APAGE IBD Working Group Guidelines on the Management of Inflammatory Bowel Disease during the COVID-19 pandemic

1. COVID-19 and the Gastrointestinal Tract

A novel coronavirus, SARS-CoV-2 which causes the COVID-19, first emerged in China in December 2019. From China, the virus has spread internationally and has now caused a pandemic.

The predominant symptoms of COVID-19 are fever, upper respiratory symptoms and shortness of breath. What is less well known is that about 20% of patients may have gastrointestinal (GI) symptoms in addition to respiratory symptoms[1,2]. In a case series of COVID-19 patients in China, 17% had diarrhoea, 1.9% had vomiting and 0.9% had abdominal pain. The diarrhoea is often not profuse and usually occurs up to three times per day. Three percent of patients in this series presented with only fever and gastrointestinal symptoms[2]. Although this particular Chinese series showed that patients with more severe COVID-19 were more likely to have GI symptoms, this finding has not been replicated in all case series of COVID-19 patients.

The GI symptoms are not a non-specific response to sepsis. It is known that SARS-CoV-2 virus infects intestinal epithelial cells through the ACE2 receptor[3]. The virus is found in stools and may continue to be shed even when the nasal and throat swab have become negative[4] .

2. COVID-19 and IBD

The inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn's disease (CD), are chronic inflammatory conditions which require long term treatment. There is currently no data to suggest IBD patients on corticosteroids, immunomodulators, biologics and small molecules are at increased risk of contracting SARS-CoV-2 or developing COVID-19. The IBD management principle should always be to maintain disease control during this difficult period while preserving patient safety.

Social Distancing

All IBD patients should practise an appropriate degree of social distancing as advised by your country's health authority and use facial mask protection when outside. Depending on age, co-morbidities and the type of medication a patient is on, some patients will be at higher risk of poor outcome should they be infected by SARS-CoV-2.

Current risk factors (which are not exhaustive) are thought to be:

1. Age >65
2. Co-morbidities e.g. hypertension, diabetes mellitus, heart disease, chronic lung disease, cancers
3. Prolonged course of high dose corticosteroids
4. Malnutrition

3. Medication for patients with IBD

The potential effect of IBD therapy on COVID-19 is uncertain given that few patients have been infected to date with no obvious detrimental effects from any single medication class. As such, **the following advice is based on theory and pooled consensus from various gastroenterological societies**. There is as yet no evidence that being on immunosuppressive therapies increases the risk of acquiring SARS-CoV-2 infection or of developing COVID-19. IBD patients should not start or stop their medications without consulting their physicians.

As mentioned previously, patients with COVID-19 may present with only fever and GI symptoms. Therefore, the IBD physician must have a high index of suspicion especially in patients with positive COVID-19 contact history or fulfil the relevant travel history to countries with COVID-19 outbreaks. In these cases, the physician should have a low threshold to test for SARS-CoV-2.

3.1 5-aminosalicylic acid compounds (5-ASAs)

Among the IBD medicines, 5-ASAs such as mesalazine do not increase the risk of infection and should be continued.

3.2 Corticosteroids

Corticosteroid-use should be minimised. Tapering of corticosteroids should be considered for doses exceeding 20 mg /day of prednisolone or equivalent, guided by the disease activity. For patients who require induction corticosteroids should have its dose tapered as quickly as disease activity permits. Alternative, topical treatment or oral budesonide (Cortiment, Budenofalk, Entocort) are considered safer alternatives.

3.3 Thiopurines/Methotrexate

Thiopurines (azathiopurine, mercaptopurine) may cause leukopenia and lymphopenia which may impair one's immunity against virus. However, patients who are already on thiopurines should continue on the drug if they are well controlled. Likewise, it is also recommended for patients to continue on methotrexate.

3.4 Biological agents

Patients already on a biological agent and in remission should continue taking the current drug. Dose reduction, if deemed necessary, might be considered in an appropriate patient who has recent documented mucosal healing upon discussion with the managing physician. A patient should not switch from an intravenous biologic (e.g. IV infliximab) to a sub-cutaneous biologic (e.g. SC adalimumab) if there is good response to the original drug, except in extenuating circumstances when infusion centres are not available. There is currently no evidence that any one particular class of biological agents is safer than another. Without further data we do not recommended switching from one class of biological therapy (e.g. anti TNF agent) to another biologic (e.g. non anti-TNF agent) if the patient is in remission.

Patients who wish to stop biological agents during this time should fulfil the same criteria for stopping biological agents as during non-pandemic times.

For patients who are considering new combination therapy (e.g. thiopurine and Infliximab), settling for monotherapy biological agents for the initial period during the pandemic may be considered in view of increased immunosuppression with combination therapy.

In patients in whom initiation of biological agents is considered, vedolizumab and ustekinumab may be better alternatives given their less systemic immunosuppressive activity. These newer agents seem to be less likely to develop immunogenicity and less reliant on immunomodulatory agent co-therapy. Vedolizumab and ustekinumab may also be preferred in higher risk elderly individuals.

3.5 Tofacitinib/ JAK inhibitors

There is no data to ascertain if tofacitinb or other JAK inhibitors increase the risk of SARS-CoV-2 infection and COVID-19. Patients in remission on tofacitinib should be maintained on the lowest effective dose.

3.6 Investigational products (clinical trials)

Patients on clinical trials should not stop their trial medications. If these patients develop SARS-CoV-2 infection or COVID 19, the trial medications should be interrupted and the study sponsors immediately updated. Some studies have currently frozen the screening of new potential cases.

4. EXCLUSIVE ENTERAL NUTRITION

Exclusive enteral nutrition is a safe and effective option to induce remission in Crohn's disease without risking the development or worsening of COVID-19. Co-management with a dietician is advised.

5. VACCINATIONS

It is recommended that patients who are receiving immunomodulators or biological agents receive up-to-date vaccinations against influenza and *Pneumonococcus*.

6. SURGERY AND ENDOSCOPY

IBD patients should not undergo elective endoscopies if detrimental effects are not expected in such postponement. Non-invasive markers, such as serum C-reactive protein and faecal calprotectin, can be used to assist with disease activity assessment.

Patients in whom endoscopic results will have a major impact on disease management in the short term should proceed with endoscopy in accordance with best practices. Screening process should be undertaken to exclude SARS-CoV-2 infection based on local and national policies and practices. They usually include exposure history, blood or nasal/pharyngeal swab confirmatory tests and chest CT Scans.

The urgent IBD related surgeries generally cannot be postponed without detrimental consequences to the patient. These should not be deferred.

7. FOLLOW-UP OF IBD PATIENTS

Where there is significant community transmission of SARS-CoV-2, doctors may consider teleconsultation with IBD patients in place of face-to-face clinic consultations.

However, in countries where IBD drugs are not usually available in community pharmacies, a mechanism may have to be employed to deliver drugs to the patient at their homes.

Patients with poor or suboptimal control of disease, a face-to-face consult should be considered on a case-by-case basis, depending on the severity of community transmission of SARS-CoV-2.

Usual indications for hospitalisations of IBD patients should prevail.

8. TREATMENT OF IBD PATIENTS WITH COVID-19

IBD patients with COVID-19 should stop thiopurines, tofacitinib and postpone receiving maintenance doses of biological agents until clearance of the virus. Patients on corticosteroids should continue on a tapering dose unless they risk hypo-adrenocortical responses in the setting of sepsis.

Patients who interrupted their IBD medications and subsequently recovered from COVID-19 can restart their medications once they are confirmed negative for SARS-CoV-2.

References

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Suggested Useful References

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