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2. Corporate Author
   The Committee on Enzymes of the Scandinavian Society of Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gammaglutamyltransferase in blood. Scand J Clin Lab Invest 1976;36 : 119 -125

Books and Other Monographs

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Pathogenesis of Gastric Cancer – A Unifying Concept

S K Lam

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Summary

There are currently two hypotheses related to tumourogenesis. The more popular gene-mutation hypothesis is in favour of a multi-step process involving an accumulation of 4-7 genes. The aneuploidy-cancer hypothesis proposes that aneuploidy, which represents an unbalanced set of chromosomes, destabilizes the karyotype and thus initiates an autocatalytic karyotype evolution, eventually reaching the threshold for a neoplastic karyotype. It is proposed that both mechanisms operate in cancer formation, so that a vicious cycle is formed that eventually leads to the transformation of normal clones of cells to abnormal clones of metaplasia, and finally to neoplastic clones.

Biomarkers can in theory identify the various stages of carcinogenesis, and can be used to mark the entrance and exit of any given stage of the process, thus facilitating the testing of potential chemopreventive agents. At present, these biomarkers are crude, and include the cancer itself, cancer pathologies such as the cancer types (intestinal or diffuse), invasion and metastasis, as well as the precancer pathologies such as atrophic gastritis and intestinal metaplasia. Proliferation and apoptosis are other frequently used biomarkers. Much attention is presently devoted to chemoeradication of *Helicobacter pylori* as a prevention of gastric cancer, using such end points as the development of cancer itself, or the progression to intestinal metaplasia or atrophic gastritis. Other potential chemopreventive agents include non-steroidal anti-inflammatory agents, cyclooxygenase II inhibitors, protein kinase C inhibitors.

A recent randomized, placebo-controlled, 7 years follow-up study showed that *Helicobacter pylori* eradication at the early stage of chronic gastritis, and not at the later stage of intestinal metaplasia, could prevent gastric cancer [1].

A decrease in E-cadherin expression appears to be an early event in carcinogenesis; in fact, this occurs at the stage of chronic atrophic gastritis and intestinal metaplasia. The decrease in expression is due to methylation at the CpG island of E-cadherin. More importantly, patients who received *Helicobacter pylori* eradication therapy showed a significant decrease in E-cadherin methylation as compared with those who received no eradication therapy [2]. These findings showed that the methylation process could be reversed and that this could be achieved by *Helicobacter pylori* eradication in patients with chronic gastritis without gastric cancer. We postulate that Helicobacter pylori induces E-cadherin methylation through the mechanism of increasing interleukin 1β, and then through the production of nitric oxide and the subsequent activation of DNA methyltransferase, thus resulting in gene methylation.

References

1. Wong B.C.Y., Lam S.K., Wong W.M. et al, & China Gastric Cancer Study Group. *Helicobacter pylori* Eradication to Prevent Gastric Cancer in a High-Risk Region of China: A Randomized Controlled Trial. JAMA 2004;291(2):187-194.
2. Chan A.O.O., Peng J.Z., Lam S.K., et al. Reversal of E-Cadherin promoter hypermethylation status after *Helicobacter pylori* eradication. Gastroenterology 2004; 126 (4 Suppl 2):333.

Treatment of Chronic Viral Hepatitis in the Asia-Pacific Region: Realities and Practical Solutions

I Merican

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Summary

Hepatitis B virus (HBV) is a global public health problem. 350 million people are chronically infected with HBV; 75% of them are Asians. Prevalence of HBV infection and patterns of transmission vary throughout the world including the Asia Pacific (AP) region (0.5 to 11%). Infection in most of the AP countries is mainly through perinatal transmission thus perpetuating the high prevalence of HBV infection in the region. The annual incidence of HCC is higher (0.6%) in Asian countries compared with western countries (< 0.2%). Drugs presently available for treatment of chronic hepatitis b (CHB) include interferon-alpha, lamivudine, adefovir and thymosin-alpha 1. The choice of treatment depends on several factors including HBeAg status, ethnicity, genotype, immune status of the host and underlying liver disease (compensated or decompensated cirrhosis).

The realities for CHB include the changing epidemiology of HBV, the changing pattern of CHB infection (i.e HBeAg positive and HBeAg negative, the risk of developing complications such as cirrhosis and hepatocellular carcinoma (HCC), late diagnosis and presence of complications at initial presentation, limitations of current therapy, questionable selection of patients for therapy, treatment initiated by generalists with limited skills in managing adverse events, inefficient patient referral mechanisms, inaccessibility to current diagnostic and monitoring tools, high costs of treatment, uncertainties regarding pre-treatment liver biopsies and scarcity of basic and clinical research in liver diseases.

Practical solutions include better treatment options and strategies, use of evidence-based guidelines for treatment, better and cheaper laboratory assessment tools, national government's commitment to reduce disease burden and provide treatment where appropriate, increased public awareness of disease and its complications, clear indications for liver biopsy, efficient patient referral mechanisms, strategic human resource development, active role of charitable organizations, patient support groups, enhanced research efforts, availability of a liver registry and expanding vaccination programmes. Trials of Pegylated IFN are in progress, both as monotherapy as well as combination. Newer agents being studied include entecavir and telbivudine. Combination treatment may be beneficial as a means of limiting resistance and achieving additive or synergistic efficacy.

Tremendous progress has been achieved in the treatment of chronic hepatitis C (CHC). Combination treatment using Pegylated IFN and Ribavirin for 24-48 weeks is now the standard treatment for patients with CHC.

The realities for CHC in the AP region include the increasing burden of CHC, the risk of developing complications such as cirrhosis and HCC, limitations of current therapy in certain patient groups, the high costs of treatment, treatment initiated by generalists with limited skills in managing adverse events, inefficient referral mechanisms, limited or no pre-treatment assessment of patients, uncertainties regarding pre-treatment liver biopsies, poor follow up of patients, poor patient adherence to therapy and scarcity of basic and clinical research in liver diseases.

Possible solutions include usage of evidence-based guidelines, treatment options and strategies based on predictors of response (eg. viral load and genotype), availability of and accessibility to better diagnostic tools for qualitative and quantitative HCV RNA tests, clear indications for liver biopsy, individualized treatment for patients who do not meet current recommendations for treatment, national government's commitment to provide treatment where appropriate, increased public awareness of disease and its complications, active role of charitable organizations, enhanced patient compliance to treatment, patient support groups, availability of a liver registry and enhanced research efforts eg non-invasive prediction of fibrosis in patients with CHC.

Early viral response (EVR) i.e negative HCV RNA or $\geq$ 2 log decrease of HCV RNA at week 12 vs baseline, can be used to guide management decisions especially in patients with genotype 1. Those with genotypes 2 and 3 can be treated for 24 weeks without the need to check for EVR. Adherence to therapy is vital as it will influence the likelihood of sustained response to therapy. New ways of ensuring adherence to therapy are being actively pursued.

Barrett's Oesophagus

R Fass

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Summary

Barrett's esophagus is a change in the lining of the distal esophagus recognized by endoscopy and documented to have intestinal metaplasia by biopsy. It is thought that it is an acquired condition resulting from chronic gastroesophageal reflux disease (GERD). Barrett's esophagus has the potential to progress to adenocarcinoma of the esophagus.

Evidence to support the association between Barrett's esophagus and GERD appears to be strong but circumstantial. The intermediate steps that lead from GERD to Barrett's esophagus are speculative and the timeline for the development of this condition remains obscure. It has yet to be demonstrated that erosive esophagitis is a necessary intermediate step for the development of Barrett's esophagus.

In spite of effective therapy, documentation that medical or surgical therapy prevents Barrett's esophagus is lacking. The goal of screening for Barrett's esophagus is ultimately to improve the survival of patients with adenocarcinoma of the esophagus. This goal has not been achieved and the evidence-based criteria for screening remain to be defined. Medical and surgical therapy of Barrett's esophagus is effective in controlling reflux, although not proven to prevent neoplastic progression of the at risk mucosa. Endoscopic techniques of mucosal injury have been applied as alternatives to esophagectomy in efforts to prevent progression to cancer. Surveillance endoscopy and biopsy is the currently accepted method aimed at early intervention and improved survival for esophageal adenocarcinoma. A working surveillance protocol to accomplish this is proposed based on dysplasia grade. If no dysplasia is found and confirmed with subsequent endoscopy and biopsy, a 3-year interval is recommended. If only low grade dysplasia is confirmed, then annual endoscopy until no dysplasia is recognized is recommended. On the basis of defined risk factors, high grade dysplasia can lead to intense surveillance very 3 months or an intervention.

Uses and Abuses of Meta-Analysis in Gastroenterology

J Q Huang

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Summary

Meta-analysis, also called a quantitative systematic review, is an invaluable scientific research method that is widely used in many disciplines of medicine. It provides a means of combining statistically raw data from all eligible primary studies addressing an identical question of interest to arrive at conclusions more precise and reliable than those presented in a single study. It differs from the traditional review with respect to the fundamentals of methodology and has many advantages over the traditional narrative review.

Since its inception in 1976, meta-analysis has received a skeptical, sometimes hostile reception. It has provoked acrimony in every discipline where it has been applied. However, with improving methodology and better understanding by the medical establishment, journal editors and policy-making bodies, meta-analysis is now widely accepted as a valuable aid to evidence-based medicine and decision-making.

A Medline search for meta-analysis-related citations to February 2004 found over 15,000 articles. Of these, 154 publications were related to peptic ulcer, 149 to *H. pylori*, 155 to hepatitis, 74 to dyspepsia, and 88 to inflammatory bowel disease. There are many good examples where meta-analysis has contributed to our understanding in the management of patients with various gastrointestinal diseases. Our two meta-analyses examining the relationship between *H. pylori* infection and cagA strains and gastric cancer have quantified the magnitude of risk for gastric cancer in patients with the infection and successfully identified several reasons why the conclusions between studies differed. Therefore, an appropriately conducted meta-analysis can significantly minimize the subjectivity and errors introduced by individual studies. However, a methodologically flawed meta-analysis may compound existing problems through its increased statistical power, be potentially misleading, create further confusion and introduce new biases.

Advances in Laparoscopic GI Surgery – What is Relevant in 2004?

S C S Chung

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Summary

The laparoscopic revolution, started by the first laparoscopic cholecystectomy in 1987, completely changed the practice of surgery. Techniques developed initially for laparoscopic cholecystectomy have now been applied to all fields of surgery and laparoscopic skills are essential for surgeons of all specialties, including thoracic surgery, urology and paediatric surgery. In the gastrointestinal tract, every conceivable operation has been successfully performed laparoscopically. Some, such as cholecystectomy, appendectomy and fundoplication have found widespread acceptance, some, for example gastroenterostomy, colon resection and splenectomy are performed routinely in specialized centers while others, such as oesophagectomy, Whipple's operation, and radical gastrectomy remained experimental. Manipulation of tissues under the laparoscope is more difficult compared to open surgery. Apart from the fact that the image on the television screen is only two dimensional and lacks depth perception, the difficulty of laparoscopic manipulation is due to the limited planes of movement of laparoscopic instruments pivoted on the abdominal wall as well as the lack of tactile sensation. This may partly be overcome by using the technique of hand-assisted laparoscopy, introducing the surgeon's hand into the abdomen whilst the procedure is preformed under laparoscopic view. Laparoscopic robots, which can (almost) reproduce the fine movements of the human hand, may also make difficult procedures easier. The final frontier of endoscopic surgery is minimally invasive surgery through natural orifices. Per-oral appendectomy has already been accomplished in humans and experimental work on cholecystectomy, gastroenterostomy and tubal ligation has been reported. The next revolution may be just around the corner.

Advances in Diagnostic Therapeutic Endoscopy

D Fleischer

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Summary

Of the numerous advances that are occurring in gastrointestinal endoscopy, four will be discussed. Capsule endoscopy (CE) introduced in 2001 revolutionized the management of digestive disease because for the first time the entire small intestine (SI) could be visualized. New information about obscure gastrointestinal (GI) bleeding, Crohn's disease, medication-related injury, celiac disease, SI tumors, and other less common conditions has been discovered. One of the acknowledged limitations of CE has been that it is currently only a diagnostic tool. Complete small bowel enteroscopy ( ) using an overtube and double balloon technique has begun to allow both diagnostic assessment and in appropriate cases therapy and this promises to serve as a useful complement to CE. Because gastroesophageal reflux disease (GERD) and its sequelae, Barrett's esophagus, are common, there has been a great deal of interest in endoscopic management of these conditions. A variety of endoscopic treatments have been applied for GERD. These include 1) radiofrequency ablation [Stretta]; 2)injection therapy [Enterryx, Gatekeeper]; 3)suture fundoplication [Endocinch]; and 4) stapling procedures. Since neither medical nor surgical treatment of GERD causes Barrett's tissue to regress, there has been an interest in endoscopic methods. The use of handheld coagulation (bipolar cautery, argon plasma coagulation [APC]) has been tedious. Photodynamic therapy (PDT) has been plagued by difficulties with administration and side effects. Endoscopic mucosal resection (EMR) has the great appeal of removing tissue for pathologic examination, but for the most part, it has been applied selectively, when dysplasia or early cancer has been found – and since intestinal metaplastic tissue remains, there is potential for future neoplasia. A new treatment modality, radiofrequency ablation (BarrX) is currently undergoing evaluation and has the appeal of potentially ablating all of the Barrett's tissue.

Current Treatment of Hepatocellular Carcinoma – An Overview

M Omata

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Summary

In Japan, approximately 30,000 patients died of hepatocellular carcinoma (HCC) last year. More than 90% of patients infected with hepatitis viruses, namely 10% for hepatitis B virus (HBV) and 80% for hepatitis C virus (HCV).

Strategy of ours is to treat cancer nodules by PTA (Percutaneous Tumor Ablation) method (PEIT, PMCT and RFA). Approximately 85% of our patients who are admitted to our Department of Gastroenterology, University of Tokyo, were treated with one of the percutaneous methods. Of 1400 treated patients, 3-year survival were 65% and 5-year survival were 45%. For the patients to receive these percutaneous methods, HCC have to be found small. For that, effective screening methods should be employed. AFP measurement is not sufficient. In our country, AFP (Alpha Fetoprotein), DCP (Des Carboxy Abnormal Prothrombin) and AFP-L3 (Alpha Fetoprotein Lectin-binding 3 Fraction) are very efficient way to screen the patients with HCC. I strongly recommend these tumor markers should be employed in Malaysia. To improve patients' prognosis, we definitely need a way treat the patients with advanced HCC. Recently, we found the chemotherapeutic regiments which might induce complete response in certain fraction of the patients, that is 5FU+interferon. More than 100 cases treated, 20% complete response was obtained. I will discuss about this in details.

Liver Transplantation – Issues and Controversies

R W Strong

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Summary

Ever since its inception in the 1950's, organ transplantation has been accompanied by many hard questions about the ethics of taking organs from the dead and the living and giving them to others. Bioethics was virtually born out of the attempt to treat organ failure with technologies such as renal dialysis and kidney transplantation. Over the decades, it has been the hope and expectation that cadaveric donor organs would meet the needs of recipients but with few exceptions, most countries have found an ever increasing gap between demand and supply. Shortage had been the driving force behind the attention that the ethics of transplantation has received and the need for more organs has resulted in increased numbers of living donors.

Many of the absolute contraindications to liver transplantation (LTX) that were evident in the early period of its introduction have now been overcome which itself has widened the spectrum of disease processes deemed amenable to liver replacement, with increase in demand. Therefore, the greatest issue confronting LTX programmes is the lack of suitable organs for transplantation and how to overcome the discrepancy. The necessity to decide who to transplant and not transplant: should the sickest or the fittest be transplanted first; is adult-to-adult living donor LTX acceptable and if so, is it justified to perform the procedure in recipients who would be regarded on medical grounds as non-acceptable candidates for a cadaveric organ.

Treatment of Chronic Hepatitis C Infection: Does it Alter the Natural History of the Disease?

M Omata

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Summary

In the past 10 years, we have conducted the nation wise survey of the patients treated by interferon, the study is called IHIT (Inhibition of Hepatocellular Carcinoma by Interferon Therapy) and we have revealed that eradication of HCV by interferon eventually induces the resolution of fibrosis (Ann Intern Med 2000;132:517-524). In fact, this reduction of the fibrosis due to the interferon treatment were related to decrease of incidence of hepatocellular carcinoma (Ann Intern Med 1999;131:174-181). We recently indicated not just hepatocellular carcinoma, but overall death was decreased in the treated (Gastroenterology 2002 ; 123 : 483-491) . Recently, we have shown that "secondary" prevention was possible in the patients who had hepatocellular carcinoma but suffering from repeated recurrence of this tumor. We treated these HCC patients by interferon after ablation of HCC. Five year survival were 83% if HCV eradicated by interferon (Ann Intern Med 2003 ; 138 : 299-306). This figure is extremely high and almost compatible to liver transplantation. So, definitely in our mind, the treatment has certainly changed the natural course of HCV infection. More so than that of HBV.

Non-Alcoholic Fatty Liver Disease – The Beginning of an Epidemic?

G C Farrell

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Summary

Non-alcoholic fatty liver disease (NAFLD) is a spectrum of metabolic liver disorders that extend from bland steatosis to some cases of "cryptogenic cirrhosis". Non-alcoholic steatohepatitis (NASH), in which fatty change is associated with lobular inflammation, hepatocyte injury and/or hepatic fibrosis, is the key pathogenic link between steatosis and cirrhosis in NAFLD. Insulin resistance (IR) is present in virtually all cases of NAFLD, and NASH can be regarded as the hepatic manifestations of the insulin resistance (or metabolic) syndrome in most (> 85%) cases. Clinicians should consider NAFLD/NASH as a primary diagnosis by its metabolic associations with obesity, insulin resistance and type 2 diabetes, rather than simply as disease of exclusion.

The present high prevalence of NAFLD in most countries (3-23%) is due to decreased physical activity and consumption of energy-abundant, high fat and/or high glycaemic diets, globally referred to as "lifestyle changes", that result in overnutrition/overweight, obesity, IR and type 2 diabetes. In Malaysia, there are good data that these factors are increasing dramatically in rural Malays in recent decades (Asia-Pac J Pub Health 1999;11:16), a trend that is being noted in all Asian countries and all ethnic groups. It is therefore likely that the increased recognition of NAFLD in all our countries is part of a wave of IR that now involves a sizeable proportion of the population; we may be in the midst of a NAFLD/NASH epidemic that heralds a harvest of cirrhosis and its consequences in decades to come.

Steatosis and obesity are also determinants of disease progression in chronic hepatitis C and possibly other chronic liver diseases (e.g. alcoholic liver disease); recent evidence implicates insulin resistance as the key pathogenic factor, so that management implications are identical to NAFLD/NASH. The logical approach to prevent or reverse NAFLD/NASH is to correct insulin resistance by lifestyle modification (dietary measures and increased physical activity). There is evidence that weight reduction improves liver test abnormalities, but further studies are required to measure the impact of these measures on prevalence of fatty liver and on disease progression/regression of chronic liver disease.

Correcting obesity, diabetes and lipid disorders are core treatment of patients with NAFLD. Among other proposed drug treatments, agents that reduce insulin resistance, particularly the PPARg agonist thiazolidinediones (rosiglitazone, piaglitazone) are most promising, but are associated with weight gain. Antioxidants (vitamin E, probuchol, curcumin and other herbs) and "hepatocellular protectants" (ursodeoxycholic acid) are also of interest, but evidence for longterm efficacy on hepatic fibrosis and liver complications is needed before routine prescribing can be justified.

Atypical Manifestations of GERD

B C Y Wong

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Summary

The prevalence of GERD is lower in Asia than in the West. However, our previous population survey showed that among patients with GERD, the frequency of association with atypical manifestations is similar in Asian population and the West. Three broad categories of atypical manifestations include non-cardiac chest pain, chronic laryngitis, and pulmonary manifestations.

Although the entity of non-cardiac chest pain is well known for some time, the prevalence, definition and diagnosis remains diverse, making it very difficult to compare data among studies. In patients with normal coronary angiogram and chest pain, about 30-50% had abnormal 24 hour pH results. The remaining patients may be caused by other oesophageal or extra-oesophageal disorders. The overall response in this group of patients to proton pump inhibitor is good. Our recent meta-analysis showed that PPI test has a high sensitivity and specificity in diagnosing acid-related non-cardiac chest pain.

Chronic laryngitis comprises of a spectrum of symptoms including hoarseness, globus, excessive throat clearing, throat pain etc, and the signs may include edema and hyperemia, posterior pharynx cobblestoing, subglottic or posterior glottic stenosis etc. There may not be good correlation between standard 24 hour pH monitoring and chronic laryngitis. Only a few small studies using PPI treatment are available to date and the results are variable.

Pulmonary manifestations of GERD include chronic cough and asthma. Around 20-40% of chronic cough may be associated with GERD. There may not be typical GERD symptoms, hence high clinical suspicion is needed. Treatment using high dose PPI with prolonged duration may be needed in some cases, especially if the cough is associated with more than one aetiology. There is a strong association between GERD and asthma. Treatment with high dose PPI for 3 to 6 months is usually associated with significant clinical improvement.

Treatment of Resistant GERD

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Summary

The most common manifestation of proton pump inhibitor failure is continuation of classic GERD symptoms (heartburn and acid regurgitation) despite PPI therapy. Other less common manifestations include antacid consumption, the presence of erosive esophagitis during upper endoscopy as well as abnormal acid exposure during 24-hour esophageal pH monitoring while on PPI. There is no clear definition, in the literature, as to what should be considered as PPI failure. Generally, it has been defined as patients who have failed to obtain satisfactory symptomatic response to a course of standard dose PPI (once a day). It has been estimated that up to 30% of the patients that consume PPI once daily continue to report typical GERD symptoms despite treatment. All patients reporting PPI failure should be assessed for compliance. Poor compliance is not unusual knowing that gastroesophageal reflux disease is primarily a symptom-driven disease. Many patients continue to take medications as long as they have symptoms. However, discontinuation of treatment primarily occurs because of loss of symptoms as the driving force for compliance with treatment. Studies have shown that up to 50% of the patients who are prescribed PPI once a day will gravitate to become on-demand takers within four weeks of initial therapy.

