Opinion

Effect of Low Dietary Protein vs. High Protein Diets on COVID-19 Infection and Mortality

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Abstract

It has been shown that populations consuming primary rice had a strong negative correlation whereas population consuming primary wheat had a strong correlation on the severity of COVID-19 Infections in humans. This suggests that diet may play an important role in mitigating or exacerbating SARS-CoV-2 infections in humans. The type of dietary ingredients, especially sulfur-containing proteins and other sulfur-containing compounds may play an important role for the intestinal microbiome. Sulfur-containing compounds may be enhancing the growth of microorganisms, including coronaviruses. Protein types may play an important role in the composition of the intestinal microbiome. Although there is an urgent need for antivirals and vaccines for coronaviruses, in the meantime, other methods based on dietary and microbiome modifications may be possible to mitigate SAR-CoV-2 infections.

Introduction

It has been shown that populations consuming primary rice had a strong negative correlation whereas population consuming primary wheat had a strong correlation on the severity of COVID-19 infections in humans [1] Rice is low in protein compared to wheat which is higher protein and other essential nutrients. This suggests that diet, especially high protein diets, may play an important role in mitigating or exacerbating SARS-CoV-2 infections in humans. The type of dietary ingredients, especially protein types may play an important role in the composition of the intestinal microbiome. Excessively nutritious diets, high in sulfur and proteins, have a dramatic effect on the pathogenicity of bacterial and viral diseases of animals [2,3]. The impact of diets high in sulfur has on the commensal microbiome and the pathogenesis of infectious diseases of animals and humans has been generally ignored. Dietary protein and sulfur byproducts may induce the microbiome of the gut to produce ammonium sulfate that is associated with the formation of protein-associated pathogenic nanoparticles that induce microthrombi linked to multiple disorders affecting the cardiovascular, respiratory, gastrointestinal, and reproductive

systems with opportunistic diseases [2,3]. The role high-sulfur and high-protein diets have on the pathogenesis of human bacterial and viral diseases, like coronaviruses, is unknown. Dietary ingredients high in protein and sulfur need to be investigated since they affect the ecosystem of the gut and commensal microbiome. A diet low in protein may be beneficial in mitigating bacterial and viral diseases and may be associated with asymptomatic infections. Conversely, diets high in protein and sulfur, essential for the growth of microorganisms, may exacerbate the pathogenicity of viral infections like COVID-19. Factors responsible for the pathogenicity of SARS-CoV-2 may be responsible for morbidities and mortalities in humans and should be investigated. Coronaviruses have been known to infect small and large animals for several decades [4] Accordingly, it has been suggested that the results of studies with animal viruses, like the animal coronaviruses should be considered when trying to understand the coronavirus SARS-CoV-2 in COVID-19 infections in humans [4,5]. There is an urgent need for treatments, based on antiviral therapeutics and vaccines. In the meantime, other intervention strategies that may reduce the morbidity and mortality associated with COVID-19 need to be explored.

Discussion

The interrelationship between dietary factors and infectious diseases in humans has received little attention. There is an urgent need to pay more attention and resources for preventive methods for COVID-19 since there are currently no known proven prophylaxes or early-stage therapies for any of the coronaviruses to prevent severe and fatal infections [6]. It has been suggested investigating individuals with no or mild signs of COVID-19 would be helpful [6].

Effect of dietary ingredients on the pathogenesis of bacterial and viral pathogens

An adequate supply of nutrients is the most important factor for the growth and infection of pathogens [7]. Following host invasion, nutrient acquisition is a basic requirement for the proliferation of pathogenic bacteria. However, a non-specific immune response by the infected host, known as nutritional immunity, may restrict the access of pathogens to nutrients to restrict bacterial growth in the host. Bacterial pathogens must develop mechanisms to evade nutritional immunity to thrive within their hosts.

Effect of High Sulfur Proteins on The Pathogenesis of Animal Diseases

Sulfur is a vital nutrient for bacteria for the biosynthesis of vital cofactors and active sites in proteins. It is present in many organic molecules, including the amino acids cysteine and methionine, coenzyme A, the antioxidant glutathione and iron-sulfur clusters [8]. Sulfur metabolic pathways are essential for survival and the expression of virulence in many pathogenic bacteria [9]. Sulfur is also involved in several cellular processes, including energy transduction, redox homeostasis, transcriptional regulation, and translation [10]. Microbial sulfur metabolic pathways are largely absent in humans and therefore, represent unique targets for therapeutic intervention [11]. Sulfur is an essential nutrient that is widely required by microorganisms including *Actinobacillus pleuropneumonia* a Gram-negative pathogen in swine that will grow in a chemically defined medium containing sulfate or methionine. The presence of other sulfur uptake systems suggests *A. pleuropneumonia* has multiple functionally redundant pathways ensuring uptake of important nutrients during infection.

