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Review Article

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Treatment Options for Patients with Inflammatory Bowel Disease During the COVID-19 Epidemic: A Review

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Abstract

The Corona Virus Disease (COVID-19) outbreak is affecting life around the world. In particular, people with basic diseases are concerned about whether COVID-19 will affect their original disease,Increasing attention is whether patients with inflammatory bowel disease (IBD) are more susceptible to COVID-19.Whether the treatment plans need to be adjusted, Summary literature shows that IBD patients have comparable infection rates as those in the general population, patients with IBD using biologics are more likely to develop asymptomatic infections and have fewer symptoms than normal populations, The use of parenteral-selective biologic agents may have a protective effect in lung function, which may be associated with its mitigation of cytokine storm syndrome. So patients with IBD should not interrupt the original biological treatment regimen. However, in preparation selection, parenteral-selective biological agents are preferred.

Keywords: Biologic therapy, COVID-19, Inflammatory bowel disease, SARS-CoV-2.

Introduction

COVID-19 is a novel severe acute respiratory syndrome (SARS), caused by the novel coronavirus SARS-COV-2.Since declared a global pandemic in SARS-CoV-2 since 12 March 2019, it has become a major threat to both public health and society worldwide [1]. Symptoms of COVID-19 include fever, pain, dry cough, and shortness of breath; however, it can also cause life-threatening conditions ranging from respiratory failure to multi-organ dysfunction. Patients with chronic underlying disease are more likely to develop COVID-19 [2]. As a kind of chronic disease, the treatment of inflammatory bowel disease and whether developing inflammatory bowel disease itself will affect COVID-19 are still controversial, it is more concern in patients with IBD using biologics; Because of endoscopic mucosal healing in IBD patients, the development of therapeutic target biotechnology for IBD, the use of biologics has been increased. However, during the COVID-19 epidemic, the guidance of biologic agent use in IBD patients is even less rare [3].

Biological Treatment of Inflammatory Bowel Disease

Inflammatory bowel disease is a chronic non-specific intestinal inflammatory disease, including Crohn's disease (CD) and ulcer colitis (ulcerative colitis, UC), the cause is not clear, in recent years it is widely believed that chronic inflammation is caused by the immune system dysfunction, immune system disorder reduces the immune tolerance of intestinal bacteria, proinflammatory cytokines and adhesion molecules, T cell overactivation and T cell apoptosis reduction is its basis
[4].

IBD treatment goal is to induce and maintain remission, conventional treatment of 5 amino salicylic acid (5-ASA), steroids and immunosuppressive drugs (including 6 sulthiopurine, azathioprine, etc.), these drugs have achieved clear efficacy in the clinic, but there are still some IBD patients conventional drug treatment, or serious adverse reactions lead to the need for additional treatment and colectomy [5]. Therefore, different biologic agents specific for immune pathways have emerged, and five biologic agents have been approved for marketing and application in IBD treatment, there are four anti-tumor necrosis factor (TNF-α) inhibitors: including infliximab (IFX), adalimumab (ADA), Goralimab and cetuzumab (CZP); and one anti-integrin Vitoriumab (VDZ); In a prospective study enrolling 200 patients with IFX for IBD for up to 3-4 years, it found a reduction in steroid

use from 51% to 10%, improved the degree of disease activity and reduced the surgery rate from 27% to 11% [6]. Another Meta-analysis of 1090 IBD patients showed that the clinical remission rate of IFX applied patients reached 60.91%, and the mucosal healing rate reached 38.10%, and the control group was significantly higher. ADA antibodies have basically similar clinical remission rate and mucosal healing rate and IFX in treating IBD, but the incidence of adverse events during treatment is small, and studies have shown that ADA can not only improve clinical symptoms, but also can positively regulate the intestinal flora of patients [7]. Golalimumab showed stable performance in clinical response and remission rates in short (6-14 weeks) and medium-long (24-54 weeks) for UC (59.3% vs 60.3%, 35.9% vs 39.2%) [8]. CZP is mainly used for moderate to severe CD that cannot be alleviated by conventional treatment, and shows good efficacy especially in patients with immune nonresponders [9]. VDZ is a novel agent with high intestinal selectivity, or IBD patients with TNF-inhibitor refractory and in a randomized clinical controlled study showed that VDZ was effective for inducing and maintaining remission in UC regardless of prior exposure to TNF-inhibitor, with slow onset time and at least 2 weeks to achieve clinical response time [10]. Although biological agents can make many benefits to patients, they may cause a certain proportion of serious infections during the use period, secondary tumors, causing autoimmune reactions, leading to neurological and hematological adverse events. The indications should be strictly selected and applied, especially in the context of the COVID-19 epidemic.