Assessment of PPI failure in patients with erosive esophagitis reveals that regardless of the PPI brand, healing rates after 8 weeks of therapy are between 90-94%. Patients with LA grade C and D demonstrate lower healing rates than patients with LA grade A and B. Interestingly, studies have shown repeatedly that there is about 15% discrepancy between mucosal healing and symptom resolution. In other words, up to 15% of the patients, with erosive esophagitis that completely heals, continue to complain about their typical GERD symptoms.

In patients with non-erosive reflux disease, PPI failure is much more common. It has been estimated that complete resolution of heartburn symptoms while on PPI once a day is achieved by only 50% of the patients with non-erosive reflux disease, after 4 weeks of treatment. Patients with non-erosive reflux disease demonstrate up to 35% lower symptom response rate than patients with erosive esophagitis. Assessment of the different subgroups that constitute the non-erosive reflux disease patient population demonstrate that those with normal (functional heartburn) or slightly abnormal acid exposure in the distal esophagus demonstrate 40-50% failure rate on PPI once daily. It is highly likely that this group of patients, which account for approximately 50% of the non-erosive reflux disease group, is the main culprit for the lower response rate to PPI of patients with non-erosive reflux disease.

There are very few studies that assess symptom response rate in patients with Barrett's esophagus using PPI once daily. Most of the studies assessed multiple dosing of PPIs and their effect on symptom

resolution. In studies that used PPI twice to four times daily, symptom resolution was observed in more than 80% of the Barrett's esophagus patients.

Factors that may affect response to PPI such as PPI resistance, rapid metabolism of PPI, *Helicobacter pylori* infection, nocturnal acid breakthrough and others, probably account for PPI failure in only a small number of patients. On the other hand, knowing that patients with non-erosive reflux disease account for up to 70% of the general GERD population and half of this patient population belongs to the functional heartburn group, which demonstrates the lowest response rate to PPI once a day, one can conclude that most of the PPI failure patients originate from the non-erosive reflux disease patient population. In non-erosive reflux disease, the functional heartburn group is likely the most common contributor to the large group of patients who fail PPI once a day.

In the last few years, GI practice has gravitated to deal primarily with PPI failure. As the PPI responders leave the center stage, gastroenterologists are forced to deal with a new type of patients that fall under the category of gastroesophageal reflux disease – the functional heartburn group.

Treatment for PPI failure has not been well substantiated. Presently the standard of care is to increase the PPI dose to twice daily. However, the proportion of patients that fail PPI once daily who reported complete symptom relief on PPI twice daily is estimated at 25%. Most of the patients that fail PPI once a day will continue to fail PPI twice daily. It has been suggested that patients who fail PPI twice daily should undergo pH testing on treatment or potentially multi-channel intraluminal impedance with pH sensor. Treatment of patients who fail PPI may include the addition of visceral analgesic in the form of tricyclic antidepressants, trazodone and selective serotonin reuptake inhibitors. In patients who fail PPI once daily, but report a shift in the predominant symptom pattern from heartburn to regurgitation/sour taste in mouth, then consideration of adding a TLESR reducer such as baclofen would be appropriate.

Management of GERD - Consensus in the Asia-Pacific Region

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Summary

This account summaries the conclusions and recommendations of a panel of gastroenterologists practicing in the Asia Pacific region. The group (GERD) recognised that although gastro-oesophageal reflux disease is less common and milder in endoscopic severity in Asia than in the West, there is nevertheless data to suggest an increasing frequency of the disease. During a 2-day Workshop, the evidence for key issues in the diagnosis and clinical strategies for the management of the disease was evaluated following which the recommendations were made and debated. The consensus report was presented at the Asia Pacific Digestive Week (APDW) 2003 in Singapore and ratified.

Upper GI endoscopy is the gold standard for the diagnosis of erosive GERD. There is no gold standard for the diagnosis of non-erosive GERD (NERD). Diagnosis therefore relies on symptoms, positive 24-hour pH study or a response to a course of PPI treatment. The goals of treatment for GERD are to heal oesophagitis, relieve symptoms, maintain the patient free of symptoms, improve quality of life and prevent complications. The proton pump inhibitors are the most effective medical treatment. Following initial treatment, on 'demand therapy', may be effective in some patients with non-erosive gastroesophageal reflux disease (NERD) or mild (GI) erosive oesophagitis. Anti-reflux surgery by a competent surgeon could achieve a similar outcome although there is an operative mortality of 0.1 - 0.8%. The decision is dependent on patients' preference and availability of surgical expertise. Currently, endoscopic treatment should be performed only in the context of a clinical trial. Treatment of patients with typical GERD symptoms without alarm features in primary care could begin with PPI for 2 weeks followed by a further 4 week before going on to on-demand therapy.

Mechanisms of Viral Resistance

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Summary

Unlike other DNA viruses, HBV is an RNA-like virus that has a reverse-transcription process (RNA to DNA, instead of DNA to RNA) catalyzed by reverse transcriptase as part of its replicative pathway in hepatocytes. Therefore, the mutational rates of HBV is higher than ordinal DNA viruses. Therefore, we established *in vitro* system to understand the replication ability of the mutants and sensitivity to different drugs. We screened 21 drugs and found that several of these are effective for blocking the mutations due to the Lamivudine. Lamivudine is not necessary to potent drug comparing to other nucleotide analogues and future generation drug could be the ones with higher proteincy and less likely to have resistant mutant developments. With these drugs, certain diseases especially end stage of liver disease could be controlled although not necessary eradicating the virus.

HBeAg⊖ Mutants - How Common is it and How Do We Best Deal with it?

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Summary

Seventy % of the HBV DNA positive patients without detectable HBeAg exhibit mutations at nucleotide 1896 in the pre-core region or at nucleotide 1762 and 1764 of the core promoter region of the HBV DNA genome, which block HBeAg synthesis but still permit HBV replication.

Of the 350 million worldwide chronic HBV carriers, HBeAg negative chronic hepatitis (CH) accounts for 7-30%, with a median prevalence of 33% in the Mediterranean area, 15% in Asia Pacific and 14% in the USA and Northern Europe. In the Asia Pacific-region about 50% of CH are infected with HBeAg-minus HBV, with a prevalence from 45% in China to 69% in Hong Kong. Rates are higher in the Mediterranean basin, from 63% in Spain to 86% and 90,5% in Greece and Italy. Only 9% and 22% of CH are HBeAg-negative in the US and France.

HBeAg-negative HBV disease is usually severe. It often progresses in a discontinuous form with multiple aminotransferases peaks accompanied by peaks of HBV viremia occuring over the years, alternating with prolonged periods of biochemical and viral quiescence.

Long-term Interferon (18-24 months therapy) may induce seroconversion from HBsAg to anti-HBs in some patients; compliance is poor. Lamivudine inhibits HBV and controls liver inflammation; its prolonged use is complicated by the frequent emergence of treatment-resistant YMDD mutants.
Continuous Adefovir therapy inhibits HBV in 75% of treated patients; drug-resistant mutants have emerged in only 3,5% after 3 years of therapy.

Endoscopic Palliative Options

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Summary

The management of esophageal cancer (EC) always begins with appropriate staging. Once it is determined that palliation is the goal of treatment, not cure, then the next question is – "what are the goals of palliation?" since one specific palliative treatment, e.g. a stent, may be an excellent choice if the goal of palliation is relief of dysphagia, whereas it would not necessarily be an appropriate choice if the goal of palliation were relief of pain. Endoscopic palliation is one form of palliation but must be considered in comparison to other forms of palliation such as surgery, radiation, chemotherapy, or simply supportive care. Endoscopic therapies may be categorized as 1) ablative (laser, coagulation, injection); 2) ablative plus (photodynamic therapy [PDT]; brachytherapy); 3) mechanical (stent, dilation); and 4) supportive (percutaneous gastrostomy). In most instances, the tumor histology (squamous cell [SCC] versus adenocarcinoma [AdCA]) does not influence the selection of therapy. However since SCC is more apt to be proximally and AdCA more apt to be distally located, it may be a factor when stent placement is considered. Stent placement should be considered as the first line of endoscopic therapy unless the is some extenuating circumstance because they have the potential to provide palliation with a single therapy, provide long-term benefit, and can allow the best relief of dysphagia. Esophageal dilation provides only short-term benefit and therefore has only as adjunctive role. Laser therapy, about which a rich literature exists, is not commonly used today because of their expense and the fact that similar benefit can generally be achieved with argon laser coagulation. Most of the information about injection therapy with either sclerosant agents or anti-neoplastic agents is anecdotal. The largest study comparing PDT to laser treatment showed comparable results. Self-expandable metal stents (SEMS) have generally replaced non-expandable plastic stents. Newly introduced self-expandable plastic stents may have a role for treatment of benign esophageal strictures, but do not appear to be advantageous for EC. A variety of SEMS are available and for the most part have been shown to be equivalent. Traditionally, stents have been placed by gastrointestinal endoscopists, but there are increasing reports of their placements by radiologists, particularly for proximal lesions. Anti-reflux stents have an appeal particularly with the increasing incidence of distal AdCA that traverses the esophagogastric junction. When the goal of palliation has been relief of dysphagia, maintenance of nutrition, and improvement in respiratory symptoms, endoscopic palliation has been good. When the goal of palliation is control of pain or prolongation of life, the benefits have not been as good.

Because the key to survival with EC is the stage of the tumor at the time of diagnosis, the most important advances in managing EC will come with strategies that lead to earlier diagnosis.

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Treatment Approaches with Special Reference to Surgery

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Summary

Cancer of the oesophagus carries a grave prognosis and the operation of oesophagectomy has a fearsome reputation. As symptoms of dysphagia does not present until the tumour has grown to considerable size, the tumour is at an advanced stage by the time the diagnosis is made. Surgical extirpation of the oesophagus, has been, up to recently, the only hope for the patients. Radical oesophagectomy is a difficult proposition because of the location of the oesophagus and the proximity of vital structures such as the trachea, the aorta, and the recurrent laryngeal nerves. The oesophagus may be replaced by the stomach, the colon, or a loop of jejunum, the stomach being the preferred choice as the operation is simpler by comparision. The fearsome operative mortality for oesophagectomy has dropped dramatically in recent years due to better selection of patients, concentration of expertise in specialized centers, advances in surgical intensive care and surgical nutrition. Minimally invasive techniques for oesophagectomy have not really lived up to its promise. Long term survival in patients with advanced tumours remains poor. Squamous cell cancer, the prevalent histological type in Asia, is sensitive to chemotherapy and radiotherapy. Up-front pre-operative chemo-irradation, using external beam irradiation and a combination of cisplatin and 5 FU, has the advantage of the ability to monitor treatment progress, to downstage the primary tumour and to sterilize any micro-metastasis, at the cost of increased surgical morbidity and mortality. With the present regime of chemo-irradation, complete responses can be seen in up to half of the patients. In the future, treatment algorithm for patients with cancer of the oesophagus may well change, with primary chemo-irradation as first line and oesphagectomy used to salvage the treatment failures.

GCA - Epidemiological Observations from Asia

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Summary

Gastric cancer is the second commonest cause of cancer-related deaths worldwide. There is definite geographical variation in gastric cancer incidence, with the highest rates seen in Asia and South America and the lowest incidences in North America, Europe and Australia.

Studies on the pathogenesis of gastric cancer suggested that it arises as a complex interaction between genetic predisposition, infection with *Helicobacter pylori* and other exogenous factors such as diet. Correa's model of gastric carcinogenesis suggested that a temporal sequence of pre-cancerous changes eventually lead to the development of gastric cancer. Inflammation caused primarily by *H.pylori* infection, as well as by exposure to toxins, results in chronic active gastritis. In a subset of patients, this leads to the development of atrophic gastritis, intestinal metaplasia, dysplasia and eventually gastric cancer. Both bacterial virulence factors, as well as individual genetic susceptibility, are believed to play important roles.

Singapore a multi-ethnic Asian country comprising 3 major ethnic groups: Chinese, Malays and Indians, and a racial difference in the incidence of gastric cancer had been reported, with the highest incidence of gastric cancer occurring amongst the Chinese. For Chinese males, the age-standardized rate (ASR) is 25.7 per 100,000 per year, while in Chinese females it is 12.6 per 100,000 per year. In contrast, the ASR in Malay males and females are 6.6 and 4.0 per 100,000 per year respectively, while that in Indian males and females is 8.4 and 6.3 per 100,000 per year respectively.

The racial difference in gastric cancer incidence in Singapore could be related to a racial difference in the prevalence of H.pylori infection, as well as gastric atrophy. A study has shown the proportion of Malays who were seropositive for *H.pylori* was significantly lower than the Chinese or Indians. *H.pylori* seroprevalence was similar between the Chinese and Indians. The seroprevalence of the bacterial virulence factors CagA and VacA was also similar between the Chinese and Indians. The lower incidence of gastric cancer in Malays compared to the Chinese and Indians could be explained by the lower seroprevalence of H.pylori. Studies on serum pepsinogen may be a surrogate marker for chronic gastritis and atrophy. The prevalence of low pepsinogen was highest in Indians compared even when adjusted for gender and the presence of *H.pylori*.

The difference in gastric cancer incidence between Malays and Chinese could be explained by differences in *H.pylori* seroprevalence. The lower incidence of gastric cancer among Indians compared to Chinese cannot be explained by differences in *H.pylori* infection or serum pepsinogen levels (chronic gastritis). Other modifying factors such as genetic and environmental factors may be important.

Helicobacter Pylori and Gastric Cancer – What is the Evidence?

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Summary

Gastric carcinogenesis is a multifactorial and multistep process involving environmental, dietary and host factors. Although the etiology is not fully understood, infection with *H. pylori* is considered the single most common factor for gastric cancer. It has been suggested that up to 80% of gastric cancer be attributed to this infection. Since *H. pylori* infection was classified as group I human carcinogen by the IARC of WHO in 1994, the relationship between the infection and the risk of gastric cancer has been further extensively studied. Evidence from animal experiments, population-based epidemiologic studies and clinical trials supports a strong causal relationship between the infection and gastric cancer.

The two most commonly used animals to model *H. pylori*-associated gastric cancer are the mouse and the Mongolian gerbils. Following a long-term infection with *H. pylori*, these animals develop gastroduodenitis, ulcers, gastric atrophy, intestinal metaplasia, dysplasia and gastric cancer resembling the gastric carcinogenic process in humans. The results from five meta-analyses of epidemiological studies have shown that the infection increases the risk of noncardia gastric cancer by 2- to 6-fold compared with non-infected control populations. The magnitude of *H. pylori* infection as a risk factor for gastric cancer in the published *H. pylori* and gastric cancer epidemiology studies may have been substantially underestimated due to the inclusion of improperly selected controls and the use of relatively insensitive testing methods for *H. pylori* infection. Increasing evidence from randomized controlled clinical trials has also shown that eradication of *H. pylori* infection regresses gastric inflammation, gastric atrophy and intestinal metaplasia. However, the results from several randomized trials using gastric cancer as the study endpoint have been inconclusive. This may have resulted from a relatively short period of follow-up, an inadequate study power or the fact that the intervention was too late to stop the progression from precancerous lesions to gastric cancer in some patients or the fact the other gastric cancer risk factors co-exist that have not been properly dealt with.

Intervention Studies in Gastric Cancer

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Summary

A biological marker is needed to mark the success of any interventional method for the prevention of gastric cancer. Histological markers are the most commonly used, and the following "precancerous" pathologies related to *H. pylori* infection are well known: chronic gastritis, atrophic gastritis, intestinal metaplasia, and dysplasia.- the gastritis-cancer pathway described by Correa. These pathologies are known to be associated with the *intestinal type* of gastric cancer, which accounts for 50-60% of patients with gastric cancer. The remaining patients have the *diffuse type* of gastric cancer, which apparently moves from chronic gastritis directly to cancer, without any intervening pathologies. It can thus be seen that any chemotherapeutic intervention should use the resolution of chronic gastritis as an initial objective, because if, for example, the resolution of atrophic gastritis is used as an objective, the intervention is unlikely to prevent the diffuse type of gastric cancer on a population basis. Atrophic gastritis is still important, of course, to an individual who presents with such histology, and it needs to be clinically tested whether resolution of atrophic gastritis will prevent cancer. If resolution of chronic gastritis, for example by *H. pylori* eradication, can be shown to prevent gastric cancer, then rigorous development of a vaccination programme on a population basis is justified, and all individuals with H. pylori related chronic gastritis should receive eradication treatment.

It is in the above light that we should receive the various reports on the success of eradication of *H. pylori* on the regression and progression of the histological markers. A one-year, population (n=587)-based study (Gastroenterology 2000;119:7-14) marginally suggested, and a six-year study with atrophic gastritis and intestinal metaplasia (n= 79) as entrance points (J Natl Cancer Inst 2000;92:1881-8) showed possible reversibility or non-progression of atrophic gastritis and intestinal metaplasia following *H. pylori* eradication. Our own seven-year, population (n=1,632)-based study in Changle, China, concluded that the progression of atrophic gastritis, and, less convincingly, intestinal metaplasia could be delayed after *H. pylori* eradication. It should be noted that intestinal metaplasia, unlike atrophic gastritis, represents an abnormal, genetically altered clone of cells. The crucial question remains whether intervention by *H. pylori* eradication will prevent cancer. Our Changle study showed that early eradication of *H. pylori*, i.e., in subjects without precancerous lesions prevented the development of gastric cancer. In subjects already having precancerous lesions, the incidence of gastric cancer could not be reduced at 7 years of follow-up (JAMA 2004;291(2):187-194).

Colorectal Cancer Screening and Surveillance

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Summary

Westernization in several Asian cities leads to a dramatic increase incidence of colorectal cancer over the past decade. Public awareness on screening is in general very low. Decision about colorectal cancer screening is more complicated than other cancers because of the various screening methods, leading to confusion among doctors and among patients. Faecal occult blood testing (FOBT) is the simplest non-invasive method with good evidence for effective colorectal cancer screening. Annual or biennial FOBT screening reduces both the incidence and mortality. At least 3 randomized controlled trials involving more than 250,000 subjects over a follow up of 13 to 18 years provided the most direct evidence of its benefit. However, single test has very low sensitivity. The sensitivity of FOBT screening increases with compliance to the annual program. Therefore the success depends on subject adherence to the program. The guaiac tests are based on the detection of pseudo-peroxidase activity found in hemoglobin. It is not specific for human hemoglobin, and dietary and drug restriction is necessary to minimize false positive and false negative results. The immunochemical tests are based on the detection of human hemoglobin and therefore potentially are more specific and without the need of dietary restriction. The choice of guaiac or immunochemical FOBT depends on the characteristics and dietary habits of the population. Other well known screening tests include flexible sigmoidoscopy with or without barium enema and screening colonoscopy. Newer methods under clinical studies include Computerized Tomography colonography and faecal DNA testing. It is important to remember that the best screening test is the test that gets done.

Identification and removal of adenoma reduce the risk of development of colorectal cancer. Post-polypectomy surveillance colonoscopy is therefore important to look for new adenomas or those missed by the original exam. The time interval between surveillance colonoscopies depends on the size, number and histology of the initial adenoma. However, this important issue is very complicated. Firstly there is no agreement among gastroenterologists on the time interval, mainly because of lack of level 1 evidence. Secondly, the real practice among gastroenterologists may be affected by various other issues, including higher perceived expectation, fear of malpractice or demand for higher level of certainty. Hence, better evidence on the effect of surveillance colonoscopy intervals for various types and sizes of adenoma is still needed.

Treatment Approaches in 2004

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Summary

Colon and rectal cancer remains the most common gastrointestinal cancer in the Western world with a rising incidence in the Far East. Advances in management, mostly relating to rectal cancer, will be discussed. Some are already significant, some promising:

1. MRI and Ultrasound Staging of Rectal Cancer: the advent of high quality imaging[1] has increased the accuracy of preoperative staging and enabled more logical decisions to be made regarding the necessity for preoperative radiotherapy or chemo/radiotherapy.
2. Total Meso-Rectal Excision (TME): the seminal work of Bill Heald[2] has for many changed the approach to surgical excision of the rectum with demonstrable decrease in the incidence of local and distal recurrence and increase in long term survival. The influence of adjuvant radiotherapy in this situation will be discussed.
3. Laparoscopy for Colon and Rectal Cancer: although technically feasible the place of laparoscopic surgery in colon and rectal cancer remains controversial. Recent American and European trial data[3] is helping to define the place of minimally invasive surgery.
4. Local Excision for Rectal Cancer: the availability of improved staging techniques together with Transanal Microsurgery (TEMS) is allowing consideration of local resection techniques for early rectal cancer (TI,T2) with clear advantage of avoiding major surgery and possible permanent stoma formation.

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Treatment of Difficult HCV Patients (Cirrhosis and Renal Failure)

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Summary

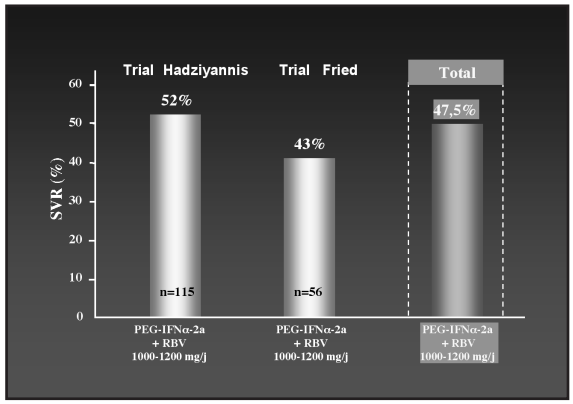
Peg-IFN and Ribavirin therapy for HCV cirrhosis aims to eradicate HCV. Side effects (neutropenia and thrombocytopenia) are more important than in non-cirrhotic patients (pts).

