



Letter To The Editor

Can a gluten-free diet be partly protective for COVID-19 infection?

The recent French observation that daily tobacco smokers have a substantially reduced risk of developing symptomatic infection with COVID-19 (1) is intriguing, since no healthcare professional would recommend smoking. So, what are the mechanisms and could something else be at play than tobacco smoking?

The French study suggested that nicotine may be the protective agent in tobacco, as nicotine has been shown to modulate the expression of the angiotensin converting enzyme 2 (ACE2) receptor (2), which is used for cell entry by SARS-CoV-2 (3, 4). Besides being present on pneumocytes, ACE2 is highly expressed on enterocytes in the small intestine, and this is suggested to mediate the invasion of virus and the gastrointestinal symptoms that are often reported in COVID-19 patients (5). Of note, nicotine is also associated with protection from ulcerative colitis (6), as well as other autoimmune diseases (7). The mechanisms are not fully elucidated, although smoking has previously been shown to reduce the intestinal permeability in healthy subjects (8, 9). Nicotine is also known to reduce pro-inflammatory cytokines and increase anti-inflammatory cytokines (10). This is relevant because pro-inflammatory cytokines can increase the intestinal permeability (11), and anti-inflammatory cytokines can have the opposite effect (12).

Highly interestingly, a gluten-free (GF) diet seems to have some of the same effects as nicotine; we have shown that a GF diet results in a less pro-inflammatory cytokine profile in mice (13). Also, in healthy subjects, a low-gluten diet reduces the pro-inflammatory cytokine IL-1beta (14), which specifically increases the tight junction permeability in intestinal cells (15). Moreover, a GF diet is well known for its ability to normalize the intestinal permeability in celiac disease patients (16). The mechanism is likely to involve the chemokine receptor CXCR3, as the gluten peptide gliadin can bind to this receptor and mediate a MyD88-mediated zonulin release and thus degradation of tight junctions (17). This may also be relevant for lung tissue, as a GF diet was shown to alleviate hemosiderose in celiac disease patients, which is likely to improve fibrosis and lung function [18, 19]. Therefore, a GF diet may normalize the permeability and protect from or dampen the severity of pulmonary infection. In addition, cytokine storm is often seen in

COVID-19 patients and might be reduced by anti-inflammatory agents like nicotine or a GF diet.

A strikingly lower incidence of COVID-19 infection is reported from Asian countries like Japan (12/100 000 persons), Taiwan, and South Korea compared to western countries like Italy (349/100 000 persons), Spain, and Belgium (Johns Hopkins University, 2020). The same trend is observed for the intake of dietary gluten, which is particularly low in Asian countries (10 g of wheat/capita/day in Japan), where rice is the predominant nutrient source, compared to western countries (33 g of wheat/capita/day in Italy) (FAO Database, 2017). Thus, the low intake of gluten in Asia should be considered as partly protective for COVID-19 infection. We propose prophylactic treatment with a GF diet, which is easy and safe, and we recommend further studies to test our hypothesis.

CONFLICT OF INTEREST

None.

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DATA AVAILABILITY STATEMENT

Not relevant as the submitted manuscript is a letter and does not contain original data.

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