With streptococcal infections as a model in horses, it was shown proteins high in sulfur from alfalfa hay had a dramatic effect on the pathogenicity of the streptococcal infections when compared to a low protein and low in sulfur diet from Timothy hay [12]. Similarly, with the Herpes-1 virus as a model, horses on a diet high in protein and high in sulfur from alfalfa hay dramatically affected the pathogenicity of the virus by inducing fatal infections, whereas infected horses on low protein and low sulfur diet from Timothy hay induced only asymptomatic infections. Similar results were observed with reproductive disorders associated with streptococcal infections in mares fed high protein and high sulfur diets including alfalfa hay [2,4]. Alfalfa is a very nutritious legume high in sulfur-containing amino acids and protein. High sulfur and protein diets seemingly have a dramatic effect on the microbiome of the gut, which includes streptococcal organisms and likely a multitude of other potentially pathogenic microorganisms. The dietary-induced overgrowth of the gut microbiome may result in excessive ammonia from proteins that reacts with sulfur compounds, and sulfur-containing amino acids, as a source of sulfur, to form ammonium sulfate. As a result, ammonium sulfate, as a metabolic byproduct may initiate the formation of protein-associated pathogenic nanoparticles that were shown to be associated with multiple lesions in fetuses and adult horses, and other livestock. The pathogenic nanoparticles induce microthrombi in small vessels throughout the body that result in a host of secondary opportunistic diseases. The pathogenic nanoparticles have a predilection for the cardiovascular system where they induce a focal myocarditis, epicarditis and lesions in the small vessels throughout the body. Seemingly, they induce heart failure in early developing fetuses. In adult horses, the pathogenic nanoparticle may induce a focal myocarditis and an endopericarditis [2]. It is not known if these pathogenic nanoparticles occur in bacterial and viral diseases in humans as in animal diseases, but this needs to be investigated in humans as microthrombi are reported to be associated with lesions in the small vessels of multiple organs in COVID-19 infections.

Effect of high-sulfur high-protein diets on the pathogenesis human infectious diseases.

Very little information is available regarding the effects of diet on the exacerbation of bacterial and viral diseases in humans. However, recent studies suggest that dietary factors affect the ecosystem of the gut and the commensal microbiome. It may be possible to look at the gut for a solution to mitigate SARS-CoV-2 infections [13]. The microbiome of the gut are beneficial if subjects are on a healthy diet. However, if the microbiome of the gut contains pathogens and if individuals are on a diet with high-sulfur and high-proteins, the growth of pathogenic microorganism may be exacerbated. Low sulfur protein diets may aid in the prevention or severity of viral diseases and secondary opportunistic bacterial and viral diseases. Since sulfur seemingly is a key factor in the pathogenicity of both bacterial and viral diseases, a therapeutic method by reducing the sulfur and sulfur containing amino acids in the diet, may be used to mitigate infectious diseases. If the microbiome of the gut is affected by excessively nutritious diets high in sulfur and proteins, the pathogens in the gut may overwhelm the beneficial normal flora. Diets high in sulfur and protein seemingly exacerbate the overgrowth of streptococcal and other microorganisms that induce multiple disorders in developing fetuses of horses and other livestock [2,3]. As demonstrated with *S. equi* infections in horses

[2], diets high in sulfur and proteins may overwhelm therapeutic drugs and immunity from natural infections and vaccines. Whereas, animals on low-sulfur and protein diets therapeutic drugs and vaccines appear rather effective. For this reason, with clinical or experimental trials evaluating therapeutic drugs or vaccines, the type of dietary ingredients needs to be addressed.

Effect of Nutrition on The Pathogenesis of Human Infections Like SARS-CoV-2

The role of diet has in the pathogenesis of SARS-CoV-2 is poorly understood. Poor diets may have detrimental effects on the immune system, thus making humans more susceptible to COVID-19 and other diseases [14, 15]. Epidemiological evidence implicates industrialization, an increasingly western lifestyle, and associated changes in the microbiome with the development of infectious bowel diseases in humans [16]. Regarding COVID-19 pandemic, currently it is reported that the United States has four percent of the world's population, yet it has approximately 25 percent of the reported cases. Could western lifestyle and diet be responsible for the increase incidence and exacerbation of COVID-19 infections? [17, 19].

Conclusion

Very little is known about the effects of excessively nutritious diets have on COVID-19 infections in humans. However, in animal diseases, there is dramatic interrelationship between diets and the pathogenicity of microorganisms and the severity of disease syndromes. Results with animal diseases associated with excessively nutritious diets may play a similar role in exacerbating COVID-19 in humans.

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