271 pts with cirrhosis were randomised to 48 weeks PEG IFN alfa-2a, 90 μg or 180 μg weekly, or conventional IFN alfa-2a, 3 MU thrice weekly. HCV-RNA was undetectable at 72 weeks in 15% and 30% of the pts treated with 90 and 180 μg of PEG IFN but only in 8% of those treated with conventional IFN. Information on combination therapy in fibrotic liver disease can at present be derived only by extrapolating the results in the minority of pts with cirrhosis enrolled in registrative trials. In a study with PEG IFN alfa 2b and Ribavirin, 44% of 136 patients with cirrhosis became sustained virologic responders, comparing with 57% non fibrotic hepatitis C. Cumulative data from the studies with PEG IFN alfa 2a and Ribavirin show the following rates of sustained virologic response (SVR) after 48 weeks of therapy.

Independent of an antiviral effect, IFN may have antifibrotic and antioncogenic effects of benefit in slowing progression and in diminishing the risk of hepatocellular carcinoma. The biochemical and virologic profile of dialysis patients with chronic hepatitis C is peculiar and apparently benign (fluctuating HCV-RNA, slightly abnormal ALT); however there is often significant necroinflammation at histology.

Ribavirin, which is eliminated by the kidney and not removed by dialysis, is contraindicated.

A metanalisys of 269 patients treated in 14 trials (most with alfa IFN 3 MU thrice weekly for 3-6 months) has shown a sustained virlogic response in 37% and therapy discontinuation in 17%. Because of its preferential hepatic clearance Peg IFN alfa 2a has a rationale in kidney failure pts; it can be used at dose of 135 μg/week even with a 20 ml/m creatinine clearance.



Management of Chronic Hepatitis C Patients Failing to Previous Treatment

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Summary

The treatment of chronic hepatitis C has been significantly improved in recent years, resulting in increasing sustained virological response (SVR). It was up to 41% when treated with interferon / ribavirin combination therapy[1] and 54 – 61% with peginterferon / ribavirin[2,3] combination therapy respectively. However, significant proportion of patients failed to respond to the treatment particularly those infected with HCV genotype 1[1-4].

Re-treatment with more effective therapy is expected to result in SVR at least in some patients. There are a number of factors needed to be considered including previous therapy regimen, character of response to previous therapy, HCV genotype, severity of disease and efficacy of therapy to be used for re-treatment. Some correctable factors (obesity, alcohol consumption, compliance and adherence to therapy) should be corrected before starting re-treatment.

The SVR rates in patients who relapsed after previous interferon mono- therapy re-treated with interferon plus ribavirin combination therapy are affected by HCV genotypes, pre-treatment HCV RNA levels and virological response during the prior course of IFN monotherapy[5,6]. In our study of re-treatment with peg-IFN alpha 2b plus ribavirin combination therapy for 48 weeks, the SVR rate was achieved in 43% (16/38) of IFN or IFN / ribavirin relapsers and an SVR increased to 62% in those who had good adherence to therapy. Re-treatment of IFN alpha 2b plus ribavirin relapsers with peg-IFN alpha 2a plus ribavirin with or without amantadine showed an SVR of 38-45%[7]. In patients who relapsed after 24 weeks peg-IFN alpha 2a plus ribavirin achieved SVR of 53% when re-treated for 48 weeks[8].

The patterns of virological response during the prior course of IFN treatment in nonresponders affect SVR rate in re-treatment. In our study of 21 patients who did not responed to the previous IFN mono or combination with ribavirin, the SVR was observed in 29% with 48 weeks peg-IFN alpha 2b plus ribavirin therapy. Re-treatment of nonresponders to IFN monotherapy or IFN / ribavirin with 48 weeks peg IFN alpha 2a plus ribavirin showed SVR of 18%, 14% and 52% in all patients, in patients with HCV genotype 1 and in patients with HCV genotype 2,3 respectively[9]. Triple therapy with peg IFN alpha 2a plus ribavirin plus amantadine in nonresponders to IFN/ ribavirin treatment showed an SVR of 24%. There is an on going study of peg IFN alpha 2a plus ribavirin re-treatment in peg-IFN alpha 2b / ribavirin nonresponders.

In conclusion, there are a number of fixed and correctable factors that need to be considered when assessing the suitability of a patient for re-treatment. Targeting re-treatment with better efficacy regimens to patients who fail to respond to previous treatment seems to be reasonable. Since an SVR is achieved in a limited number of patients, studies of new strategies are clearly needed to improve treatment efficacy.

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Differences in the Pattern of Gastric Carcinoma Between North-Eastern and North-Western Peninsular Malaysia: A Reflection of *Helicobacter Pylori* Prevalence

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Objective

To compare the demographics of gastric carcinoma between Hospital Pulau Pinang (HPP) and Hospital Universiti Sains Malaysia (HUSM), Kelantan.

Materials and Methods

Demographic data of all gastric carcinoma cases was retrieved from pathology records of HPP for the year 2000, and compared to a similar study conducted by the main author in HUSM.

Results and Discussion

The incidence of gastric carcinoma was much higher in HPP (32 cases in one year) compared to HUSM (23 cases during a 5-year period). The tumour was most common in Chinese, male, and median age of patients was about 60 years in both studies. There was a higher rate of non-cardia location of gastric carcinomas in HPP(23/32 or 72% cases), an area with higher *H. pylori* infection rates compared to a preponderance of cardia-located tumours in HUSM (14/23 or 61% cases) where the *H. pylori* infection rate is exceptionally low. Histologically, there were 23 intestinal type (including 2 cases of early gastric cancer), 8 diffuse and 1 mixed type in HPP. The ratio was similar to the HUSM study with 16, 5 and 2 cases respectively, with absence of early gastric cancer.

Conclusion

The incidence and site of gastric carcinoma closely parallels Helicobacter pylori infection rates.

Incidence of *Helicobacter Pylori* in Non-Variceal Upper Gastrointestinal Bleed in HUSM, Kelantan

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Objective

Our objective is to study the incidence of *Helicobacter Pylori* infection as a cause of non-variceal upper gastrointestinal bleeding (NVGIB)and compare the effectiveness between using pronto-dry test and tissue biopsy in HUSM, Kelantan.

Materials and Methods

Retrospective data of 142 patients who were scoped for NVUGIB was collected in HUSM, Kelantan from January 1999 to December 2003. The presence of *H.pylori* infection was tested using Pronto dry test and simultaneously, tissue biopsy was sent for histopathological examination. Data collected was analysed using SPSS version 11.0.

Results

Incidence of *H.Pylori* present in this study is 7%. Of this, 8 patients were positive from pronto-dry test while 6 patients were positive from HPE. Only 4 patients were positive from both pronto-dry test and HPE. Specificity of pronto-dry is 97% whereas sensitivity is 66.6%. Among the ethnic distribution, 8 Malays (6.3%) and 2 Chinese were positive to *H. pylori* infection.

Conclusions

H.Pylori infection is a common cause for peptic ulcer disease leading to upper gastrointestinal bleeding. In this series, the incidence of *H. pylori* infection is low (7%) in Kelantan. Comparing between the 2 methods, we found that specificity to pronto-dry is 97% and sensitivity is 66.6%.

Study on Risk Factors of *Helicobacter Pylori* Infection and it's Prevalence Among Adult Indigenous Orang Asli (Aborigines) Population in Gua Musang District of North Eastern Area of Malaysia

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Background

Helicobacter pylori (H. pylori), a bacteria consistently found in the gastric mucosa biopsy of patients suffering dyspeptic symptoms and subsequent investigation by endoscopic biopsy confirmed its presence. The discovery was considered a landmark because it changed the way the medical fraternity view and treat peptic ulcer disease particularly since *H. pylori* was subsequently isolated in almost all gastric mocosa biopsies in patients suffering from peptic ulcer disease. Subsequent studies confirmed *H. pylori* as the main contributing factor in the development of peptic ulcer disease. *H pylori* infection prevalence among various ethnic communities in Malaysia were well known with variation to the prevalence of infection depending on the ethnicity and geographical location of the affected communities, a high prevalence rate was seen in the Indian and Chinese community but a consistently low prevalence was seen among ethnic Malays. However, there was no report regarding the prevalence rate of *H. pylori* infection among the indigenous Orang Asli population as they were not well established. There was also lack of data regarding risk factors that may have important clinical consequences towards the rate of *H. pylori* infection rate in the indigenous Orang Asli (Aborigines) community.

Objective

The objective of this study was to determine the prevalence rate of *H. pylori* infection among adult indigenous Orang Asli population in the area of Gua Musang, Kelantan. The second major objective was to determine the various risk factors that contribute to the prevalence of *H. pylori* infection which has important health and socioeconomic impact.

Materials and Methods

The study involved adult indigenous Orang Asli (Aborigines) population in Gua Musang, Kelantan. The study proposal was reviewed and approved by the University Sains Malaysia Research and Ethical Committee. The consent from the relevant government agency i.e. Jabatan Hal Ehwal Orang Asli

(JHEOA) was taken. The study population was calculated using Windows Power And Sampling (PS) software, with the power of the study 80.0%, which calculated the sample size as 480 subjects. The study involved data and blood samples collection upon visits to the indigenous Orang Asli community. The identified adult Orang Asli will undergo a randomisation process and the selected subjects were given lengthy information and any queries about the study were fully explained. Each subject was required to give their consent by signature or thumbprint by filling the prepared consent forms. The selected subjects were then interviewed by the researcher using a set of prepared questionnaire and blood sample were taken for the purposes of detecting the presence of antibody IgG against *H. pylori*. These tests were done using ELISA method of detection. Validation tests for the ELISA serological tests was done based on gastric mucosal histopathological diagnosis by Pathologist from tissue samples taken during gastroscopy examination in University Sains Malaysia Hospital. Relevant data were then statistically analysed and the risk factors were reviewed to find any relationship and correlation with the end result of the prevalence study using SPSS. Sympthomatic subjects positive for *H. pylori* are treated with eradication regime according to Asia Pacific Guidelines For H. pylori eradication.

Results

480 subjects were selected through a randomization process. We found *H. pylori* infection among 19.0% of subjects, of which males made up 57.1% and females 42.9% . Of those infected with *H. pylori*, 70.3% had no background of formal education at all, with 84.6% were cigarette smokers. However, the majority of those infected, which was 84.6% had never consumed alcoholic drinks . An interesting finding in the study was that all the subjects who tested positive for *H. pylori* boil their drinking water and a further 65.9% had never taken any non steroidal anti inflammatory drugs in their lifetime. The subjects positive for *H. pylori* also practiced eating exotic food items which include tapir and porcupine making up 92.3 %. These subjects also had a positive family history of dyspeptic symptoms which was seen in 69.2% and 74.7% of these subjects also received clean piped water supplied by the government.

Conclusion

The prevalence rate of *H. pylori* infection among adult indigenous Orang Asli (Aborigines) population in Gua Musang, Kelantan is 19.0 %, a low rate of infection comparable with the ethnic Malays of 22.0 % infection rate.

Cost Analysis of a *Helicobacter Pylori* Test and Treat Strategy VS Prompt Endoscopy in the Management of Young Asian Patients with Dyspepsia: Preliminary Results from A Randomised Trial

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Introduction

It is uncertain if a non-invasive management strategy in an Asian setting can be cost effective in a chronic relapsing condition like dyspepsia.

Aims

To perform a direct cost analysis of a *Helicobacter pylori* test and treat approach versus prompt oesophagogastroduodenoscopy (OGDS) in young patients with dyspepsia.

Materials and Methods

Consecutive patients with dyspepsia (aged < 45 years) were randomized to either a C^{13} Urea Breath Test (UBT) or prompt OGDS, given *H. pylori* eradication if positive, and subsequently followed up for 6 months. Direct costs of the initial investigative tool, all medication required, further investigation, clinic visits and hospital admissions during the subsequent 6 months were calculated.

Results

201 patients were enrolled (April 2002 to January 2003) and 181 (98 UBT, 83 OGDS) were followed up for 6 months. Demographic details were similar between both groups of patients, apart from a higher proportion of Chinese ethnicity in the UBT group (47% vs 25%). 8 (8%) of UBT patients and 3 (3.6%) of OGDS patients underwent a further endoscopy during the 6 months. The mean number of clinic visits was 14 ± 3 (UBT) and 13 ± 2 (OGDS) (p=NS) whilst mean hospital visits for both groups were 2 ± 0.5 (UBT) and 2 (OGDS) respectively. Continued medication for dyspepsia, represented as means, are as follows: antacids 22 UBT vs 14 OGDS (p=0.01), H2 antagonists 14 UBT vs 16 OGDS (p=NS), proton pump inhibitors 5 UBT vs 10 OGDS (p=0.001) and motility agents 2 UBT vs 8 OGDS (p=0.001). The mean cost of both UBT and OGDS patients at the end of 6 months were RM 335.31 ± 535 and RM 596.52 ± 507 (p< 0.0001), respectively.

Conclusion

A non-invasive *Helicobacter pylori* test and treat strategy is more cost effective than prompt endoscopy in the management of young Malaysian patients with dyspepsia, up to a 6 month period.

Satisfaction of a Non-Invasive Management Strategy for Young Asian Patients with Dyspepsia : Preliminary Results from a Randomised Trial

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Introduction

Although most young Malaysian patients with dyspepsia do not have any serious pathology, it is uncertain if local patients would be satisfied with a non-invasive approach to managing their condition.

Objectives

To assess patient satisfaction with a *Helicobacter pylori* test and treat strategy compared to prompt endoscopy for initial management of dyspepsia.

Materials and Methods

Consecutive patients aged < 45 years with a history of uncomplicated dyspepsia attending the primary care department in this hospital were randomized to either a C13 Urea Breath Test(UBT) or prompt oesophagogastroduodenoscopy (OGDS), given *H. pylori* eradication if indicated and followed up for a period of 6 months. Prior to randomization, all patients were asked about their anxiety as to the cause of their dyspeptic symptoms, and of any family history of gastrointestinal malignancy. Satisfaction of either management strategy was assessed at the end of 6 months using a 4-point Likert scale from 1 (very dissatisfied) to 4 (very satisfied).

Results

Of 201 patients recruited, 181 patients (98 UBT, 83 OGDS) were followed up for 6 months. No significant differences in terms of anxiety about cancer (33.7% vs 39.8%) nor of ulcer disease (36.7% vs 37.3%) existed between both groups (p=0.67). 12.2% of UBT patients and 9.6% of OGDS patients had a family history of gastrointestinal malignancy (p=0.57). During the follow up period, 8 (8.1%) UBT patients and 3 (3.6%) OGDS patients underwent further OGDS (p=0.001). A higher proportion of patients in the OGDS group were on proton pump inhibitors (10% vs 5%, p=0.001) and motility agents (8% vs 2%, p< 0.0001) during this period as well. The mean satisfaction score at the end of 6 months was 3.01 ± 0.62 for UBT patients and 3.16 ± 0.59 for OGDS patients (p=0.11, mean difference -0.15; 95% CI – 0.33 to 0.33). The initial anxieties about cancer or peptic ulcer disease as well did not have any significant correlation to the final satisfaction score.

Conclusion

A non-invasive *Helicobacter pylori* test and treat approach is an acceptable alternative to young Malaysian patients with dyspepsia, compared to the standard 'endoscope and treat' practice.

Clinical Efficacy of a Helicobacter Pylori Test and Treat Strategy VS. Prompt Endoscopy in the Management of Young Asian Patients with Dyspepsia: Preliminary Results from a Randomised Trial

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Background

Most young patients with dyspepsia in our population do not have serious pathology. It has been suggested that a non-invasive approach based on *Helicobacter pylori* testing and subsequent eradication may be an alternative to standard oesophagogastroduodenostomy (OGDS). This may not necessarily be the case in Asia.

Aims

To assess the clinical effectiveness of a *Helicobacter pylori* test and treat management strategy versus prompt OGDS in young patients with dyspepsia in an urban Asian population.

Materials and Methods

Consecutive patients aged < 45 years with uncomplicated dyspepsia lasting more than 4 weeks, attending this institutions primary care unit, were enrolled into the study. Following screening, they were randomized to either a C^{13} Urea Breath Test (UBT) with *H. pylori* eradication if positive, or prompt OGDS with appropriate treatment. During the next 6 months, patients' symptoms and the need for further medical attention were documented. The primary endpoint was based on the Leeds Dyspepsia Questionnaire (LDQ), which was assessed in all patients prior to randomization and at the end of the study period.

Results

201 patients were recruited (April 2002 to January 2003) and 181 (98 UBT, 83 OGDS) completed the study. No significant differences were noted in basic demography, apart from a higher proportion of Chinese patients in the UBT group (47% vs 25%). The overall prevalence of *H. pylori* was 26% (UBT 33%, OGDS 17%). The LDQ at the beginning for both groups was 19.8 ± 6.5 (UBT) and 22.2 ± 6.3 (OGDS). No significant differences were noted between the 2 groups in terms of number of clinic visits (14 ± 3 UBT vs 13 ± 2 OGDS), severity of symptoms and hospital visits (2 ± 0.5 UBT vs 2 OGDS). More subsequent endoscopies were done in the UBT group (8% vs 3.6%, p=0.001) but a higher proportion of patients in the OGDS group were on proton pump inhibitors (10% vs 5%, p=0.001) and motility agents (8% vs 2%, p< 0.0001). At the end of 6 months, the mean change in LDQ for both groups was 14.8 ± 7.1 (UBT) and 16.1 ± 7.6 (OGDS), p=0.25.

Conclusion

The non-invasive *Helicobacter Pylori* test and treat approach is as effective as standard OGDS in the management of young Malaysian patients with dyspepsia.

High-Dose Lansoprazole/Amoxicillin in the Eradication of *Helicobacter Pylori* Infection: Rescue Therapy

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Objectives

To assess the efficacy of high-dose Lansoprazole/Amoxicillin dual therapy in the eradication of Helicobacter pylori(H.pylori) infection in patients who had failed to respond to standard first-line and second-line regimes before.

Materials and Methods

Patients with history of two previous unsuccessful attempts on *H.pylori* eradication regimes were included in the study. The first-line therapy consisted of one week duration of pantoprazole 2 x 40mg, clarithromycin 2 x 500mg and amoxicillin 2 x 1g., whereas the second-line therapy consisted of 2 weeks duration of pantoprazole 2 x 40mg, bismuth subcitrate 4 x 120mg, tetracycline 4 x 500mg and tinidazole 2 x 500mg. The rescue therapy included high dose lansoprazole 3 x 30mg and amoxicillin 3 x 1g for 2 weeks duration. H.pylori status was determined 4 weeks after end of therapy by ^{13}C Urea Breath Test.

Results

Nine patients (6 males and 3 females) with history of two previous unsuccessful attempts on *H.pylori* eradication regimes were included in this study. *H.pylori* infection was eradicated in 6/9 (66.7%) patients. The mean Delta Over Base (DOB) was 29.8 in patients with successful *H.pylori* eradication and 24.9 in patients failed *H.pylori* eradication.

Conclusion

Our data suggest that dual therapy with high-dose Lansoprazole/Amoxicillin is an effective rescue therapy in eradicating *H.pylori* infection in patients who experienced at least two previous treatment failures. No significant correlation was noted between pre-treatment mean DOB and *H.pylori* eradication rate.

Distinct Genetic Diversity of *Helicobacter Pylori cagA* Gene

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Background

The prevalence of *cagA*-positive *H. pylori* strains varies between different geographical regions and populations. In Western countries, *cagA*-positive strains is significantly associated with peptic ulcer disease and gastric cancer. However, data from studies done in Asian showed no association between *cagA*-positive strains and clinical outcome of disease. In our previous study, three type of *cagA* variants (type A, B and C) was detected in our clinical isolates.

Aim

To investigate the sequence diversity of the *H. pylori cagA* gene in strains isolated from the Malaysian populations.

Materials and Methods

PCR technique was used to amplify *cagA* gene and the product was visualized by agarose gel electrophoresie. Sequence of the gene was determined in both directions by automated sequencer (ABI Prism, Applied Biosystem).

Results

Sequence analysis of the cagA subtypes revealed that *cagA* subtypes in local *H. pylori* isolates were characterized by two repeat sequences which were different among each other. Repeat sequence in *cagA* subtypes were characterized by 54 bp sequence in type A, 39 bp sequence in type B and 30 bp sequence in type C. Phylogenetic analysis of the three cagA subtypes formed two different groups with genetic distance of about 2.2. Alignment of the deduced amino acid sequences of *cagA* subtypes (nucleotide position at 2991 to 371) in local *H. pylori* strains showed high polymorphism compared to strains from Western countries (strain J99 and 26695).

Conclusion

Sequence analysis of cagA variant in local *H. pylori* strains suggested the existence of distinct *cagA* variants. The sequence of the 3' region of the *cagA* gene in Malaysia differs markedly from the primary sequence of *cagA* gene from Western isolates.

Clinical Relevance of the *babA2*-Positive *Helicobacter Pylori* Clinical Isolates in Malaysia

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Background

H. pylori blood group antigen-binding adhesion (BabA) mediates bacterial adherence to human blood group antigens on gastric epithelium. In Western countries, it has been suggested to be of high clinical relevance and is a useful marker for patients with peptic ulceration and gastric adenocarcinoma.

Aim

To determine the association of *babA2*-positive *H. pylori* strains with peptic ulceration in Malaysian clinical isolates.

Materials and Methods

PCR technique was used to amplify the *babA2* gene in 191 *H. pylori* isolates. Presence of the gene was visualized by agarose gel electrophoresis.

Results

babA2-positive was detected in 25% of the isolates. The gene was present in 30% of isolates from peptic ulcer patients and 23% of isolates from non-ulcer patients. There was no correlation between the *babA2*-positive genotype and peptic ulceration ($p = 0.303$). Among the *H. pylori* isolates, *babA2*-positive was present in 18% of isolates from Malays, 23% of isolates from Chinese and 47% of isolates from Indians. Results showed there was no association between the *babA2*-positive *H. pylori* genotype and ethnicity of the host ($p = 0.12$).