The Perpective of Patients with Inflammatory Bowel Disease in COVID-19 Pandemic

At present, more and more studies show that the elderly and immune compromised, as well as patients with basic diseases of complex and even fatal COVID-19 disease risk is higher, long-term patients with IBD are highly afraid of infection, in the use of biologic patients this phenomenon is particularly obvious, some patients think that the use of biological agents can lead to novel coronavirus (SARS-COV-2) prone to infection,in response, a cross-sectional survey of 415 IBD patients in a Danish IBD clinic found that IBD patients using biologics were more afraid of entering public places, Such as hospitals, private practice, Large supermarkets, etc. They leave less frequently from home than their peers without IBD; 90 percent of IBD patients wash their hands more frequently; Patients applying biologics were more concerned with the interaction studies between drugs and COVID-19, However, this phenomenon is not true in patients using 5-ASA; Drugs mainly rely on Internet news and television for guidance, electronic media counseling is an effective way for young people to obtain medication guidance, elderly people have significantly less access to guidance than young people; Despite the many concerns, 96.4% of patients can still adhere to their due treatment regimen [11]. For patient concerns and doubts, the current focus is on the need to deliver the COVID-19 information effectively related to the IBD.

Performance of SARS-CoV-2 Infection with IBD Patients Treated with Biologics

What is the prevalence of COVID-19 in IBD patients treated with biologics? A multicenter study of 1816 IBD patients showed that the cumulative incidence of COVID-19 was 7/1816, comparable to the prevalence of 3% in the general population in California, and did not show a higher incidence; the hospitalization rate was 57%, and the case fatality rate was 29%. The type of biological agents was the only risk factor for SARS-CoV-2 infection (P=0.01), and the patients using parenteral selective biologics were lower after COVID-19 infection, and the clinical symptoms were lighter than the control group (P<0.05); lower prevalence of IBD patients using biologics was COVID-19 compared to the general population (3.9 vs 8.5/1000, P=0.03); comparison of IBD patients using and without biologics was in a group of COVID-19 using biologics (7.5% vs 18%, P<0.001) [12]; there is a lack of evidence of SARS-CoV-2 infection among patients with IBD, especially those receiving immunosuppressive therapy, including the elite IBD consortium of seven IBD referral centers in China in nearly 191000 adult IBD patients, which showed 262 opportunistic infections with a significantly reduced risk of anti-TNF monotherapy compared with patients receiving thiopurine monotherapy [13]. An Italian study selected 103 IBD patients with symptoms of SARS-CoV-2 infection and close contacts, all with mild or asymptomatic infections, and 13 patients under 18 (12.6%) and 90 were serologically tested, with 19 patients having positive IgG, IgM or both, with a positive rate of 21%. There was no significant difference in global and age-stratified seroprevalence (P>0.05), notably in women, elderly and symptomatic patients; multivariate variable analysis, which confirmed the protective effect of men, increased the risk of positive serology compared with young adults, and no positive cases were found in children, another 11 patients (58%) were asymptomatic despite their positive serological results [14].

The use of biologics does not increase the prevalence of COVID-19 in IBD patients, but it may instead reduce the symptoms after SARS-CoV-2 infection.

Conclusion

With the deepening of COVID-19 research, Several studies have mentioned that patients with severe COVID-19 have cytokine storm syndrome, mainly secondary hemophagocytic lymphohistiocytosis, a poorly recognized hyperinflammatory syndrome, characterized by fulminant and fatal hypercytokine emia with multiple organ failure, in COVID-19, cytokine IL-2, IL-7, TNF-α, GSF elevation, the onset of COVID-19 may be an excessive inflammatory response driven by viral infection [15]. Another study also showed that the plasma concentration of granulocyte-macrophage colony-stimulating factor (GM-CSF) as inflammatory response mediators was significantly increased in COVID-19 patients, a phenomenon more pronounced in severe patients [16]. With a monoclonal antibody to the GM-CSF receptor, Mavrilimumab treated 40 hospitalized COVID-19 patients, on day 14,12 (57%) in the treatment group and 9 (47%) in the control group

(odds ratio 1.48,95% CI0.43-5.16, P=0.76), no treatment-related deaths, no adverse events, no significant statistical difference in survival rate and cessation of oxygen therapy in each group, given the wide confidence interval, the efficacy of maffimimumab in this patient group has not been confirmed [17]. But it is observed that drugs blocking TNF-αand interferon G signaling seem to be harmless in patients infected with SARS-CoV-2.

Although there is no evidence of higher susceptibility of IBD patients to COVID-19, IBD patients often require immunosuppressive therapy to induce or maintain clinical remission and whether these drugs should be continued or discontinued, with the main concern that immunosuppressive therapy can cause infection-related complications, however, it may be protective in cytokine storm-driven inflammatory responses. Furthermore, experimental evidence suggests that commonly used parenteral-selective biologics, IBD treatment, may have protective effects in lung function [18]. In our daily outpatient visits, there was a clear uncertainty about the impact of the disease and medication in IBD patients on COVID-19 disease. However, there is no evidence that IBD patients using biological agents are more likely to infect SARS-CoV-2; for IBD patients already infected with SARS-CoV-2, biological agents may reduce the infection symptoms; therefore, the author believes that IBD patients should not interrupt their original biological treatment regimen during the COVID-19 epidemic, but tend to choose parenteral selective biological agents.

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