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Short Communication

Gut Dysbiosis, Probiotics and COVID-19

Andrew P Smith*

Centre for Occupational and Health Psychology, School of Psychology, Cardiff University, UK

***Corresponding Author:** Andrew P Smith, Centre for Occupational and Health Psychology, School of Psychology, Cardiff University, UK.

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The impact of COVID-19 is well documented, with over sixteen million people infected and 665,000 deaths [1]. With any infection it is necessary to consider countermeasures which can improve immune functioning and the immunological response to vaccination. Our bodies are host to large numbers of bacteria which colonise the skin and the digestive system. These organisms are referred to as microbiota and interest here lies in the gut microbiota. These show large individual variation [2], which may plausibly explain differences in susceptibility to and severity of disease. An abnormal gut microbiota is referred to as gut dysbiosis, and this has been shown to be a risk factor for disease. For example, hypertension is linked to gut dysbiosis [3], as is coronary heart disease [4]. Similarly, patients with both Type 1 [5] and Type 2 [6] diabetes show signs of gut dysbiosis. Susceptibility to, and the severity of COVID-19 has been shown to be associated with the same diseases that lead to gut dysbiosis. This suggests that one plausible method of preventing and managing COVID-19 might be by beneficial changes in the gut microbiota. This could involve the use of probiotics or possibly prebiotics that lead to positive changes in gut flora.

Probiotic bacteria compete with pathogenic bacteria for nutrients and also interact with the epithelium of the gut and immune tissues in the digestive system [7]. These effects may be due to chemical changes or direct contact between cells. There is evidence that some probiotics can enhance phagocytosis and natural killer cell activity [8]. There is also evidence that probiotics may improve the immunological responses following vaccination [9]. The Handbook of COVID-19 Prevention and Treatment [10] describes COVID-19 patients who have had abdominal pain and diarrhoea which may be caused by infection of the intestinal mucosa. The dysbiosis seen in these patients [11] suggests that probiotics might be beneficial. However, this conclusion is based on the existing literature rather than evidence from clinical trials [12]. The gut bacteria, particularly lactobacilli and bifidobacteria, do seem to also reduce the incidence and severity of upper respiratory tract infections [13]. This, again, suggests that they may have some efficacy in the prophylactic and therapeutic treatment of COVID-19. This view is supported by results from a recent study from China [14]. In this Chinese study, the researchers isolated 20 proteins associated with disease severity of COVID-19 patients. The proteins were then used to create a risk score that could predict the severity of the disease. They then correlated the risk scores with the quality of the gut microbiome as analysed from faecal samples. The results showed that a poor microbiome score was a better predictor of symptom severity that traditional indicators of health (e.g. body mass index, blood pressure and age). The results of this study have to be treated with caution due to the small number of COVID-19 patients.

Evidence from Italy [15] also suggests that probiotics, combined with other compounds, may have benefits for COVID-19 patients. The study started with the observation of frequent gastrointestinal problems in COVID-19 patients. Probiotic administration led to a remission of diarrhoea and other gastrointestinal symptoms in nearly all of the group. In contrast, half of those not given probiotics showed a persistence of the symptoms. The removal of the digestive tract symptoms is not unexpected. However, those given the probiotics also showed an eight-fold lower risk of developing respiratory failure compared to those not given probiotics. The impact of gut microbiota on lung function is an established concept, namely the "gut-lung axis" [16]. Patients with gastrointestinal disorders often have a higher incidence of pulmonary disease, which might reflect gut-derived metabolites priming myeloid cells

in the bone marrow, which then migrate to the lungs and change inflammation. Therefore, while the results of the Italian study are plausible, replication is required to examine whether effects generalise to a more diverse sample of patients and other probiotic formulations. Other authors [17] have been more specific about the probiotic regime necessary to combat COVID-19. They argue that a preventative dose would be one capsule with at least 10^9 Colony Forming Units of Lactobacillus or Bifidobacterium species during a meal [18,19]. Those with COVID-19 should take two such capsules three times daily. If the patient is on invasive mechanical ventilation they should be given two opened capsules three times a day by enteral feeding.

The above account suggests that the gut microbiota may play a major role in COVID-19. This suggests that probiotics may be important, but one should also remember that a healthy diet, rather than supplements, plays a role in maintaining a healthy gut microbiota. The literature contains many examples of clinical trials that have investigated beneficial effects of probiotics. In the case of COVID-19, such trials will initially aim to demonstrate that probiotics lead to a reduced risk of developing the disease. It is also possible that they may reduce symptom severity, and even, as in the Italian study, increase the likelihood of remission of gastrointestinal symptoms present in those with COVID-19. Overall, one can now suggest that nutritional studies should be part of the prevention and management of COVID-19. It is also important to point out that changing the gut microbiota is one of many approaches to treating COVID-19. Indeed, even within the area of nutrition, there are other approaches which may turn out to be extremely useful [13]. For example, a severe infection of the respiratory epithelium leads to ARDS, which is characterised by a cytokine storm. This is often observed in severe cases of COVID-19. Studies of ARDS in the context of other diseases has shown that the cytokine storm can be controlled by the n-3 fatty acids EPA and DHA. This suggests further interventions and the need for a holistic approach to the prevention and management of COVID-19.

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