Discussion and Conclusion

These results indicate that *H. pylori babA2* status is not of high clinical relevance in Malaysia. Given their low prevalence, *babA2* may not be a useful markers for predicting patients with high-risk to severe *H. pylori*-associated disease in Malaysia. Data from this study showed that the strains circulating in Malaysia may be different from those among the Western populations.

The Polyflex Technique : A Novel and Effective Technique in Palliation for Non-Operable Oesophago-Respiratory Stenosis and Fistulae

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Summary

Self-expanding metallic stents have to-date provided acceptable palliation of non-resectable stenosis of the oesophagoeal tract. Lately, a revolutionised technique employing a plastic stent - the "Polyflex", made of polyester netting and embedded in silicone has been developed and has proved to be very successful in relieving patients presenting with non-operable oesophageal stenosis or eosphagorespiratory fistulae.

This presentation will discuss the fundamental principles of the intervention process, associated risks and contraindications and will recommend the Polyflex Technique as an immediate addition to the armamentarium currently available in Malaysian hospitals.

Incidence and Epidemiological Study of Non Variceal Upper Gastrointestinal Bleed in HUSM, Kelantan

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Objective

The aim of the study is to determine the epidemiology and incidence of non-variceal upper gastrointestinal bleed in HUSM, Kelantan.

Materials and Methods

This is a retrospective study on patients who had undergone upper gastrointestinal endoscopy at Endoscopy Unit in Hospital USM, Kelantan from January 1999 to December 2003. They were examined for the presence of non-variceal upper gastrointestinal bleed. Epidemiology data was collected and analysed using SPSS version 11.0.

Results

A total of 142 patients were confirmed to have acute upper gastrointestinal bleeding during this period. There are 97 males and 45 females. Their age ranges between 18 – 89 years old and a mean of 65.5 years. Ethnic distribution are 128 Malays (90.1%), 14 Chinese (9.9%) and 0 Indians. Symptomatically, 27% presented with haematemesis, 46.5% with maelena and 34.5% with both haematemesis and maelena. The common risk factors for bleeding are non-steroidal anti-inflammatory drugs other than aspirin are (54.2%) followed by aspirin (18.3%), warfarin (3.5%) and others (23.5%). On admission, mean haemoglobin levels were 7.3%. Endoscope findings showed that 57.7% of the patients presented with Forrest classification ulcer grade 3, 38% grade 2 and 2.1% grade 1. 45.8% of patients did not require any endoscopic treatment, 49.3% of the patients were injected with adrenaline and heat probe while 4.2% were treated with diathermy or APC with or without adrenaline injection. All patients were also covered with proton-pump inhibitors.

Conclusion

In Kelantan, Malays are the predominant ethnic group thus showing a higher preponderance for bleeding ulcer and it is also common in males. From our series, peptic ulcer disease secondary to NSAIDS is the most common cause of non variceal upper gastrointestinal bleeding and the most common presenting symptom is maelena.

Comparative Study Between Intravenous Bolus Proton-Pump Inhibitors Versus Continuos Infusion in Non-Variceal Upper Gastrointestinal Bleed – HUSM, Kelantan

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Objective

To compare the incidence of rebleeding between using intravenous bolus and continuous infusion proton-pump inhibitors in patients presenting with non-variceal upper gastrointestinal bleed in HUSM.

In conclusion, there are a number of fixed and correctable factors that need to be considered when assessing the suitability of a patient for re-treatment. Targeting re-treatment with better efficacy regimens to patients who fail to respond to previous treatment seems to be reasonable. Since an SVR is achieved in a limited number of patients, studies of new strategies are clearly needed to improve treatment efficacy.

Materials and Methods

This is a retrospective study of 142 patients who presented with acute upper gastrointestinal bleed confirmed clinically and endoscopically. Endoscopic findings are compiled and anaylsed using SPSS version 11.0. The ulcers or bleeders are graded according to Forrest Classification.

Results

A total of 142 patients were recruited during this period comprising of 97 males and 45 females. Endoscopy findings of the NVUGIB were classified according to Forrest Classification grade 1 (2.1%), 2 (38%) and 3 (57.7%). Ninety six patients were treated to intravenous bolus PPI while 46 patients were treated to continuous infusion. Sixteen patients (16.7%) treated to IV bolus PPI rebled and needed to be rescoped compared to 10 (27.1%) patients on continuous infusion. In total 8.5% (12) of all patients required surgery. Of the 12 patients, 5 (41.7%) patients on intravenous PPI bolus required surgery compared to 7 (58.3%) patients on PPI continuous infusion. (p=0.045)

Conclusion

Proton-pump inhibitors are the current mainstay of management of patients with upper gastrointestinal bleeding. Continuous infusion of PPIs has been proven to be effective in controlling acute upper GI bleeds. In our series, there is a statistically significant difference in controlling upper gastrointestinal bleed between using IV bolus PPI and continuous infusion PPI.

Gastroesophageal Reflux is More Prominent in Western Dyspeptics – A Prospective Comparison Study of British and South East Asian Patients with Dyspepsia

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Background

There is a paucity of data directly comparing the incidence of gastro-esophageal reflux disease (GERD) in Western and Eastern populations. We therefore compared clinical symptoms, epidemiological factors and endoscopic diagnoses in two sample populations with dyspepsia from the United Kingdom and Asia in a cross-sectional study.

Materials and Methods

Patients with uncomplicated dyspepsia attending endoscopy units in both institutions were prospectively interviewed and underwent subsequent endoscopy from January 1999 to June 2001 (Leeds, UK) and between January and August 2002 (Kuala Lumpur, Malaysia).

Results

693 patients from Kuala Lumpur and 392 patients from Leeds of Caucasian race were included in the analysis. The mean age was 48.7 ± 15.8 and 47.5 ± 13.8 years for the Malaysian and British patients respectively (p=NS). There was a higher proportion of cigarette smoking (39.5% vs 13.4%, p< 0.0001), alcohol consumption (32.5% vs 2.5%, p < 0.0001), NSAID use (33.2% vs 23.4%, p=0.005) and *H. pylori* infection (45.3% vs 23.5%, p< 0.001) amongst the British patients. GERD symptoms were more common in British compared to Malaysian patients (heartburn (66.2% vs 37.4%), regurgitation (60.1% vs 30.2%) and dysphagia (23.7% vs 6.7%) p < 0.0001). This correlated to an increased endoscopic finding of reflux oesophagitis (29.6% vs 5.8%) and Barrett's oesophagus (3.8% vs 0.7%) amongst British patients (p< 0.001). A logistic regression model revealed that Caucasian race (OR 9.1; 95% CI=4.2 to 20.1), male sex (OR 2.0; 95% CI=1.2 to 3.2) and *H. pylori* infection (OR 0.4; 95% CI = 0.2 to 0.6) were independent predictors for reflux oesophagitis. Heartburn had a 75% sensitivity and 38% specificity for detecting oesophagitis in British patients compared to a 45% sensitivity and 63% specificity in Malaysian patients.

Conclusions

GERD is more predominant in Western patients and their symptoms are more predictive of pathology compared to their South East Asian counterparts.

An Audit on Gastroscopies (OGDS) Performed in the Kuala Lumpur Hospital

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Background

Kuala Lumpur Hospital is Malaysia's largest tertiary public referral hospital with a busy endoscopy unit performing more than 6500 procedures per year. We offer an open access endoscopic service.

Aim

To audit the gastroscopy referrals in the Kuala Lumpur Hospital.

Materials and Methods

Consecutive patients presenting to our endoscopy suite during office hours from 1st March to 30th April 2004 for OGDS were audited. Only patients referred for endoscopy from various medical clinics and medical wards were enrolled in the study. The gold standard was the American Society of Gastrointestinal Endoscopy's guidelines of 2000. Data was analysed using SPSS software (ver. 12.0).

Results

A total of 300 patients were audited. 164 (54.7%) were males and 136 (45.3%) were females. Mean age was 54.4 years (range 78, SD=14.9). One hundred and thirty-one (43.7%) were Malays, 83 (27.7%) Chinese, 75 (25%) Indians and others comprised 11 (3.6%). Based on ASGE guidelines, the most common reason for referral was " upper abdominal distress that persisted despite trial of therapy" (75 patients, 25%), followed by 66 (22%) with "presumed chronic blood loss/ iron deficiency anaemia", 33 (11%) who underwent "variceal surveillance or elective banding", 28 (9.3%) who required "tissue sampling", 27 (9%) with "symptoms suggesting serious disease", 21 each (7% each) with "reflux symptoms" and overt "upper gastrointestinal bleed", 12 (4%) with "dysphagia or odynophagia" and another 12 (4%) who required endoscopic "treatment of bleeding lesions". Thirteen patients (4.3%) did not meet the guidelines. The common findings on OGDS were endoscopic gastritis(including erosive and haemorrhagic gastritis) in 34.7% of patients, peptic ulcers (15.4%), oesophagitis (10.3%) and esophageal or gastric varices (10.7%). Eighty-two patients (27.3%) had normal findings. The most common indications in which the endoscopy was normal were "upper abdominal distress" and "anaemia" (25 and 16 patients respectively). The average waiting period for an elective OGDS was 28.4 days (range 180, SD=29.5).

Conclusion

A wide range of indications were observed in this study. Despite having an open access system, most indications conform to guidelines.

Percutaneous Endoscopic Gastroenterostomy Tube: A 2 Year Audit

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Background

The need to avoid prolonged starvation in patients is well recognized. Without intraluminal feeds, intestinal integrity may deteriorate and translocation of gut bacteria may set in. One means to combat nutrient deprivation and simultaneously to keep the local defense barrier of the intestine intact is tube feeding. Percutaneous Endoscopic Gastroenterostomy (PEG) has developed into an acceptable procedure accounting for over 200,000 procedures per year worldwide.

Objective

To audit demographics, indications, complications and 1 month survival of PEG insertion in our unit.

Materials and Methods

Case records from our endoscopy unit of patients undergoing PEG tube insertion from January 2002 to March 2004 were analysed.

Results

A total number of 54 PEG tubes were inserted in 40 patients comprising of 20 males and 20 females out of which 17 were Malays, 10 Chinese,11 Indians and 2 Sikhs. The average age at insertion was 57.5 years. Fourteen patients needed replacement tubes during this period. The PEG was fashioned for feeding in 21 patients with Strokes, 6 with Hypoxic Ischaemic Encephalopathy, 5 with Carcinoma of the Oro-Pharynx, 3 with Motor Neuron Disease, 2 with Spinocerebellar Degeneration, 1 with Multiple Cerebral Infarct, 1 with AIDS Dementia Complex and 1 with Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) who subsequently had the PEG tube removed after 3.5 months due to recovery of the swallowing reflex. There was no mortality or bleeding related to the procedure. Ten patients were found to have infection at the PEG site. One patient had bleeding from a "buried bumper syndrome" due to tight apposition of the external bolster to the abdominal wall. Thirteen of the patients are still alive,16 have passed away whereas the status of the remaining 11 patients are unknown. Survival at one month approached 87.5%.

Conclusions

PEG tube insertion is a relatively safe and well tolerated procedure. Survival at 1 month, a commonly reported end point in PEG studies (80-90% in most reports) approached 87.5% in our audit.

Bleeding in Peptic Ulcer Disease - The HKL Experience

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Background

Endoscopy is a necessary tool to define the cause of upper gastrointestinal haemorrhage (UGIB), to provide prognostic information and to achieve haemostasis. The endoscopic stigmata of recent UGIB's using the Forrest Classification (F) is a standardized method of assessing ulcers and it's propensity for rebleeding. Various modalities of hemostatic therapies are currently available for arresting UGIB's.

Objective

To assess the risk of rebleeding using the Forrest criteria and the effectiveness of various hemostatic therapies.

Materials and Methods

A total of 100 case records of patients presenting with UGIB's secondary to bleeding PUD were assessed.

Results

Seventy-two patients presented with F3 ulcers (clean base ulcers) with 5 patients experiencing rebleeds (6.9%), 11 with F2c ulcers (ulcers with haematin covered base) with a rebleeding rate of 9.1%, 12 with F2b (non bleeding ulcers with adherent clot) with rebleeding seen in 3 patients (25%), 8 patients with F2a ulcers (non bleeding ulcers with visible vessel) with rebleeding seen in 3 patients (37.5%) and 12 patients with F1b ulcers (non spurting active bleed) with rebleeding in 5 (41.6%). There were no patients with F1a ulcers (spurting vessel) during this period. A total of 25 interventational procedures (25%) were performed, with 19 patients received only Adrenaline injection with 9 rebleeds (47.3%), 2 patients with Adrenaline injection and heater probe administration,1 with Adrenaline injection, heater probe and haemoclip fashioned and 3 patients with Adrenaline injection and haemoclip; none of which experienced rebleeding.

Conclusion

The Forrest Classification of stigmata of Upper Gastrointestinal Bleeding in our centre approached recognized international values. Intervention with Adrenaline alone may not suffice in controlling bleeding ulcers. The utility of coadministering heater probe and haemoclip offered the best modality for haemostasis.

Patients' Perception of Dyspepsia and their Health Seeking Behaviour

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Objective

To study patients' perception of dyspepsia and their health seeking behaviour.

Materials and Methods

A cross sectional study of participants attending a public forum on *H.pylori* in year 2001.

Results

Two hundred and fifty participants perceived themselves as having dyspepsia. There were 45.2% male, 53.6% female; 80.8% Chinese, 6.8% Indians, 6.8% Malays. The mean age was 43.8 years (SD 11.5). Duration of dyspepsia ranged from 1 day to 40 years. The 5 most common perception of dyspepsia were upper abdominal bloating (54.8%), belching/burping (52.4%), periodic stomach discomfort/pain (51.6%), pain or burning all over the upper abdomen (39.6%), heartburn (36%). 37.2% had endoscopy, 36.8% had no investigations. 75.6% consulted doctors, but only 2.4% sought treatment from traditional healers. The mean number of visits to doctors in the past 1 year for all illnesses and for dyspepsia was 4.4 (SD 3.9) and 3.6 (SD 3.3) respectively.

Discussion and Conclusion

The most common perception of dyspepsia is upper abdominal bloating. However, nearly 40% included heartburn in their definition of dyspepsia. Physicians should therefore elicit history of heartburn from patients presenting with dyspepsia. Most had consulted doctors and this poses a heavy health burden. The study is limited by its design of a biased population.

Current Practices in the Management of Peptic Ulcer Disease in Malaysia

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Background

The aim of this study was to assess the current opinions and practices in the endoscopic management of bleeding peptic ulcer disease (PUD) in Malaysia.

Materials and Methods

A pretested questionnaire was given to 150 delegates during the annual national gastroenterological conference (International GUT Meeting) in August 2003. Chi-squared test were performed for the statistical analysis of comparative non-parametric data.

Results

One hundred and six valid questionnaires were tabulated and analysed. Ninety-four (89%) of respondents were hospital gastroenterological practitioners, 53 (50%) and 41 (39%) of who were gastroenterologists and surgeons respectively. The remaining 11% were family physicians with an interest in gastroenterology. Public health sector practitioners accounted for 58% (61) of respondents while the rest were physicians from private hospitals 22% (23) and academic institutions 9% (10) respectively. The majority (93%) of hospital practitioners prescribed intravenous proton pump inhibitors for bleeding PUD while 79% employed injection of adrenaline as their main method of endoscopic therapy for bleeding PUD. Over half of all doctors incorporating the 3 different establishments preferred injection of adrenaline for clot-bearing PUD ulcers while a conservative approach was preferred for patently non-bleeding ulcers. A small percentage of doctors, both surgeons (15%) and physicians (17%) indicated prescribing *Helicobacter* eradication therapy despite negative rapid urease test following acute PUD bleeding. Overall, there were no significant differences in the pattern of practice between surgeons and physicians ($p>0.05$) in managing bleeding PUD even though surgeons preferred early endoscopic evaluation ($p>0.05$).

Conclusion

Based on this survey, there appears to be minimal variation amongst surgeons and gastroenterologists in the management of patients with bleeding PUD. Both group of practitioners appear to conform and utilise optimal management pathways in managing this condition even though certain non-evidence-based clinical practices continues to be utilised.

Aggressive Surgical Management of Oesophageal Perforations - The Mainstay of a Successful Outcome

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Summary

The management of oesophageal perforation continues to be a formidable challenge. Prompt diagnosis and effective treatment optimizes the chance of a successful outcome. However, controversy exists on the best method of treatment. The management is rendered more difficult when the perforation is diagnosed late. Although treatment needs to be individualized, there is an increasing trend towards aggressive surgical intervention.

We report three consecutive cases of oesophageal perforation, two of which were referred late. All three patients were managed successfully with aggressive surgical intervention, two patients having had emergency subtotal oesophagectomy. We stress the importance of proactive surgical intervention in this group of patients to procure an effective outcome.

Achalasia Registry: The Kuala Lumpur Hospital Experience

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Background

Achalasia cardia is an uncommon disease that is often detected late and is associated with significant morbidity. It is a primary esophageal motility disorder diagnosed based on a good history, barium swallow, upper endoscopy and a standard esophageal manometry.

Materials and Methods

We reviewed complete available records of treatment naïve patients with achalasia cardia from 1st January 2000 till April 2004.

Results

A total of 40 patients, with average presenting age at 44±16 (range 19-73) years with 14 males: 26 females with 20 Malays: 15 Chinese: 5 Indians, were suitable for further analysis. The classical symptom of dysphagia to liquids and solids were noted in all cases (100%). These patients learnt that water and sometimes-aerated drinks aid in flushing food down. Symptoms of regurgitation (36 patients-90%), heartburn (15 patients-37.5%), weight loss (10 patients–25%), nocturnal cough (16 patient-40%), retro-sternal chest discomfort (2 patient-5%) and hemetemesis (2 patient-5%) was noted. One patient had aspiration pneumonia and another had concomitant active pulmonary tuberculosis and 8 had concomitant constipation (20%). In this series the duration of illness before diagnosis was 5±6 (range 0.3- 30) years and their presenting weight was 53±13 (range 33-82) kg. Barium swallow diagnosed Achalasia in 27 patients (67.5%) and a dysmotility disorder in 7 cases (17.5%). There were 10 patients with mega-esophagus and two had epiphrenic diverticulum. There was no pseudoachalasia. Standard esophageal manometry, performed in 36 cases, demonstrated aperistalsis with one vigorous achalasia. The manometric assembly failed to pass through the sphincter in 14 cases and hence LOS assessment was not possible. Four cases demonstrated normal LOS pressure but demonstrated incomplete relaxation (normotensive achalasia). Pneumatic dilatation was performed in 38 newly cases without any complications with excellent symptomatic relief and a 3-12 month post procedural weight gain of 7±5 (range: 0-19) kg. Six patients required a second dilatation and another required two further dilatation. The durability of the total 45 pneumatic dilatations during this short study period was excellent at 24±12 (range 2-48) months.

Conclusion

A primary esophageal motility disorder must be excluded in any patients who present with dysphagia, with or without regurgitation and a "normal" upper endoscopy. Achalasia is not uncommon, often delayed in diagnosis and has a varied presentation. Although there is no cure for achalasia, but early detection and treatment certainly relieves symptoms and prevents complications. Pneumatic dilatation in our center has excellent durability without any complications.

Dilatation of Oesophageal Strictures Without Fluoroscopy Guidance Using Savary-Gillard Dilators: Is it Effective and Safe?

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Introduction

Oesophageal dilators have been used since the Middle Ages and its technique has evolved considerably in recent years. Endoscopic oesophageal dilatation is currently the first line of treatment for benign oesophageal strictures and occasionally used in selected cases of malignant strictures. Many centers use radiographic screening during the procedure to ensure safety.

Objective

To review the efficacy and safety of performing endoscopic oesophageal dilatation using Savary Gillard dilator without fluoroscopy guidance in our center.

Materials and Methods

The efficacy and safety of Savary Gillard dilators were evaluated retrospectively from April 2001 to April 2004 in 18 patients with oesophageal strictures. Forty-five dilatations were performed within the 3 years period as outpatient basis. All dilatations were performed under sedation and opiate analgesia using guide wire as guidance. The stricture would be gradually dilated once the wire is felt to pass easily into the stomach. Preliminary barium studies were performed on cases of corrosive strictures. A complete endoscopic examination would be performed immediately after dilatation.

Results

A total of 45 dilatations were performed on 18 cases of oesophageal strictures. There were 10 males and 8 females (F:M, 4:5 ratio). Age range was between 13 to 74 years old. Eleven cases required only single dilatation. Seven patients required multiple dilatations ranging from 2 to 12 dilatations. Indications for dilatation were post surgery anastomotic strictures (7 cases), benign strictures (7 cases), corrosive strictures (3 cases) and malignant stricture (1 case). Site of dilatations were upper third oesophagus in 11 cases, middle third 4 cases and lower third in 3 cases. All patients experienced immediate significant improvement in the ability to swallow. Complication in the form of oesophageal perforation and false tract formation occurred in one patient which was treated conservatively. There was no mortality.

Conclusion

Oesophageal dilatation with Savary Gillard dilator without fluoroscopy guidance is effective and relatively safe. It can be done on an outpatient basis and limits radiation exposure to the patient and medical staffs.

Palliation of Malignant Dysphagia – From Alcohol Injection to Metallic Stenting: HUKM Experience

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Introduction

Oesophageal carcinoma incidence is increasing both in the developed and developing countries. Hospital Universiti Kebangsaan Malaysia (HUKM) serves a multi ethnic community comprising of Malays, Chinese, Indians and other ethnic groups. Oesophageal cancer appears to affect patients from the lower socio-economic group. Earlier, metallic stents were extremely expensive and intratumoral alcohol injection was used to palliate the dysphagia. Subsequently metallic stents were used when the price became affordable and subsidy was provided by the hospital.

Objective

To review the efficacy and safety of alcohol injection and metallic stenting in the palliation of malignant dysphagia in HUKM.

Methods and Results

From March 1991 to November 2001, 24 patients with advanced oesophageal cancer underwent endoscopic alcohol injection to induce tumour necrosis. Four had grade 4 dysphagia while the rest had grade 3. Following ethanol injection, the median grade dysphagia improved significantly to 2 in 18 patients while in the other 6 patients they improved to near normal swallowing (Grade 1). The mean duration of dysphagia free was 35.6 days.

From January 2001 to January 2004 there were 32 patients diagnosed to have oesophageal carcinoma with 11 of them deemed inoperable. They were treated with palliative metallic stents and another patient was stented for a complicated recurrent postoperative stricture. Two patients with advanced lung carcinoma were stented for malignant dysphagia secondary to tumour infiltration. All the 14 patients showed significant improvement in the ability to swallow. There was only one mortality involving a patient with lung carcinoma who developed severe aspiration pneumonitis following the stenting. Four cases (28.5%) had tumour overgrowth that was dealt with at a later stage. One case had a restenting procedure due to a malignant tracheo-oesophageal fistula formation and another for stent migration.

Conclusion

Palliating malignant dysphagia with alcohol injection is simple, cheap and effective but painful plus may require repeated sessions. Metallic stenting is very effective but costly.

A Modification of Pneumatic Dilation Technique

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Background

Based on studies and some clinical practice pneumatic dilatation utilizing the widely available wire-guided polyethylene pneumatic dilator system using a 30mm balloon inflated for 15 seconds upon loss of waist noted (during fluoroscopy) at 7 to 10psi obtains optimal disruption of the lower esophageal sphincter. We employed this technique till August 2001 without any complications (notably perforation) with good clinical outcome and durability.

Aims

To study the efficacy of pneumatic dilatation with the pneumatic balloon dilated only till loss of waist.

Materials and Methods

A total of 10 treatment naïve achalasia patients enrolled from August 2001 till July 2002 were dilated till loss of waist and the outcome and durability was compared with our historical controls.

Findings

A total of 10 patients with age 45±18 (range 22-67) years with 8 females: 2 males and 5 Malays: 5 Chinese with 3 patients with megaoesophagus underwent pneumatic dilatation using a 30 mm Rigiflex ® pneumatic dilator till loss of waist was noted during fluoroscopy at 7psi and the balloon deflated immediately. All the patients reported symptomatic improvement in dysphagia, regurgitation and demonstrated a 3-12 month post procedural weight gain of 6±5 (range: 1-15) kg. One patient required a second dilatation only after 13 months. All the remaining patients remain well till today after the initial single dilatation. The durability of the dilatation was 27±7 months (range: 13-33) months. There were no complications noted. There were no complaints of excessive reflux. This data was compared with our historical control (patients before August 2001), i.e. the pneumatic dilator inflated for 15 seconds upon loss of waist, and there was no difference in clinical outcome, or the durability of dilatation or the duration of stay post procedure.

Conclusion

Forceful disruption of the lower esophageal sphincter utilizing the pneumatic dilator is effective but is associated with a 1-5% risk of perforation. We obtained identical results without loss of clinical improvement or durability utilizing our technique compared to the traditional method. Since August 2001 all our dilatations were performed in our unit utilizes this simplified method. We have yet to report a perforation after pneumatic dilatation.

Oesophageal Manometric Characterization of Patients with Achalasia Cardia

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Background

Achalasia is a rare but important cause of dysphagia often missed and diagnosed late. Absence of oesophageal peristalsis is a prerequisite for manometric diagnosis of achalasia. The confirmatory diagnostic criteria are incomplete lower esophageal sphincter (LES) relaxation and/or elevated LES pressure.

Aims

To define the standard esophageal manometric features in our series of patients with achalasia. To further evaluate if manometry would serve as a gold standard for the diagnosis of Achalasia.

Materials and Methods

Manometric tracings from 36 patients with suspected achalasia/ functional dysphagia from 1st January 2000 till April 2004 who underwent manometry were reviewed. Manometry was performed using a low compliance pneumohydraullic pump with either an 8 channel water perfused catheter (4 distal ports arranged radially) or an 8 channel water perfused catheter with a Dentsleeve. Various techniques and tricks were required to aid the catheter must pass the LES for sphincter assessment.

Results

All 36 patients exhibited absence of esophageal body peristalsis with simultaneous contractions (mean amplitude 15±9 (10- 46)) mmHg of the esophageal body. One patient had vigorous achalasia with amplitudes around 45-47 mmHg. Approximately six months prior to enrollment one patient with dysphagia and regurgitation had evidence of intermittent lumen occlusive peristaltic esophageal contractions but lost them in the subsequent study.

The catheter failed to pass the oesophageal sphincter in 14 patients giving a LES intubation success rate of 61%. A total of 7 out of 10 (70%) patients with megaesophagus failed LES intubation while only 7 out of 26 (27%) patients without megaesophagus failed LES intubation ($p < 0.05$).

The basal LES pressure, following the standard nomenclature in reference to the gastric baseline, was 17±7 (range 5-40 mmHg). Four patients had normal LES pressure (18% - normotensive achalasia) but demonstrated the hallmark of failure of relaxation. The remaining 18 patients had LES pressures above

10 mmHg. The percentage relaxation of the LOS with reference to gastric baseline varied from 0- 90% (mean: 50±40%).

Discussion

Dysphagia and aperistalsis can also occur in scleroderma and non specific esophageal motor disorder. Technical difficulty in intubating the LOS frequent occurs especially in advanced achalasia (with megaoesophagus) but in these patients the barium swallow is usually characteristic. Failure of LES intubation frequently occurred in patients with megaesophagus.

Conclusion

Manometry is superior in the diagnosis of early achalasia but has limitation in advanced disease due to technical reasons. Ideally the diagnosis of achalasia cardia is made on the full complement of a good history, endoscopy, barium swallow and manometry.

Cervical Osteophyte Induced Dysphagia

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Summary

A 60 year old man was referred to the hospital with a history of difficulty in swallowing solid food for 6 months. He also complained of cervical pain radiating to both upper limbs. There was no history of pharyngeal paralysis, nasal regurgitation of foods or odynophagia. However, he did complain of pain in the knee joints for the past few years. On investigation, he had normal haemogram, liver function and renal function tests, including serum calcium. Cervical spine radiography revealed severe cervical spondylosis with large osteophytes at C5-6 level. Barium swallowed revealed narrowed sections of oesophagus in hypo-pharyngeal region and upper portion of oesophagus with reflux at the gastro-oesophagal (GE) junction. Upper gastro-oesophagal endoscopy showed indentation of posterior oesophagus at 15cm from incisor teethwith a 5cm hiatus hernia at GE junction. There was no evidence of any growth and endoscopic biopsy taken at level of indentation was normal. He was treated with cisapride and omeprazole for reflux and diclofenac sodium for joint pain. With these measures, his cervical pain and dysphagia improved. Six months later the dysphasia was better but not gone completely.

Discussion

Cervical osteophtes and other hypertrophic changesin the aging cervical spine are common and frequently occur in those with generalized osteoarthritis. In most of these patients, spurs are asymptomatic while in others they may be associated with neck stiffnessand localized or radiating pain. Dysphagia secondary to compression of the oesophagus is unusual. In reviewing 116 patients with known cervical exostosis of sufficient magnitude to warrant treatment, Saffouri and Ward founf only seven (6%) had dysphagia. The usual complaint is difficulty in swallowing solid foods, but patients also occasionally complain of odynophagia, a foreign body sensation, hoarseness, cough, or an urge to clear the throat.

Cervical osteophytic dysphagia may be related to single or combined mechanism. First, these lesions, if large enough, may compress the oesophagus sufficiently to cause partial obstruction. Peri-oesophageal inflammation may occur secondary to irritation contributing further to dysphagia. Frequently (70%), only one pair of vertebra are involved. Anatomically, the oesophagus is anchored at the level of the cricoid cartilage and thus it is most likely to be compressed at the C5-6 or C6-7 level as was in our patient. In addition, our patient also had gastro-oesophageal reflux and this could be contributing to his dysphagia as partial improvement did take place after institution of omeprazole and cisapride. However, as the recovery was incomplete and he continues to have dysphagia on follow up despite these measures suggests compression of oesophagus.

The management of cervical osteophyte induced dysphagia depends on the nature and severity of the disease. Symptomatic therapy has been the most common initial approach, particularly in cases where no obvious large obstructing lesion exists. Occasionally, surgical excision of the osteophyte is required for those who have profound symptoms.

Use of Lidocaine Spray for Pain Relief in Terminally Ill Cancer Patients

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Summary

Pain relief is the top priority in palliative care given to terminally ill cancer patients and contributes significantly in improving quality of life (QOL). These commonly present with: pain from open wounds, dysphagia and pain/discomfort of mucositis. Lidocaine is the drug for surface anaesthesia. This study used lidocaine spray with a long nozzle to reach inaccessible areas for relieving symptoms. Spray was used on superficial painful areas found in 15 patients (75%) from the head and neck cancer group and 5 patients (25%) from others.

The spray contained 100 mg of lidocaine in 80 ml of ethanol (30% v/v), each metered dose contained 10 mg. The spray was in a glass bottle with a long nozzle, the cannula length being 10cm, with the internal diameter of the nozzle orifice being 0.4mm. The plastic nozzle could be easily sterilized and reutilized.

Lidocaine is soluble in alcohol. Ethanol is a penetration enhancer and an antibacterial. Penetration behaviour changes with changes in the vehicle composition, and changes in the evaporation and moisture uptake. The degree of relief depends upon the reach of the drug to the affected areas. Shortened nozzle length affects the spray function. Lidocaine in alcohol achieves anaesthesia in a shorter time. Effects of the drug also last for a short time. Short duration of action ensures decreased toxicity of the drug.

Quality of life (QOL) was assessed on the following basis- pain, dysphagia, intake, weight, mobility, nutrition and mood. QOL was determined on admission and subsequently at the end of the treatment. The spray with a long nozzle produced substantial symptom relief, both qualitatively and quantitatively within 3-35 days. A 1.25% solution of lidocaine in 30% alcohol applied as a spray through a long nozzle was successful in relieving pain in 19 of 20 patients and dysphagia in 15 of 16 patients. It improved nutrition in 19 of 19 patients, improved the reduced mobility in 10 of 10 patients, and restored depressed mood in 18 of 19 patients. Eleven patients also gained weight. There was a significant enhancement in QOL of patients. Lidocaine was well tolerated except in one patient, in whom the spray was discontinued due to an allergic reaction. Good palliation was achieved in terminally ill patients.

The Prevalence of Gastroesophageal Reflux Disease (GERD) in Asthmatic Patients

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Background

The association of gastroesophageal reflux disease (GERD) and asthma has been observed for a long time. GERD is thought to cause asthma or worsen pre-existing asthma. On the other hand asthma medications have been implicated in causing GERD.

Objective

To determine the prevalence of GERD in patients with moderate to severe asthma.

Materials and Methods

Patient with moderate to severe persistent asthma as defined by the GINA guidelines were recruited from University Malaya Medical Center asthma clinic. All patient were administered a detailed questionnaire, underwent EGD and a 24-hour esophageal pH monitoring. Patients were defined as having GERD when there was reflux esophagitis (Los Angeles classification) at endoscopy, or the 24-hour esophageal pH test was positive using the DeMeester score or when they had predominant symptoms of heartburn or acid regurgitation at least once per month for the past 6 months.

Results

Thirty patients were recruited for the study: The mean age was 51.9 $\pm$ 12.3 years, male: female ratio-6: 24. Seventeen patients (56.7%) were found to have GERD: 10 patients had reflux esophagitis, the majority, 8 (80%) had grade A changes and 2 of grade B changes. Only 3 had a positive 24-hour esophageal pH test. 6 (20%) patients were diagnosed to have non-erosive reflux disease, 3 had a positive 24-hour esophageal pH test. One patient was asymptomatic clinically but had a positive 24-hour esophageal pH test.

Conclusion

The prevalence of GERD in asthmatic patients was high. The majority of patients had NERD or mild grades of reflux esophagitis.

The Role of Gastroesophageal Reflux Disease in Asthma: Response to Treatment with Potent Acid Suppression in "Difficult-to-Control" Asthma Patients

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Background and Objectives

Gastroesophageal reflux disease (GERD) is thought to cause or exacerbate pre-existing asthma. Treating GERD in asthma patients with potent acid suppression may therefore result in improvement in asthma control. The aim of this study is to determine the effect of proton-pump inhibitor (PPI) therapy on the severity of asthma.

Materials and Methods

Patients with moderate to severe asthma with or without GERD were prescribed an 8-week course of lansoprazole 30mg daily. A baseline and an "end-of-treatment", one-week pulmonary symptom severity score (PSS), one-week reflux symptom severity score (RSS), peak expiratory flow rate (PEFR) and forced expiratory volume in one second (FEV1) were recorded. Symptoms were assessed by an investigator who was blind to the GERD status of the patient. Efficacy of treatment was assessed by comparison of the pre and post treatment mean scores of the above variables.

Results

Thirty patients were recruited. Twenty-seven patients completed the treatment and were available for analysis (16 - GERD, 11- non-GERD). Twelve (75%) patients reported improvement in asthma symptoms with a significant reduction in mean PSS (p=0.002). There was no significant change in the mean PEFR and FEV1 (p=0.075, p=0.147 respectively). Amongst the non-GERD patients, the mean PSS did not show significant improvement (p=0.317). There was also no improvement in the PEFR and FEV1. The change in the mean PSS, PEFR and FEV1 pre and post treatment was significantly higher in GERD vs non-GERD patients.

	Δ Mean PSS	Δ Mean PEFR	Δ Mean FEV1
GERD	-15.6	25.0	0.10
Non – GERD	-0.64	-1.4	-0.11
Difference GERD vs non-GERD	p=0.010	p=0.040	p=0.017

Conclusion

PPI therapy was effective in improving asthma symptoms only in patients with GERD. The difference in the change in severity of asthma and lung function tests pre and post treatment was highly significant in GERD compared to non-GERD patients underlining the critical role of GERD in a subset of patients with "difficult-to-control" asthma.

Emergency Endoscopy Reduced Mortality in Patients Presenting with High-Risk Upper GI Bleeding

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Introduction

Acute upper gastrointestinal bleeding (UGIB) is associated with high mortality in patients with risk factors including co-morbidity and hemodynamic instability at presentation. Whether urgent endoscopy with therapeutic intervention in such patients improves the outcome is unknown.

Aim

To identify predictive factors for mortality in patients presenting with high risk acute UGIB and to determine if urgent endoscopy in these patients has an impact on their mortality.

Materials and Methods

Patients who presented with acute UGIB were triaged at presentation by a gastroenterologist and urgent endoscopy was performed for any of the risk indices; frank hemetemesis, hemodynamic instability and/or suspected/known cirrhosis. All patients were endoscoped within 24 hours. We prospectively collected data from a consecutive series of such patients over a one-year period. Parameters including patient over a one-year period. Parameters including patient age, gender, hemodynamic status at presentation, co-morbidity, cirrhosis, and time between presentation and endoscopy were analyzed with respect to in-hospital mortality.

Results

Of 320 patients included in the study, 217 (67.8%) were men. Their ages ranges 17-92 (median: 64) years. Two hundred and four (62.2%) had comorbid disease on presentation. Endoscopic therapy was required in 142 patients (43.3%). Thirty-four (10.2%) died during the hospital stay. Using multivariate logistic regression, hypotension at presentation (OR 11.96, $p<0.0001$) and presence of comorbidity (OR 9.6, $p=0.003$) are independently predicted increased in-hospital mortality. In contrast, endoscopy within 4 hours of presentation was an independent predictor of reduced in-hospital mortality (OR 0.36, $p=0.047$).

Conclusion

Hemodynamic instability and comorbidity were predictors for increased in-hospital mortality in patients who present with high risk UGIB. Endoscopy within 4 hours of presentation predicted reduced mortality in such patients. Therefore, early endoscopy should be considered in these high risk UGIB patients.

Metal Stenting of a Case of Duodenal Obstruction Due to Advanced Cholangiocarcinoma

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Summary

A 57 years old male who was diagnosed as cholangiocarcinoma in April 2003, had biliary wall stent inserted for palliation. He presented again after a year with symptoms of gastric outlet obstruction. Clinically he was cachectic, pale but not icteric. Abdomen was distended with succussion splash. Ultrasound abdomen revealed dilated stomach with irregular mass noted at duodenum, Bile ducts were not dilated. Gastroscopy revealed stricture and obstruction at first part of duodenum. He underwent a series of therapeutic upper GI endoscopic procedures and later 2 metal stents were successfully placed that made him well for the next 5 months. The rarity of the clinical presentation and management prompted us to report this case.

IBS in East Malaysia: Does Socio-Economic Status Make a Difference?

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Aims

To ascertain the influence of socio-economic status of IBS (Irritable Bowel Syndrome) subjects in a multi-ethnic Malaysian society.

Materials and Methods

This is a state-wide telephone interview protocol, the first of its kind conducted in Malaysia. A telephone directory provided by a major telecommunication provider in Malaysia was used. Samples selection utilized a systematic cluster sampling based on alphabetical ascending order list. Statistical analysis was performed using SPSS® v.12 statistical software. Test of significance using Pearson Chi-Square with a p-value set at a significant level of < 0.05.

Results

A total of 402 subjects were interviewed via telephone call. Out of them 178 (44.3%) were male and 224 (55.7%) were female. The majority of subjects falls under the category of age ranging from 35-44 and 45-54 with a prevalence of 27.1% and 28.4% respectively. The Chinese (49.8%) remains the largest group in the population surveyed, mainly due to the telephone subscription pattern in this state. The types of educational level in our population surveyed shows a predominance of education level up to upper secondary level (77.9%). Comparing IBS and non-IBS subjects with regards to level of educational attainment, there is no significant difference noted ($p=0.355$). Subgroup analysis also does not show any significant different; in C-IBS ($p=0.793$) or in the D-IBS($p= 0.481$). Most of our IBS subjects (66 or 55.93%) are gainfully employed as employees. This is significant as compared with other job descriptions such as being self-employed ($p=0.047$). Most of our subjects interviewed had a combined monthly income of less than RM2,000, however this was not significant when compare with other income groups (a Chi-Square analysis shows a p-value of 0.262). There was no significant different with regard to race amongst IBS and non-IBS subjects in Sabah ($p=0.926$).

Conclusions

Irritable Bowel Syndrome in Sabah, East Malaysia does not appear to be associated with educational level, economic status or race. However, working as an employee appear to be more at risk of getting IBS.

IBS in East Malaysia: Consultation Pattern

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Aims

To ascertain the consultation pattern of IBS (Irritable Bowel Syndrome) in a multi-ethnic Malaysian society in East Malaysia.

Materials and Methods

This is a state-wide telephone interview protocol, the first of its kind conducted in Malaysia. A telephone directory provided by a major telecommunication provider in Malaysia was used. Samples selection utilized a systematic cluster sampling based on alphabetical ascending order list. Statistical analysis was performed using SPSS® v.12 statistical software. Test of significance using Pearson Chi-Square with a p-value set at a significant level of < 0.05

Results

Out of the 402 subjects interviewed, the prevalence of (IBS) was 29.4%. Of all the 402 subjects interviewed, 4.5% (18 subjects) had consulted doctors for their abdominal symptoms. Of these 17 (14.41%) had a diagnosis of IBS and only one was not diagnosed as IBS. The difference between IBS and non-IBS with regard to Consulters and Non-Consulters is significant. *(Pearson Chi-Square, P= 0.000)*. IBS subjects consult doctors more frequently than non-IBS subjects. Apparently there are more diarrhea predominant subjects (12 or 70.59%) who seek medical help. However there is no difference in consultation pattern between constipation predominant (C-IBS) and diarrhea predominant (D-IBS) subjects (p=0.918). Out of the 402 subjects interviewed, 8 or 2.0% of the subjects were told by their health care provider that they have IBS. Seven of them were diagnosed to have IBS by ROME II criteria. Only one subject did not fulfill the criteria. The only one alternator subject was never diagnosed by the health care provider as having IBS. The IBS group were aware of the diagnosis of IBS made by their health care provider (p=0.001). Among the C-IBS and D-IBS groups there was no difference in terms of whether they were informed by their physician of the diagnosis of IBS (p=0.626). Six (7.32%) of the D-IBS said they were informed while only 1 (2.86%) of the C-IBS was informed. Of all the 402 subjects, 39 (9.7%) had actually taken some forms of medication for their abdominal symptoms. A small proportion (37 or 31.36%) of IBS subjects took some form of medication for relief of abdominal symptoms. This finding is significant (p=0.000). There is no difference between C-IBS and D-IBS groups with regard to intake of medication for abdominal symptom relief (P=0.070). Out of the 402 subjects, 17 (4.2%) had taken prescription medications from their doctors. The number of IBS patient who took prescription medication (16 or 13.56%) from their doctor is very significantly low (p=0.000). There is no difference in prescription-seeking behaviour between C-IBS and D-IBS subjects. Thirty-one subjects of C-IBS (88.57%) and 70 subjects of D-IBS (85.36%) did not seek prescriptions from doctors (p=0.830). Of all

subjects interviewed, 7 or 1.7% had taken over-the-counter (OTC) drugs for abdominal symptom relief. The difference between IBS and non-IBS subjects with regard to OTC usage is significant (p=0.000). One hundred and eleven or 94.07% IBS patient do not take OTC medications. Among the 402 subjects, 27 (5.5%) had taken herbal drugs or natural remedies. The number of IBS subjects who took alternative medicine (20 subjects or 16.95%) is significantly low (p=0.000). There is no difference between C-IBS and D-IBS subjects with regard to alternative therapy. Only 3 subjects of C-IBS (8.57%) and 17 subjects of D-IBS (20.73%) who seek *alternative therapy* (p=0.249).

Conclusion

IBS subjects in East Malaysia seek help from doctors more frequently than non-IBS subjects. There was however no different in consultation pattern between constipation predominant and diarrhea predominant subjects. All IBS subjects in this study were well informed about the diagnosis of IBS by their health care provider even before There is no difference between C-IBS and D-IBS groups with regard to being informed of the diagnosis. Most IBS subject do not take prescription medication and there is no difference between C-IBS and D-IBS groups. The number of IBS patient who took OTC medications and/ or alternative therapy is significantly low.

IBS in East Malaysia: A Prevalence Study

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Objective

To ascertain the prevalence of IBS (Irritable Bowel Syndrome) in East Malaysia and the characteristic of IBS in a multi-ethnic Malaysian society.

Materials and Methods

This is a state-wide telephone interview protocol, the first of its kind conducted in Malaysia. A telephone directory provided by a major telecommunication provider in Malaysia was used. Samples selection utilized a systematic cluster sampling based on alphabetical ascending order list. Statistical analysis was performed using SPSS® v.12. Test of significance using Pearson Chi-Square with a p-value set at a significant level of < 0.05.

Results

A total of 402 fixed-line telephone users were interviewed via telephone by a single, well trained research assistant. 178 (44.3%)of the subjects were male and 224 (55.7%) were female. The prevalence of IBS was 29.4% (118 subjects). On sub-group analysis, the prevalence of Constipation predominant IBS (C-IBS) is 8.7% (35 subjects). This reflects a 29.7% or 35 subjects within the IBS diagnosed group. The Diarrhea predominant IBS (D-IBS) group was identified in 82 subjects or 20.4% of the entire population under survey. Subgroup analysis shows that 82 subjects (69.5%) are diarrhea predominant within the IBS diagnosed group. Comparing IBS and non-IBS group, more female (75) are having IBS as compared with male (43). However, this is non-significant (p=0.079). There is only one alternator IBS subject who is a female. Most IBS subjects are in the age range of 35-44 followed by 45-54 and 55-64. However, this is not significantly different from the non-IBS group (p=0.654). The prevalence of IBS among the Kadazan-Dusun, Chinese, Malay, and Bajau are 29.0%, 28.5%, 27.65% and 24.2% respectively. There is no ethnic distribution variability between IBS and non-IBS subjects (Pearson Chi-Square, p=0.926). There is no gender difference in the D-IBS (p=0.364) nor in the C-IBS (p=0.249) groups. D-IBS and indeterminate (mixed) group had not shown any significant pattern of different among the different races in east Malaysia (P=0.550). C-IBS also shows no significance pattern of different among the different races (p=0.278). overall, there is no difference in the prevalence of IBS among males and females (p=0.079) as well as the various ethnic groups (p=0.926) in Sabah.

Conclusion

The prevalence of IBS in east Malaysia was noted to be 29.4%. The prevalence of C-IBS and D-IBS were also determined according to the ROME II criteria. There were no different in the IBS, C-IBS and D-IBS prevalence with regards to gender, age and race.

Duodenal Diverticulum and Pancreaticobiliary Disease: Analysis of 127 Patients Undergoing ERCP

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Objective

To detect prevalence of juxtapapillary duodenal diverticulum in patients undergoing ERCP and its role in pancreaticobiliary disease.

Materials and Methods

All patients who had ERCP for various pancreaticobiliary disease from February 2002 till March 2004 were analyzed. Patients with juxtapapillary duodenal diverticulum were analyzed according to age, sex, race and nature of pancreaticobiliary disease.

Results

A total of 127 patients had ERCP, 17 (13.3%) were identified to have juxtapapillary diverticulum. Seventy-five males (59%) and 52 females (41%) had ERCP for pancreaticobiliary diseases. Diverticulum was seen in 11 males (64%) and 6 females (36%). Age ranged from 40 to 65 years with a median of 50. In patients with diverticulum, 7 (41%) were Malays, 9 (52%) were Chinese, and 1 (7%) patient was Indian. We encountered difficulty in cannulation of the ampulla in 60% of patients with diverticulum compared to 20% in patients without diverticulum. There were no excessive post sphinterotomy bleeding in patients with diverticulum.

Conclusion

Prevalence of duodenal diverticulum in our hospital is comparable with other studies. In our study it is more commonly seen in males more than 50 years. Duodenal diverticulum is more prevalent in Chinese patients. In patients with diverticulum, cannulation of the ampulla was more difficult compared to those without diverticulum. All patients had common bile duct stones secondary to gall stones. Potential mechanism would include altered motility of common bile duct or Ampulla of Vater, mechanical obstruction, and bacterial overgrowth either as primary or secondary.

Duodenal Diverticulum Found During ERCP – Hospital Alor Setar Experience

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Objectives

To determine the incidence of duodenal diverticulum found during ERCP.
To describe the types of duodenal diverticulum in relation to its papilla.
To identify the complication rates during ERCP in the presence of duodenal diverticulum.

Materials and Methods

ERCP findings of 431 surgical patients were retrospectively reviewed during a two year period from January 2000 till December 2001. Data such as age, sex, race and ERCP findings of the common bile duct, common hepatic duct, intrahepatic duct, gall bladder, ampulla and duodenum with its associated complications and interventions were analysed.

Results

Duodenal diverticulum is found in 8% of the patients with a female preponderance rate. Occurrence of duodenal diverticulum increases with age. Three types of duodenal diverticulum were described and it depends on the location of the papilla in relation to the diverticulum. Cholelithiasis was found in 40% of the patients and choledocholithiasis; in 14% of the patients. 8.5% of the patients have a combination of cholelithiasis and choledocholithiasis.

Conclusion

The incidence of duodenal diverticulum was incidentally found during ERCP. Three types of duodenal diverticulum found during ERCP are papilla inside the diverticulum, at the border of the diverticulum or outside the diverticulum. The difficulty in cannulating during ERCP is due to the anatomical structure of the papilla which led to stenosis and stone formation.

Peginterferon Alfa-2a(Pegasys) Plus Ribavirin in the Treatment of Chronic Hepatitis C: A Preliminary Report of Local Experience

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Objectives

To assess the efficacy and safety of Peginterferon (PegIFN) alfa-2a plus ribavirin in patients with Chronic Hepatitis C (CHC) treated locally.

Materials and Methods

All patients had Hepatitis C Virus (HCV) RNA detectable in sera by PCR. These included naïve patients and those with previously failed treatment with PegIFN alfa-2b plus ribavirin. Majority of patients had liver biopsy done which showed features consistent with chronic hepatitis with or without fibrosis. All patients had persistently raised serum alanine aminotransferase (ALT). Patients with decompensated liver cirrhosis were excluded. Quantitative HCVRNA by PCR were measured on several occasions : before starting treatment, during treatment at 12 weeks and end of treatment as well as 24 weeks after completed treatment. All patients received PegIFN alfa-2a subcutaneously at a dose of 180ug weekly plus oral ribavirin 1-1.2g/day for 24 weeks in the case of genotype (G) 2 or 3 and 48 weeks in the case of genotype 1. Early viral response (EVR) was defined as > 2 log decrease or negative HCVRNA at 12 weeks of therapy. End of Treatment Response (ETR) was defined as negative HCVRNA at the end of treatment. Sustained Virological Response (SVR) was defined as undetectable HCVRNA 24 weeks after stopping therapy. EVR is a good predictor of SVR. Therapy was discontinued after 12 weeks if patients failed to achieve EVR and they were considered as non-responders (NR). For those with EVR, therapy was continued for a total of 48 weeks in genotype 1 and 24 weeks in genotype 2 or 3. All side-effects were recorded on follow up and the dose of PegIFN and ribavirin were adjusted if necessary.

Results

Fifteen patients received the combination therapy. Eight of these patients who completed at least 3 months of therapy were included in this study. There were 4 females and 4 males with a mean age of 47.3 years (range 17-57 years). Three Malaysians and 5 Indonesians with 7 Chinese and 1 Malay participated in this study. The mean pre treatment ALT level was 94.5U/l (40-242 U/l). All of them carried genotype 1a/1b. The mean pre treatment HCVRNA was $190.1x10^3$ IU/ml ($6.1x10^3$ -$500x10^3$ IU/ml). The mean HAI score was 6.6 (4-13) with biopsy proven fibrosis in 3 patients. The source of infection was transfusion-related in 3/8 (37.5%) and sporadic in 5/8 (62.5%). 4/8 (50%) were naïve patients and 4/8 (50%) had prior PegIFN alfa-2b plus ribavirin therapy. EVR was achieved in 5/8 (62.5%). Side-effects were tolerable in most patients which included anaemia, leucopenia, thrombocytopenia, fever, fatigue, headache, rigors, myalgia, anorexia, nausea, pruritus and rash.

Conclusion

Peginterferon alfa-2a (pegasys) plus ribavirin is an effective and safe therapy for Chronic Hepatitis C. The EVR rate of 62.5% in this study was comparable with other published international trials.

Peginterferon Alfa-2b(PegIntron) Plus Ribavirin in the Treatment of Chronic Hepatitis C: A Local Experience

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Objectives

To assess the efficacy and safety of Peginterferon (PegIFN) alfa-2b plus ribavirin in patients with Chronic Hepatitis C (CHC) treated locally.

Materials and Methods

All patients had Hepatitis C Virus (HCV)RNA detectable in serum by PCR. These included naïve patients and those with previously failed treatment with standard interferon alfa-2b plus ribavirin. Majority of patients had liver biopsy done which was consistent with chronic hepatitis with or without fibrosis. All patients had persistently raised serum alanine aminotransferase (ALT). Patients with decompensated liver cirrhosis were excluded. Quantitative HCVRNA by PCR were measured on few occasions : before starting treatment, during treatment at 12 weeks and end of treatment as well as 24 weeks after completed treatment. All patients received PegIFN alfa-2b subcutaneously at a dose of 1.5ug/kg weekly plus oral ribavirin 1-1.2g/day for 24 weeks in the case of genotype(G) 2 or 3 and 48 weeks in the case of genotype 1. Early viral response(EVR) was defined as > 2 log decrease or negative HCVRNA at 12 weeks of therapy. End of Treatment Response (ETR) was defined as negative HCVRNA at the end of treatment. Sustained Virological Response (SVR) was defined as undetectable HCVRNA 24 weeks after stopping therapy. Therapy was discontinued after 12 weeks if patients failed to achieve EVR and they were considered as non-responders (NR). For those showing EVR, therapy was continued for a total of 48 weeks in genotype 1 and 24 weeks in genotype 2 or 3. All side-effects were recorded on follow up and the dose of PegIFN and ribavirin were adjusted if necessary.

Results

Thirty-three patients received the combination therapy. There were 5 defaulters and 1 patient who stopped treatment prematurely due to side-effect of the drugs. Twenty-seven patients completed the treatment with only 21 patients accessible for analysis as the remaining 6 patients are still awaiting HCVRNA testing at 24 weeks post-treatment. There were 13 females and 8 males with a mean age of 52 years. Fourteen Malaysian, 6 Indonesian and 1 Japanese patients were involved in this study. The mean pre treatment ALT level was 129.9U/l (32-371.8 U/l). HCV genotype distribution were as follows:3 G1a (14%), 11 G1b (52%), 2 G2a/2c(10%),5 G3a(24%). The mean pre treatment HCVRNA was 561.2x103 IU/ml ($0.9x10^3$ -$2,780x10^3$ IU/ml). The mean HAI score was 6.3(1-13) with biopsy proven fibrosis in 6

patients. The source of infection was transfusion-related in 9/21 (42.9%) and sporadic in 12/21 (57.1%). Fifteen (71.4%) were naïve patients and 6 (28.6%) had prior standard interferon alfa-2b plus ribavirin therapy. EVR was achieved in 15/21 (71.4%) with ETR in 14/21 (66.7%) and SVR in 9/21 (42.9%). 7/21 (33.3%) were non-responders and 5/21 (23.8%) were relapsers. The SVR rate was 5/14 (35.7%) for G1a/1b and 4/7 (57.1%) for G2a/2c/3a. In naïve patients, overall SVR rate was increased to 7/15 (46.7%) with SVR rate of 3/9 (33.3%) for G1a/1b and 4/6 (66.7%) for G2a/2c/3a. Side-effects were tolerable in most patients with anaemia noted in 13/21 (61.9%), leucopenia in 18/21 (85.7%) and thrombocytopenia in 8/21 (38.1%). Average drop of haemoglobin, leucocyte and platelet count below lower limit of normal range was 1.6g/dl, 1.4 $x10^9$ /l and 78x 10^9 /l respectively. Other side-effects included fever (47.6%), rigor (33.3%), myalgia (47.6%), headache (57.1%), pruritus (14.3%), fatigue (38.1%), nausea (28.6%), rash (9.5%), alopecia (42.9%) and weight loss (19%).

Conclusion

Peginterferon alfa-2b(PegIntron) plus ribavirin is an effective and safe therapy for Chronic Hepatitis C. Overall SVR rate of 46.7% in this study was lower compared with 54% achieved in other international trials, and this could be due to the relatively lack of adherence in patients treated outside a research center.

Efficacy of Standardized Extract of Phyllanthus Niruri, EPN 797 in Inducing HBeAg Clearance and Seroconversion in the Immune Tolerant Phase of HBV Infection: Three Case Reports

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Summary

Immune tolerant phase of Human Hepatitis Virus (HBV) infection is characterized by the presence of HBeAg and high levels of serum HBV DNA but normal ALT. During this phase, there is a very low rate of spontaneous HBeAg clearance and treatment is usually ineffective in inducing seroconversion. We describe three cases where patients in immuno tolerant phase treated with the combination therapy of lamivudine 100mg and EPN 797 1500mg or monotherapy with EPN 797 1500 mg alone for a duration of treatment ranged from three to seven months, had achieved HBeAg clearance in all three cases and seroconversion in two cases. Throughout the treatment period, these three patients had normal ALT level. These three cases suggested that the use of EPN 797 alone or combination with lamivudine might be useful in treating patient in immuno tolerant phase, in which drug treatment is generally thought to be ineffective.

Efficacy of Standardized Extract of Phyllanthus Niruri, EPN 797 in Inducing HBeAg Clearance and Seroconversion HBV Infection: Three Case Reports

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Summary

Active viral replication in hepatocytes is indicated by the presence of hepatitis B e antigen (HBeAg) in serum. HBeAg is thus a surrogate marker for the presence of hepatitis B virus DNA. There are recent data that show the relationship between the risk of developing hepatocellular carcinoma (HCC) with the activity of the virus. There is a markedly increased risk of developing HCC in those individuals with chronic hepatitis B who are also e-antigen positive. We describe three cases where patients with positivity of HBeAG treated with the combination therapy of lamivudine 100mg and EPN 797 1500mg or monotherapy with EPN 797 1500 mg alone for a duration of treatment ranged from 3 to 7 months, had achieved HBeAg clearance in all three cases and seroconversion in 2 cases. Throughout the treatment period, these three patients had normal ALT level. These three cases suggested that the use of EPN 797 alone or combination with lamivudine might be useful in inducing HBeAg clearance and seroconversion that could possibly reduce the risk of developing hepatocellular carcinoma (HCC).

Mucinous Adenocarcinoma of the Gallbladder Presenting with Empyema and Cholecystoduodenal Fistula – A Case Report

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Summary

Carcinoma of the gallbladder is a rare malignancy and cholelithiasis exists in most of the patients. Preoperative diagnosis is difficult because the clinical manifestations are nonspecific and often indistinguishable from those of acute or chronic cholecystitis. Histologically most gallbladder tumors are adenocarcinomas with mucinous adenocarcinoma being an extremely rare variant. We report a case of an elderly male who presented with features suggestive of empyema of the gallbladder. An emergency laparatomy revealed an empyema of the gallbladder with patchy areas of necrosis. There were no gallstones present. There was a fistulous communication between the neck of the gallbladder and the third part of the duodenum. Histopathological examination confirmed the diagnosis of mucinous adenocarcinoma. The rare association of mucinous carcinoma and gallbladder empyema with cholecystoduodenal fistula is discussed with a brief literature review.

KeyWords: Gallbladder carcinoma, Mucinous adenocarcinoma

Cholecystectomy Preference Amongst Hospital Staff

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Introduction

Laparoscopic cholecystectomy has been an available option for about a decade. It is associated with less morbidity, less scarring but increased costs and a very marginal increased incidence of bile duct injury when compared to open cholecystectomy. A study was undertaken to determine cholecystectomy preferences amongst hospital staff.

Materials and Methods

Design: Survey using self administered questionnaire. Setting: Tertiary Referral Centre. Subjects: Hospital Staff.

Results

Of 150 questionnaires distributed, 104 (69.3%) were returned by 69 (66.3%) females and 34 (32.7%) males, (gender not stated -1). The majority, 84 (83.4%) were aged less than 40. They consisted of 49 (47.1%)nurses, 42 (40.4%) medical officers and 11 (10.6%) medical assistants. Of these 104, 59 (56.7%) had experienced working in the operating room and 50 (48.1%), 15 (14.4%) and 62 (59.6%) had witnessed the procedures of open, mini (small incision) and laparoscopic cholecystecotmy respectively. Cholecystecomy preference was found to be 83.7% (87), 2.9% (3) and 1.9% (2) for laparoscopic, mini and open cholecystecomy respectively with 11.5% (12) patients being uncertain of their preference. The proportions of subjects who stated they were willing to pay 300%, 200%, 150%, 125% and 100% the cost of an open cholecystectomy for a laparosopic cholecystectomy were 10.6%, 14.4%, 25.0%, 17.3% and 25% respectively.

Discussion and Conclusion

Although only 56.7% had operating room work experience and less than 60% had witnessed the different types of cholecystectomy, the preference of the subjects in the study was overwhelming in favour of laparoscopic cholecystectomy (83.7%). This is probably because of the good results rather than from scrutiny of the intricate technical details of the different operations.

Hospital Based Hepatitis B Database – Preliminary Results

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Background and Aims

Hepatitis B remains an important health problem in Malaysia. We are developing a database to capture vital information among hepatitis B patients in Hospital Kuala Lumpur. This database will enable us to study the clinical characteristics and problems of local patients as well as to facilitate future research.

Materials and Methods

We collected bio-clinical data, utilizing a self designed comprehensive data capture form, during outpatients' visits and we reviewed all available clinical records retrospectively. Inclusion criteria were patients with HBsAg positive with follow up more than 6 months. This on-going database collection began on 1st October 2003.

Results

To date 450 patients met the eligibility criteria but at the moment only 294 patients had complete data suitable for analysis. The mean age of HBsAg was first detected was 32 ± 11.9 (range of 12 -70) years and 92.2% patients were below 50 years of age. At diagnosis 64.6% of patients had anti-HBeAb positive and 35.7% had HBeAg positive. A total of 25.9% of patients had positive first degree family history of hepatitis B infection and 6.3% of this cohort had documented risk of parental transmission. A total of 49.7% of patients were diagnosed during routine health screening. Only 3.4% of patients presented with acute hepatitis and 0.7% of patients had presented with complications related to liver cirrhosis. Further 45.9% of this cohort was first diagnosed after blood donation, whereby 27.4% of this group had a positive first degree family history of hepatitis B infection. After a follow up of 74.4 ± 55.3 (range: 7 – 254) months, 74.5% of patients had the profile "HBeAg negative & anti-HBeAb positive" and 2.7% of patients were confirmed cirrhotic. A total 39 patients or 35.2% of HBeAg positive patients seroconverted during follow up, 74.4% of this group had spontaneous seroconvertion and 25.6% received antiviral treatment. The duration of documented seroconversion was 2 -168 months from the diagnostic date of infection and 76.5% had acute hepatitic illness with 1% had decompensation of liver function during seroconversion.

Conclusion

Our preliminary results reveals that most patients (92.2%) were diagnosed below 50 years of age and the majority (64.6%) were anti-HBeAb positive at diagnosis. Analysis of this cohort revealed significant numbers of patients were detected first time for hepatitis B infection during blood donation activity despite 27.4% of patients being aware of a first degree relative with hepatitis B infection. Only more than a third of HBeAg positive patients seroconverted during follow up with a quarter of them receiving antiviral therapy, and majority of them suffered from acute hepatitic illness with 1% risk of decompensation during seroconversion. We propose to continue and complete our database to expand our knowledge on Hepatitis B.

Postoperative Analgesic Efficacy with Bupivacaine Infiltration in Needlescopic Cholecystectomy

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Background

Since its introduction in the early 1990s, laparoscopic cholecystectomy has become the standard operation for patients with gallstone disease. Now needlescopic cholecystectomy (the technique that reduces the keyhole-type wound to a needlehole-type wound), has taken patient care a step beyond laparoscopy. In our center it has been standard practice for both laparoscopic and needlescopic choelcystectomy to employ local wound infiltration of bupivacaine in order to reduce postoperative pain.

Materials and Methods

To assess the analgesic effects of local wound infiltration with 10ml of 0.5% bupivacaine in reducing post-operative pain following needlescopic cholecystectomy. In terms of pain relief using pain scores, time to first analgesic request, and supplementary analgesic consumption as compared with control.

Methodology

This was a prospective, randomized, placebo-controlled, double-blinded study. All patients with ASA physical status 1, 11, and 111 scheduled for needlescopic cholecystectomy in Hospital Universiti Kebangsaan Malaysia from July 2003 to April 2004 were included in the study. They were randomized to two groups – one receiving local infiltration with bupivacaine and the other with normal saline.

Results

A total of 56 patients were involved in this study and the majority of patients were females 62% (35). The most frequent age group did not differ significantly between the males and the females. There was no significant reduction in the mean pain scores in the group that was randomized to receive bupivacaine local infiltration. The difference in between the two groups was statistically not significant (p value = 0.079). The average time to the first analgesic request was the same in both groups, and the mean difference between the two groups was statistically not significant (p value = 0.58). The mean amount of analgesic requirements between the two groups was also not statistically significant (p value = 0.22)

Conclusion

Local wound infiltration with bupivacaine is a widely employed method of minimizing postoperative pain however, we were unable to demonstrate a benefit of employing this technique in patients undergoing needlescopic cholecystectomies.

Common Bile Duct Stone Extraction at ERCP: Our Experience in Hospital Universiti Kebangsaan Malaysia

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Introduction

Endoscopic sphincterotomy with stone extraction during ERCP has been the standard procedure for the management of common bile duct (CBD) stones.

Objective

To review our experience in the extraction of CBD stones during ERCP in our center.

Materials and Methods

All cases of CBD stones managed by ERCP between January 2000 and April 2004 were retrospectively reviewed. The data was collected from the ERCP reports.

Results

A total of 261 patients were confirmed to have CBD stones at ERCP. The female to male ratio was 1.2 : 1. Two hundred and eleven patients (80.8%) were more than 40 years of age. One hundred and fourteen patients had single stone while the other 147 had multiple stones. Successful extraction of stones during the first attempt of ERCP was achieved in 197 patients (75.5%). 44 (16.8%) patients required 2 or more attempts of ERCP before complete removal of CBD stones. The overall total success rate of complete extraction of CBD stones in our center was 92.3% (n: 231). There was no ERCP related mortality and the morbidity rate was minimal. Twenty patients (7.7%) required open or laparoscopic exploration for CBD stone clearance. The factors that influence the failure of extraction of CBD stones during ERCP include junior endoscopists, ascending cholangitis with sepsis, patient restlessness, bleeding, multiple stones and single large stone.

Conclusion

In our population, CBD stones were more prevalent in patients above 40 years of age. Our overall success rate of endoscopic extraction of CBD stones was 92.3%.

Risk Factors for Post ERCP Pancreatitis

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Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) has revolutionized the diagnosis and management of hepatobiliary and pancreatic diseases. Complication occurs in about 10% of patients undergoing ERCP and post ERCP pancreatitis incidence is reported to vary between 1.2% to 5.4%.

Objective

To review the prevalence of post ERCP pancreatitis and identify the independent risk factors.

Materials and Methods

All cases of ERCP performed in Hospital Universiti Kebangsaan Malaysia (HUKM) from 1st January 1999 to 31st December 2003 were retrospectively reviewed. Post ERCP pancreatitis was defined as those who developed upper abdominal pain with serum amylase of more than 1000 IU/L while a serum amylase of 300 to 1000 IU/L were termed as hyperamylasemia. Data was collected from the ERCP reports and the patients' case notes. Statistical analysis was performed using SSPS version 11. The risk factors studied were age, sex, choledocholethiasis, pancreatic duct cannulation, history of pancreatitis, raised liver enzymes, ascending cholangitis, previous ERCP, sphincterotomy and experience of the endoscopist. The binary logistic regression analysis was used to identify the independent risk factors for post ERCP pancreatitis and hyperamylasemia.

Results

There was 1253 ERCP procedures performed during the study period and 1004 were included. There were 42 (4.1%) cases of post ERCP pancreatitis. On analysis however, none of the independent risk factors were significant statistically. There were 83 (8.3%) cases of hyperamylasemia. The statistically significant independent risk factors for development of post ERCP hyperamylasemia were female, presence of choledocholithiasis, younger age (< 50) and pancreatic duct cannulation.

Conclusion

The rate of post ERCP pancreatitis in our center is comparable to other centers however we were not able to identify any significant risk factors.

Knowledge, Attitude and Practice Associated with the Risk of Hepatitis B Virus Infection Among Medical Students and Staff of the Faculty of Medicine and Health Sciences of Universiti Putra Malaysia

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Background

Hepatitis B virus (HBV) is one of the most easily transmitted blood borne pathogen, putting medical students and staff at high risk for contracting the virus. A cross-sectional study was carried out among the medical students and staff of the Faculty of Medicine and Health Sciences of Universiti Putra Malaysia to determine their knowledge, attitude and practice associated with the risk of hepatitis B virus infection.

Materials and Methods

Self-administered pre-tested questionnaires were given, of which 192 medical students and 68 staff had responded.

Results

Eighty percent of medical students and 89.7% of staff knew the various universal precautions well while 85.4% of medical students and 77.9% of staff were aware of the needle stick injury protocol in their study/work place. More staff than medical students knew that HBV could also be transmitted via sharing personal items. Forty-one percent of medical students and 48.5% of staff knew that a HBV infected person may recover fully. About 32% of medical students and 41.2% of staff admitted that they were unsure of the treatments available for HBV infected patients. Almost all medical students and staff felt that screening for HBV status before entering medical school should be made compulsory. Thirty-five percent of medical students and 33.8% staff felt that infected medical students/staff should be allowed to carry out invasive procedures. Seventy-nine percent of medical students and 77.9% of staff wore gloves while carrying out lab work or when in contact with patients. Almost all the medical students as compared to only 66.2% of staff were vaccinated against hepatitis B.

Conclusion

There is room for improvement on the knowledge, attitude and practice associated with the risk of HBV infection.

Association of Diabetes Mellitus and Hepatitis C Virus Infection and its Comparison with Hepatitis B Virus Infection

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Summary

While patients with liver disease are known to have a higher prevalence of glucose intolerance, preliminary studies suggest that hepatitis C virus (HCV) infection may be an additional risk factor for the development of diabetes mellitus. Diabetes mellitus effects approximately 30 million people worldwide, is usually irreversible and although patients can have a reasonably normal lifestyle, its late complications result in reduced life expectancy and considerable uptake of health resources. It has been observed that patients with chronic hepatitis C in Egypt were three times more likely to develop DM than HCV seronegative patients. A study of high prevalence of diabetes mellitus among adult beta thalassaemic patients with chronic hepatitis C concluded that the frequency of diabetes in adult thalassaemic patients is significantly increased by HCV infection, even in the absence of cirrhosis. Another study conducted in Pakistan of HCV viraemia in clinical and biochemical perspective found that HCV viraemic persons had increased association with chronic renal failure and diabetes mellitus. The presented study was aimed to study and determine a relationship between the relative proportion of diabetes mellitus in patients suffering from HCV infection.

Materials and Methods

This Cross Sectional Study was designed and conducted at Hepatitis Clinic Services Hospital affiliated with Post Graduate Medical Institute, Lahore, Pakistan. Approved by "Advanced Studies and Research Board" of Punjab university, Pakistan. Diagnosis of Hepatitis C and Hepatitis B was done by Elisa, Diagnosis of dibetes was assigned after fulfilling the American Diabetic Association Criteria.

Results

A total of 318 patients were registered, out of which 269 cases fulfilled the inclusion criteria, 169 Hepatitis C infected and 98 Hepatitis B infected cases. 11.83% Hepatitis C infected cases were diagnosed as diabetics while 5.10% Hepatitis B infected cases were diagnosed as diabetics.

Conclusion

This study suggests the presence of Association and relationship of Diabetes Mellitus and Hepatitis C virus infection when compared with Hepatitis B virus infection".

Non-Alcoholic Fatty Liver Disease (NAFLD): A Clinical, Biomechanical and Histopathological Study in Malaysian Patients

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Background and Objectives

Non-alcoholic fatty liver disease (NAFLD) appears to be increasing rapidly in the Asian-Pacific region. However, there has been a paucity of studies on Asian patients and no studies hitherto on Malaysian patients. The aims of this study are: 1). investigate the demographic, anthropometric and biochemical characteristics of patients with NAFLD in Malaysia and 2). Study the association of NAFLD with insulin resistance and abnormalities of glucose tolerance.

Materials and Methods

Patient with persistently raised liver enzymes, particularly ALT and/or fatty liver on ultrasonography with biochemical exclusion of other liver disorders were recruited. Demographic, anthropometric and biochemical data were recorded for all patients. Insulin resistance was assessed using the HOMA score. A liver biopsy was performed in all cases for grading (for steatohepatitis) and staging (for fibrosis) of NAFLD).

Results

Forty-five patients were recruited for the study. The mean age of subjects was 47.8 ± 11.7 years with female preponderance (male: female, 21.24). The mean BMI value was 27.4 with 73.3% being obese (n=33), 43.2% were diabetic (n=19) and 20.4% had impaired glucose tolerance (n=9). Biochemical studies revealed that 38 patients (84.4%) had elevated levels of either ALT or AST with 31 patients (70.5%) having raised total cholesterol levels and 51% (23/45) with raised triglyceride level. The mean HOMA value was 5.24. Forty-one of 42 patients (97.6%) were noted to be insulin resistant. Twenty-eight liver biopsy samples were available for review: Benign steatosis, non-alcholic steatohepatitis and cirrhosis histologically were seen in 5 (17.9%), 20 (71.4%) and 3 patients (10.7%) respectively.

Conclusion

All patients had biopsy changes compatible with NAFLD and the full spectrum of histologic changes associated with NAFLD was seen; including 3 patients (10.7%) with liver cirrhosis. Almost all patients (97.6%) were insulin resistant, with majority being obese and either diabetic or had impaired glucose tolerance.

An Audit on Colonoscopies Performed in the Kuala Lumpur Hospital

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Background

Kuala Lumpur Hospital, being Malaysia's largest tertiary referral hospital, has an endoscopy suite performing a variety of cases. Colonoscopy is one of the most common procedures undertaken.

Aim

To audit the colonoscopies performed in our hospital.

Materials and Methods

One hundred consecutive patients presenting for colonoscopy mainly from medical outpatients or medical wards were audited in March and April 2004. The gold standard was the American Society of Gastrointestinal Endoscopy's (ASGE) guidelines of 2000. Data was analysed using SPSS software (ver.12.0).

Results

Out of 100 patients, 47% were females and 53% were males. Chinese 42%, Malays 37%, Indians 20% and others 1%. Mean age 55.6 years (range 71,SD=14). Two caecal intubations failed. The common indications falling under ASGE guidelines were for screening or surveillance for colonic neoplasia in patients with previous polyps or cancer (19%), haematochezia (17%), significant diarrhoea (17%), unexplained iron deficiency anaemia (16%), abnormalities on radiological examination (3%), assessment of colitis activity (3%), treatment of vascular malformations (2%) and stool occult blood positive (1%). Nine patients had polypectomies. Failure to meet ASGE guidelines were seen in 20% and these were mainly for constipation (6%), abdominal pain (4%), weight loss (2%) and metastases (2%). 53% had normal colonoscopies, out of which 13% were in patients with indications falling outside the guidelines. The average waiting period for elective colonoscopy was 44.2 days(range 179, SD=39.3).

Conclusion

Complete colonoscopy was achieved in 98%. Eighty percent of colonoscopies conform to guidelines. Some remaining indications (chronic abdominal pain, irritable bowel syndrome) were still permissible under ASGE guidelines in exceptional circumstances.

Telomerase Activity in Human Colorectal Cancer

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Introduction

Telomerase is a ribonucleoprotein enzyme that function in the elongation of telomere repeats TTAGGG at the end of chromosomes. Telomerase is believed to have potential as a tumor marker as it has been found to be active in nearly all tumours but low in all normal somatic tissues.

Materials and Methods

We have determined telomerase activity of 50 frozen tumour samples and matching normal colon tissues from colorectal cancer patients using the TRAPeze Telomerase Detection Kit (Serologicals Co.). The ladder of TRAP products with 6 base increments starting at 50 nucleotide were visualized with DNA Silver Staining kit.

Results

The results showed that 32 of 50 (64%) samples were positive for telomerase activity (using 1.0, 0.5 and 0.05 mg/ml protein). The telomerase activity shows significant correlation with degree of tumour differentiation (χ^2 = 14.507 ; $p<0.05$) and age of patients ($p<0.05$). Very weak telomerase activity were detected for the matched normal tissues taken from the same colorectal cancer patients.

Conclusion

Although more samples need to be analysed, telomerase activity may be an important biomarker in the diagnosis of colorectal cancer.

Carcinoma of the Rectum with Ocular Metastasis

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Summary

We present a case of a 32-year-old woman who after 10 months of abdomino-perineal resection and total mesorectal excision for a locally advanced mucinous adenocarcinoma of the rectum, presented with a local recurrence as well as metastases to the breast, spine, the left eye and orbit. Following surgery, due to patient's personal reasons, adjuvant chemo-radiation was not given. The patient died 2 months after, with disseminated cancer. To the best of the author's knowledge, ocular metastases in a patient with mucinous adenocarcinoma of the rectum has never been reported and therefore needs to be documented.

KeyWords: Mucinous adenocarcinoma of the rectum, ocular metastasis.

Mutational Analysis of APC Genes in Mutation Cluster Region (MCR) in Colorectal Cancer

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Introduction

The age-standardized incidence rate for colorectal cancer (CRC) in Malaysia is 25.6. and 17.9 per 100,000 men and women respectively (National Cancer Registry, 2002). The adenomatous polyposis coli (APC) gene is the main tumor suppressor gene implicated in the development of CRC. Previous published data have shown that mutations of APC occurred in 80% of all CRCs. The vast majority of these mutations are insertions, deletions, and nonsense mutations that lead to frameshifts and/or premature stop codons in the resulting transcript. This results in a stable truncated APC protein without the carboxyl-terminus. A mutation cluster region exists within the 5' end of exon 15, between nucleotides 3000 and 4800 and represents approximately 60% of reported somatic mutations.

Materials and Methods

As the incidence rate of APC mutations in CRC's in Malaysia have yet to be determined, we examined 11 pairs of CRC tissues with apparently normal adjacent tissues for APC mutations in its mutation cluster region (MCR) from nt 3801 to nt 4576 [geneBankTM accession number: NM_000038]). Genomic DNA was isolated from CRC tissues, PCR performed followed by direct sequencing of PCR products.

Results

APC mutations were found in 4 out of 11 CRC tissues examined. 4 out of 5 mutations were point mutation at nt 3999 (4 cases), 4043 (4 cases), 4069 (4 cases), 4047 (3 cases), 4065 (3 cases), and 4074 (3 cases). The point mutation that occurred at 4096 in the other 4 samples generated a stop codon UGA. No APC gene mutations were observed in the remaining 6 CRC tissues. The results from APC gene analysis at the mutation cluster region were in accordance with immunohistochemical staining which showed that truncated APC was present in 23 /47 (49.9%) of CRC tissues.

Conclusion

Inactivating mutations of APC may play a causative role in colorectal carcinogenesis in Malaysia and further analysis with larger sample size will be required to support this finding.

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Dieulafoy's Lesion of the Rectum

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Summary

Dieulafoy's lesion of the rectum is an uncommon but potentially life threatening cause of lower gastrointestinal haemorrhage. The condition is being increasingly reported as afflicting the lower gastrointestinal tract and we have recently managed two patients with chronic renal failure who presented with torrential rectal bleeding secondary to a Dieulafoy's lesion. Diagnosis of rectal Dieulafoys is best achieved during proctoscopic and endoscopic visualization and in cases where there is profuse and torrential haemorrhage, angiography may help clinch the diagnosis. There are a few endoscopic treatment options available, all of which have varying degree of success even though operative peranal intervention for accessible lesions in the lower rectum can control the bleed in an expedient manner. It is imperative for the attending surgeon to have a high degree of suspicion in cases of profuse lower gastrointestinal haemorrhage and attempt endoscopic visualization of the bleeding source, which may be lying in an accessible location for prompt surgical control. The association of rectal Dieulafoy's and chronic renal failure is further elaborated upon in this report.

Attitudes Towards Colorectal Cancer Screening

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Introduction

Colorectal cancer screening is increasingly advocated. However, it's acceptance or otherwise has not been widely addressed. A study was undertaken to evaluate the acceptance of colorectal cancer screening

Materials and Methods

Design: Interview utilizing structured questionnaire. Issues Evaluated: Willingness to(i)undergo rectal examination,(ii)collect faeces for haemoccult testing,(iii)collect water near faeces for occult blood testing and(iv)undergo colonoscopy. The exposure to colorectal cancer such as having relatives and/or friends with the disease, experience of a a previous endoscopy, and willingness to pay for the screening was also evaluated.

Results

Of the 30 individuals included,13.3% (4) had a relative and 23.3% (7) had a friend who had suffered colorectal cancer, and 3.3% (1) had a friend with metastatic colorectal cancer. A colostomy was present in a relative or friend of 3.3% and 6.6% subjects respectively. Apart from the willingness to undergo a once only rectal examination (46.7%) less than 25% were willing to collect faeces for haemoccult testing, collect water near faeces, or undergo colonoscopy. Only 23.3% stated that they were willing to pay for the costs of colorectal cancer screening.

Discussion and Conclusion

Although a relatively substantial proportion had relatives (13.3%) and friends (23.3%) who had suffered colorectal cancer, willingness to undergo colorectal cancer screening was not widespread. This may be due to reluctance to collect faeces or endure colonoscopy. Perhaps acceptance can be enhanced by avoiding the collection of faeces and the discomfort of colonoscopy by utilizing virtual colonoscopy for screening of colorectal cancer.

Repeat Colonoscopy: Spectrum, Outcome and Efficacy

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Introduction

A study was undertaken to determine the spectrum of indications, findings and efficacy of repeat colonoscopy.

Materials and Methods

Design: database review. Period:42 months. Inclusion: all undergoing colonoscopy within 6 months of previous colonoscopy.

Results

Of 3114 colonoscopies, 207 (6.6%)were repeat procedures and were performed on 157 patients. They were undertaken because of(A)inadequate previous bowel preparation in 77 (37.2%), (B) reassessment of previously seen and/or treated lesions in 107 (51.7%), (C) Reassessment of previously normal colonoscopy in view of new clinical features in 7 (3.4%) and (D) previously incomplete examination not due to inadequate bowel preparation in 16 (7.7%). Of the 77 performed because of previously inadequate bowel preparation (A), there were abnormalities in 16 (20.8%) including cancers in 3, polyps in 3, ulcers in 5 and inflammation in 3. Of the 107 colonoscopies undertaken for reassement of previously seen or treated lesions (B), 94 (87.9%) were performed because of ongoing clinical features (Bi) and 13 (12.1%) for new clinical features (Bii). Of the 94 (Bi), findings similar to previous lesions or normal findings were found in 80 (85.1%) and new findings unrelated to previous lesions were found in 14 (14.9%). These 14 included cancer in 1, polyps in 4, ulcers in 2 and inflammation in 1. Of the 13, performed in patients with previously seen and/or treated lesions, because of new clinical features (Bii), 3 (23.0%) were normal and 10 (76.9%) were abnormal. Of the 7 repeats because of new worrying symptoms (C), 5 (71.4%) were normal and 2 (28.6%) abnormal showing a polyp and proctocolitis.

Discussion and Conclusion

Abnormalities were found in 20.8% of colonoscopies repeated because of inadequate bowel prep. New abnormalities were found in 14.9% of examinations performed to assess previously seen or treated lesions and 76.9% of those performed in patients with previously seen or treated lesions who had new symptoms. Repeat colonoscopy is efficacious and should be performed when indicated.

Complicated Diverticular Disease

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Introduction

Complicated diverticular disease of the colon is a very common problem with the prevalence increasing with age, varying from < 10% in those < than 40 years and 50-60% of patients > 80 years. We review a total of 9 cases of complicated diverticular disease needing surgery that was managed in Hospital Seremban between the year 2000 and 2003.

Results

There were a total of 9 patients and the male female ratio was 6:3. The median age was 59 years. Six patients presented with perforated diverticular disease with peritonitis, 2 with bleeding diverticular disease and one vesico-sigmoid fistula. There was 0% mortality rate with our patients.

Conclusion

Though diverticular disease of the colon is fairly common with 120 cases diagnosed with colonoscope, there were only 10 patients that developed complications requiring surgery. As surgery involves the elderly patient who is either septic due to peritonitis or unstable due hypovolemia, early diagnosis and adequate resuscitation is absolutely essential in assuring favourable results. When surgery was offered it was often a resection of the affected colon and or diverting stoma.

A Report of Colorectal Carcinoid Tumour

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Summary

Carcinoid tumour is a slowly developing neuroendocrine tumour. The incidence rate is 1.5/100,000 populations and they make up 1% of colorectal carcinomas. It can be localized in the appendix, small bowel, colon, rectum and bronchi. Here we present our experience with two patients with rectal carcinoid tumours.

Case 1: A 74-year-old Malay patient presented to our clinic with history of hematochezia associated with constitutional symptoms. A colonoscope done showed a large proliferative growth at the mid rectum which on histological examination was unremarkable. An anterior resection was done and the histological report was Carcinoid tumour. Immunohistochemistry was positive to chromogranin and cytokeratin. CT scan of the abdomen did not show any distant metastasis.

Case 2: a 79 year old Chinese lady was referred to with diarrhoea and loss of weight. Colonoscope examination revealed a sessile 1.5cm polyp in the mid rectum, which was snared off. The histopathological report came back as carcinoid tumour of the rectum. Repeat colonoscope showed an ulcer in the mid rectum. Low Anterior resection was offered to the patient.

Though carcinoid tumours of the rectum are a rare entity, it must be entertainment in all patients with rectal growths or polyp. The diagnosis and management of carcinoid tumour of the colon and rectum are discussed in this paper.

A Case Report of Emergency Total Colectomy for PR Bleeding Secondary to Severe Ulcerative Colitis: Seberang Jaya Hospital Experience

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Summary

Emergency total colectomy is common for failed medical management of ulcerative colitis complications such as toxic megacolon and intractable diarrhoea. However, massive bleeding requiring total colectomy is common.

We are reporting an emergency total colectomy for torrential bleeding secondary to ulcerative colitis.

A 19-year-old Chinese male G.B.H, presented to our unit with massive intractable bloody diarrhea. Colonoscopy showed features of severe ulcerative colitis. Random biopsies were taken for histopathological examination. He was initially managed conservatively with Pentasa 1gm tds and IV Hydrocortisone 100mg qid and nil orally. Despite this, he still had torrential per rectal bleeding after 10 days of conservative treatment. A decision to operate was made on the basis of failed medical treatment and torrential intractable per rectal bleeding.

He underwent a total colectomy and ileostomy with a further plan of ileo-J pouch formation at a later date. Post-operatively the bloody diarrhoea stopped and he was discharged home well. Gross and HPE of the specimen confirmed severe ulcerative colitis involving the entire colon

Risk Factors for Low Rectal Anastomosis Leakage – Hospital Universiti Kebangsaan Malaysia Experience

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Background

Colorectal cancer is the third commonest cause of death in Malaysia with rectal cancer alone constituting about 50% of colorectal deaths as stated in the national census. Colorectal cancer surgery has become a common procedure performed in our hospitals. The most important surgical complication following colorectal resection is symptomatic anastomotic leakage, which is associated with mortality rate of 6 – 22%. There is also significant morbidity associated with leak.

Aim

The aim of this retrospective study was to evaluate the risk factors for clinical anastomotic leakage after anterior and low anterior resection for rectal cancer.

Materials and Methods

A retrospective analysis was performed on 64 patients with rectal carcinoma who were operated from November 2001 till August 2003 in our center. Ten patients who had anastomotic leakage were analyzed for the risk factors. Factors analyzed were age, sex, type of surgery performed, ASA classification, preoperative albumin level, preoperative adjuvant therapy and distance of tumour from anal verge.

Results

The preoperative variables that have been shown to have significant correlation with anastomotic leakage include low preoperative albumin, types of surgery performed, distance of tumour from anal verge and the use of neoadjuvant radiotherapy. However, this review failed to demonstrate any statistically significant relationship between the factors above and the leak rate except for tumour distance from the anal verge ($p=0.03$). The group of patients with diverting stoma showed lower leak rate however, this was statistically not significant.

Conclusion

Distance of tumour from anal verge is a significant factor of anastomotic leakage. These patients undergoing low rectal anastomosis should be considered for temporary diversion stoma.

Anal Eroticism with Aerosol Spray Cannisters – A Report of Two Cases

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Summary

Foreign bodies found in the rectum and anus seems to be limited only by the human imagination. In all societies, individuals have introduced foreign bodies into the rectum, penis and vagina, for sexual gratification or for some unusual psychological reasons. When the object eventually either causes pain or becomes irretrievable, the patient presents to the emergency department.

We present two separate cases of such predicament. Both were male patients who presented with a similar history - an aerosol spray cannister that accidentally got lodged in the rectum. In one patient the aerosol spray can was successfully retrieved with a rigid sigmoidoscopy and grasper while in the other a laparotomy had to be resorted to.

Awareness, Attitude and Knowledge Towards Prevention and Screening of Colorectal Cancer Among Patients Attending the UPM Physician Clinic in Hospital Kuala Lumpur

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Background

Colorectal cancer is the third commonest form of cancer mortality in Malaysia. Screening for colorectal cancer in the general population with normal risk has not been adapted into the routine practice in Malaysia due to various factors like cost-effectiveness, inadequate local data to support the effectiveness, acceptability and presence of other more important health conditions that need more immediate attention.

Objectives

To determine the level of awareness, knowledge, attitude and acceptability of colorectal cancer prevention and the various modalities of screening procedure.

Materials and Methods

One hundred and twelve patients that attended the UPM physician clinic in Hospital Kuala Lumpur between 5th and 22nd April 2004 or their relatives were interviewed with a pre-tested questionnaire.

Result

Only 35 respondents (31.3%) indicated that they knew what colorectal cancer is. Among them, 14 respondents (40%) obtained the information from health clinic and hospital, 11 (31.4%) from their own relatives, 8 (22.9%) from their friends, 25 (71.4%) from mass media and 4 (11.4%) from school / college / university / workplace. Only 19 patients were aware of the availability of colorectal cancer preventive measures. There was a significant relationship between knowledge and awareness of colorectal cancer prevention with educational level ($p<0.05$). Factors that patients believed to increase the risk of colorectal cancer were smoking (56.3%), increasing body fat (51.8%), history of rectal adenoma (6.3%), family history of colorectal cancer (27.7%), age above 50 (32.1%), inflammatory bowel disease (4.5%), adenomatous polyps (1.8%), diet from animal sources (2.7%) and physical inactivity (8.9%). There were

38 patients who were aware of a proposed colorectal cancer screening programme. Although only few knew about the screening programme before the interview, 102 (91.1%) of them would agree to undergo screening if it was available. The preferred screening procedures were yearly FOBT (64.3%), 10 yearly full colonoscopy (28.6%), annual digital per rectal examination (3.6%), 3 to 5 yearly sigmoidscopy (1.8%), 3 to 5 yearly double contrast barium enema (1.8%).

Conclusion

There is a need to further educate the public on the availability of colorectal prevention measures.

Crohn's Disease in Adults: Observations in a Multiracial Asian Population

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Background

Although Crohn's disease (CD) is an uncommon disease in Asia, it appears to be increasing in recent years, in our part of the world. This increase appears to be more amongst some ethnic groups compared to others. The aims of this study is firstly to determine the demography and clinical presentation of CD and secondly to determine any racial differences amongst our multiracial Asian population in Malaysia.

Materials and Methods

Patients and with CD who were seen in 2000-2003 in the University of Malaya Medical Centre (UMMC) were included into the study. Prevalence of disease was calculated for the group as a whole and by race with hospital admissions per ethnic group as the denominator.

Results

Thirty-four patients were diagnosed to have CD. Basic demographic data of patients; Male: Female 17:17; mean age 29.1 years (± 13.5); ethic group: Malay 5 (14.7%), Chinese 12 (35.3%) and Indian 17 (50%). Seven (20%) patients were smokers and none had a family history of CD. The commonest presenting complaints were diarrhoea 29 (85.3%), abdominal pain 25 (73.5%), rectal bleed 17 (50%) and weight loss 15 (44%). Thirteen (38.2%) patients presented acutely with intestinal obstruction and diagnosis was made at surgery. The commonest sites of involvement were ileocolonic (53%), colon only 24% and terminal ileum only (15%). Stricturing complications were seen in 17 (50%) and penetrating complications (fistula, abscess) in 19 (55.9%) patients. Sixteen (47.1%) of patients had undergone at least one operation.

The prevalence of CD was 41.7 overall, Indians - 28.9, Chinese - 7.0, and Malay - 5.8 per 100,000 admission per ethic group. The difference between Indians vs Malay and Chinese was highly significantly p=0.005; OR 5.00 (1.512, 18.33) and p=0.015; OR 4.13 (1.24, 15.13) respectively.

Conclusion

The clinical presentation of CD is similar to the western experience. Although, the overall prevalence is low, there appears to be a clear racial predominance among the Indians.

Appropriateness and Diagnostic Yield of Colonoscopy in a Tertiary Hospital in Malaysia

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Background and Objectives

Guidelines on appropriateness of endoscopy have been drawn up to guide clinicians as to the rational utilization of endoscopic procedures. Referrals for colonoscopy have increased dramatically in recent years and appropriateness of colonoscopy becomes therefore, a relevant and important issue. The aim of this study are firstly to determine the appropriateness of colonoscopies performed in the endoscopy unit of University Malaya Medical Centre (UMMC) using the guidelines from the American Society of Gastrointestinal Endoscopy (ASGE) 2000, and secondly to search for a relationship between appropriateness of colonoscopy and the presence of colorectal cancer (CRC) and other lesions.

Materials and Methods

Consecutive colonoscopies performed in UMMC, where an open access endoscopy system exists for doctors working within the hospital were included. Indications were judged "appropriate" or "inappropriate" using the ASGE criteria 2000. Referrals were categorized as from gastroenterologists, surgeon-endoscopists, primary care physicians and other specialists. Colonoscopic findings were recorded as positive or negative and the presence of CRC was specifically noted.

Results

Three hundred and eighty patients were enrolled. Two hundred and twenty (57.9%) were classified as appropriate, 49 (12.9%) as inappropriate and remaining 111 (29.2%) presented with conditions not categorizable by the ASGE criteria. Gastroenterologists had the highest rate of appropriate referrals (78.4%), followed by the surgeons-endoscopists (56.7%), primary care physicians (48.1%) and "others" (48%). The most common appropriate indication was unexplained haematochezia 79 cases (20.8%). The most common inappropriate indication was the inappropriately timed colonic cancer surveillance, 32 cases (8.4%). Chronic constipation, 36 cases (9.5%), was the most common "unlisted" indication. A positive finding was detected in 36.4% of cases with appropriate indications, 34.7% with inappropriate indications and 30.6% with unlisted indications. CRC was found in 36 patients. Multivariate analysis revealed that rectal bleeding and smoking were significantly independent positive predictive factors for CRC.

Conclusion

The percentage of appropriate referrals varied between doctor groups but was highest amongst gastroenterologists. However, the percentage of CRC was similar in patients with appropriate, inappropriate and unlisted indications. An appropriate indication did not result in a higher diagnostic yield of CRC.

Review of Operated Pediatric Intussusception Cases in Hospital USM from January 2000 - December 2003

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Aims

To review all operated cases of pediatric intussusception in view of clinical presentations, clinical findings, diagnosis and indications and complications of surgery.

Materials and Methods

Retrospective analysis of paediatric patients who underwent laparotomy for intussusception in HUSM from Jan 2000 to December 2003. Twenty-seven patients below 12 years old (21 boys and 6 girls were included. Clinical presentations, age, diagnosis, use of therapeutic reduction, decision for laparotomy, findings and complications were reviewed and analyzed.

Results

Twenty-four (89%)of patients presented with vomiting, 22 (81%) with PR bleeding and 14 (52%) with irritability or abdominal pain. Twenty (74%) found to have abdominal mass on palpation and 21 (78%) have red currant jelly stool on PR. USG was used to confirm diagnosis in 19 (70%) with 94.7% sensitivity and 10 (52%) proceeded with Ba reduction before laparotomy. Five (18%) underwent Ba examination on clinical suspicion (total Ba examination - 15 (55.5%)). Causes for deference to proceed to Ba examination were long history, long segment on USG and free fluid in the abdomen on USG. The most common findings intra-operatively were ileo-colic intussusception with 26 (96%) manually reduced, 1 needed resection and anastomosis. There were 3 (11%) incidence of re-laparotomy and 1 needing R hemicolectomy due to gangrenous bowel. Mortality were 2 (7.4%) and causes of death were overwhelming sepsis and multi-organ dysfunction. Long term complication was adhesion colic 3 (11%).

Conclusion

Intussusception in the most common cause of acute intestinal obstruction in infants and young children. Untreated, it is a potentially life-threatening condition. Laparotomy is indicated in cases of failed Ba reduction and is generally safe. Mortality is usually contributed by the condition of the patient on diagnosis.

Changing Trends in Endoscopic Findings in a Private Gastroenterological Center in Kuala Lumpur

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Introduction

With the effective detection and eradication of Helicobacter pylori, better understanding of the detriments of NSAIDS and Aspirin and effective acids suppressants, peptic ulcer disease is on the decline. This study is to evaluate the changes in the demographics pattern of gastrointestinal diseases over the past 14 years.

Materials and Methods

A comprehensive search of all available records of endoscopic findings was made from 1st January 1990 till 31st December 2003 and the endoscopic findings were reviewed.

Findings

Peptic ulcer disease and erosive oesophagitis were the two common endoscopic findings in our series. In 1990 till 1992, duodenal ulcers were the commonest endoscopic diagnosis followed by gastric ulcers then GERD. However, in 1993, GERD overshot peptic ulcer disease and remained the dominant diagnosis till today. From 1993 till 2001, there was a plateau in the number of cases of GERD with an average of 210 ± 47 cases seen per year. However there was an explosion in the number of cases in 2002 (471 cases) and 2003 (574 cases). Notably there has been a constant slow decline in the number of cases of duodenal and gastric ulcers over the years from 1992. Duodenal ulcers were always commoner than gastric ulcers. But from 1996 the difference in the number of cases was not tremendously great.

Conclusion

There is a major change in the demographic pattern of acid related diseases based on our study. There is a decline in both gastric and duodenal ulcers but there seems to be an explosion in the number cases with erosive oesophagitis. This is clearly in line with the better understanding of GERD and the widespread utility of the Los Angeles Classification for GERD.

Spontaneous Retroperitoneal Hematoma Secondary to Myeloproliferative Disorder Presenting as Acute Abdomen

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Summary

A elderly patient with acute abdomen, mimicking intestinal obstruction with peritonitis was presented to us. Intraoperatively, a huge retroperitoneal hematoma was found at the right side (zone II), extending across midline. In view of the nonexpanding, nonpulsatile nature of the retroperitoneal hematoma, no exploration or attempt evacuation of clot was done. Instead, a postoperative contrast CT-scan was done to exclude aneurysmal bleed. Hematologist consultation was obtained. He is currently on hematological management. Patient recovers and discharges without further bleeding.

Relaparotomy for Pseudomyxoma Peritonei

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Summary

Pseudomyxoma peritonei is an uncommon disease, characterized by the accumulation of extracellular gelatinous fluid collection and non invasive mucinous implant on the peritoneal surface and omentum. The recent development of immunohistochemistry and cross-sectional imaging has led to better understanding of the aetiology and the pathogenesis of this disease. We report a case of a 72-year old lady who had undergone a right hemicolectomy and local debulking procedure for a well-differentiated mucinous adenocarcinoma of the caecum four years before. A relaparotomy was indicated due to symptoms of abdominal compartment syndrome secondary to increasing intra abdominal pressure exerted by progressive reaccumulation of the gelatinous fluid. This is an uncommon indication for relaparotomy in patients with pseudomyxoma peritonei as the latter is more often indicated in patients who develop subacute or acute bowel obstruction. This report is complemented by a brief literature review on the current management of this uncommon condition.

KeyWords: Pseudomyxoma peritonei, Mucinous adenocarcinoma.

Is Diagnostic Abdominal Ultrasound Appropriately Utilised

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Introduction

Diagnostic abdominal ultrasound (U/S) is frequently utilized as it is noninvasive and of almost no risk. Occasionally requests for U/S examinations are not appropriate. A study was undertaken to determine whether this was prevalent.

Materials and Methods

Setting: Tertiary Referral Centre. Subjects: Patients undergoing abdominal U/S. Indications for the U/S examination and whether U/S was an appropriate form of investigation was assessed from the information on available on the request form and in medical case records. On completion of the U/S examination, findings were analysed with respect to (i) indications for the examination, (ii) whether U/S was an appropriate investigation, (iii) whether clinically suspected pathology was found, and (iv) whether U/S findings, (clinically suspected or otherwise) could account for the clinical features.

Results

Of the 43 patients included, 67.4% (29) had appropriate indications from information available on the request form, whilst 86.0% (37) had appropriate indications, from, information available in the medical case records. Abdominal U/S was an appropriate imaging modality in 90.7% (39) of the patients. Although clinically suspected pathology was found in only 27.9% (12), some form of pathology was found in 74.4% (32). The pathology found on U/S could account for clinical features in 48.8% (21) of the patients. No pathology was found in 25.6% (11).

Discussion and Conclusion

Although the sample is small, the study shows that diagnostic abdominal U/S was appropriately utilized. A substantial proportion of patients had appropriate indications and had pathology found on diagnostic abdominal U/S.

Mesenteric Vein Thrombosis – Our Experience

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Summary

Mesenteric ischaemia can be caused by both arterial occlusive disease and venous thrombosis. Of these, mesenteric vein thrombosis is less common but can be potentially more extensive and fatal. In this paper we would like to share our experience in treating 3 patients with mesenteric vein thrombosis. The ages range from 35 to 50. In one patient oral contraceptive were attributed as the etiological factor and the other two had no obvious etiological factors. Two patients presented with acute abdominal pain with features of peritonitis and in one patient had severe abdominal pain with no abdominal signs of peritonitis. Radiological examination in all 3 patients showed small bowel dilatation. As mesenteric ischaemia was entertained, ultrasound Doppler was useful in clinching the diagnosis in one patient. The ischaemic segments were resected in all the patient.

Conclusion

Though a rare entity it must be entertained when the symptoms are more severe than the abdominal sign of peritonitis. Other modalities like ultrasound Doppler and CT scan of the mesenteric veins are helpful in clinching the diagnosis. Early diagnosis with resection of the involved segments is important in reducing mortality and morbidity. Rarely a second look surgery is useful when assessing if the thrombosis has had further extension and these are normally done electively 48 hours after the initial laparotomy.

A Survey of Practices and Patient Satisfaction on Consent Taking for Patients Undergoing Gastroenterological Endoscopy in UPM Medical and Surgical Endoscopy Unit in Hospital Kuala Lumpur

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Background

Shared decision making by patients and clinicians has been advocated as the ideal for medical management. However, little is known about patients' degree of participation, amount of information received and level of satisfaction in decision-making prior to endoscopic procedure in Malaysia. The depth and content of information given to patients are often variable.

Materials and Methods

A cross-sectional study based on interviews using a questionnaire was carried out on patients undergoing endoscopic procedures by UPM endoscopy unit in Hospital Kuala Lumpur to determine information received during the consent taking and the level of satisfaction.

Results

The study showed that 53.8% patients were informed about technical aspects of the procedure, 76.3% on the indication, 96.8% about preparation before procedure, 50.5% about events after procedure, 24.7% about complication, 53.8% about advantages of the procedure and 32.3% of the patients are given option of using sedation by their doctors. Ninety five percent of patients were satisfied with the information received. Among the patients who were satisfied, 38.2% felt that information was adequate to assist them to make decision and 61.8% thought that their doctor will be the best person to make the decision on their behalf, thus is not necessary to know too much. The younger age group patients appear to receive more information ($p=0.022$). Patients from white-collar occupation category also received more information compared to blue collar and non-working patients ($p=0.01$). The amount of information received by patients was also proportionate to their education level ($p<0.001$).

Conclusion

Overall, the majority of patients played a passive role in medical decision-making. Most of the patients still adhere to paternalistic model in making decision for their medical plan.

The Utility of Imatinib Mesylate in the Treatment of Metastatic Gastrointestinal Stromal Tumour (GIST)

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Summary

We report a 55 year-old Malay gentleman who presented with progressive abdominal swelling and fullness, loss of appetite and weight for 3 months. On examination he was bed-ridden and cachetic with massive hepatosplenomegaly and an irregular mass at his epigastric region. Ultrasound showed a mass arising from stomach, with hypoechoiec lesion in liver and spleen. CT scan confirmed a stomach mass with metastasis to the liver and spleen and marked ascites. Endoscopy revealed a large sumucosal mass at the corpus along the lesser curvature with central ulceration. Histopathology is consistent with a malignant GIST with positive CD117. He was initially started on Imatinib mesylate 100mg bd. He was able to ambulate with minimal support on day 5 of therapy. We note marked symptomatic improvement within one week of therapy. A repeat CT scan after 1 month and 2 months of therapy showed the previous mass lesions becoming cystic with minimal reduction in tumour volume; Repeat Endoscopes revealed a reduction in size of the submucosal lesion but the mucosal area maintained to be denuded.

Imatinib mesylate is a tyrosine kinase inhibitor of the 2-phenylaminopyrimidine class target the activated portion of the BCR-ABL oncoprotein, and the following subgroup III receptor tyrosine kinases: c-kit receptor, PDGF receptor, and stem cell factor receptor. Two phase 2 trials have shown encouraging results with 90% symptomatic relief with partial or complete responses to the treatment.

This gentleman with advanced metastatic GIST (CD117 positive) showed improvement in his functional status, wellbeing, clinical symptoms and signs, biochemical parameters and radiological imaging soonest after initiating Imatinib.

Pediatric Gastroenterology and Hepatology Practice in Malaysia – Implications for Training of Trainees

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Background and Aim

Guidelines for structured training in pediatric gastroenterology and hepatology (PG&H) in North America and Europe have been implemented to facilitate formal training of trainees. The practice of PG&H from a referral centre in a developing country was prospectively reviewed to ascertain the appropriateness of the unit as a training centre for training of trainees.

Materials and Methods

The Division of Gastroenterology and Nutrition, Department of Paediatrics, University of Malaya Medical Centre, Kuala Lumpur, is one of two tertiary referral centers in PG&H in Malaysia. This was a prospective study documenting all the clinical and research activities carried out in the Division from January 2002 to December 2002.

Results

During the study period, a total of 490 episodes of outpatient (75 new referrals, 415 follow-up cases) and 149 episodes of inpatient consultations (including 38 in-patient referrals from other hospitals, and 29 interdisciplinary referrals within the same department) were carried out in the Division. The 5 commonest gastroenterological (GI) conditions seen in out-patient follow-up were: recurrent abdominal pain (RAP), gastroesophageal reflux and related disorders, food allergy, chronic constipation, and cyclic vomiting; while the 5 commonest new GI referrals were: RAP, recurrent vomiting, GI bleeding, chronic diarrhea and chronic constipation. The 5 commonest hepatology conditions out-patient follow-up were: biliary atresia, neonatal hepatitis, chronic hepatitis B, post-liver transplant, and chronic hepatitis C; while 4 commonest new hepatology referrals were: neonatal cholestasis, chronic hepatitis, acute liver failure, and portal hypertension. The 2 commonest indications for interdisciplinary referrals were oncology patients with GI symptoms while undergoing chemotherapy and post-chemotherapy chronic hepatitis B or C infection. Procedures performed were: upper GI endoscopy (41), colonoscopy (15), percutaneous liver biopsy (20), pH monitoring (15), rubber banding (8) and sclerotherapy (1) for bleeding oesophageal varices, and percutaneous endoscopic gastrostomy (2). The Department of Paediatrics also has an infectious diseases ward, with 430 cases of acute gastroenteritis being admitted in 2002. Based on the clinical work done mainly in the Division, 6 abstracts were presented in national / international conferences, and 9 papers were published in peer-reviewed journals.

Conclusions

The pattern of PG&H practice seen in a center from Kuala Lumpur was largely similar to that seen from other developed countries, enabling existing training guidelines from developed countries, with minor modification, to be adapted and be used for the training of PG&H in Malaysia. Rotation to other center in Malaysia and oversea training in established training centers will the enhance quality of the training.

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