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The Effect of Ketogenic Diets on the Gut Microbiota

Short Review

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Abstract

The ketogenic diet (KD) has gained a lot of media attention in the last few years. Some athletes have adopted this diet for performance and body composition changes. While studies have reported mixed results on performance, the KD has shown consistent results in improving body composition, as well as improving other health conditions. What is unclear is how KD diet affects athletes' gut microbiota. The gut microbiota is comprised of 10-100 trillion microbial cells known to influence overall health and disease of the host. A microbiota rich in diversity and beneficial bacteria has been associated with health, while a low diverse and decrease in beneficial bacteria microbiota has been associated with disease. Diet, exercise, stress, and other lifestyle factors have been shown to influence gut microbial composition and diversity. KD studies have been done primarily in mice or individuals with health conditions. KD experiments in mice have revealed a decrease in diversity; however, there is an increase in the number of beneficial bacteria. In humans, KD studies have resulted in correcting gut microbial imbalances in epileptic children; on the contrary, it may increase bacteria species associated with inflammation in obese subjects.

Key Words: athletes, nutrition, health

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Introduction

The ketogenic diet (KD) is defined as consuming a high fat, very low carbohydrate, and moderate protein diet.[1] Many athletes have adopted this diet to change their body's fuel source from glucose to primarily fat to help increase performance and lose body fat. [2] As researchers have come to better understand how KD affects an individual's health, performance, and body composition, there has also been a growing interest in studying how KD and other diets affect the gut microbiota. The gut microbiota has been shown to play a major role in health and disease, with diet being a major influence on its bacterial composition and overall diversity.[3] Therefore, The purpose of this review is to present research on the effects of ketogenic diet on the human gut microbiota.

What is a Ketogenic Diet?

The ketogenic diet (KD) has become a popular diet not only for treating epilepsy, type 2 diabetes, obesity, neurodegenerative disorders among other diseases.[1] It has also become a popular diet for body composition, and performance among athletes.[2] The KD diet is defined as a high fat (>60% of energy), very low carbohydrate (<10% of energy) and sufficient protein diet.[4] The original version of KD consisted of 80% of daily energy intake from fat, 15% of protein, and 5% of

carbohydrate.[5] Since then, modifications have been made with decreasing total daily fat % and increasing daily protein and/or carbohydrate %, as well as not restricting total caloric intake.[5] By eating a very low carbohydrate diet, the body switches from glucose as the primary fuel source to fat.[2,5] Fat metabolism produces water-soluble ketone bodies, known as ketogenesis.[2]

Human Gut Microbiota Defined

According to Ursell LK et al (2012) human microbiota is comprised of 10-100 trillion microbial cells, primarily in the gastrointestinal tract, which comprises more than 70% of the microorganism colonization.[6,7] The number of these microorganisms (bacteria, viruses, fungi) is collectively called the microbiota, and the genes that harbor these cells comprises the human microbiome.[6,7] The gut microbiota is primarily comprised of anaerobes (99%), facultative anaerobes, and aerobes.[8] The primary bacteria in the gut are Firmicutes and Bacteroidetes.[8] A healthy intestinal flora is characterized by a majority of potentially beneficial species, mainly Fimicutes and Bacteroides, with a low presence of potentially pathogenic species, Proteobacteria.[7]

The intestinal flora greatly influences an individual's health and disease.[3] A growing number of studies have demonstrated the influence of the gut microbiota on obesity, digestive disorders, inflammatory, endocrine, and auto-immune disorders.[9] The immune system and the gut microbiota interact, giving signals to promote the immune cell maturation, and normal immune system function development.[3] The diversity of the gut microbiota also plays a role in overall health; for example, low gut diversity has been linked to inflammatory bowel disease and obesity.[10] Exercise, and a diet rich in fiber, fruits, vegetables, whole grains and legumes has shown to boost the number of beneficial bacterial species, as well as increase overall diversity, which has a beneficial effect on the individual's health.[9] Genetic diversity within our gut microbiota plays a crucial role in the ability to extract energy from the foods consumed; microbes ingested with food may be providing the individual's microbiome with new genes to digest different foods.[6]

The normal microbiome faces challenges when there are changes to diet, stress, or physiology.[11] Diet changes can significantly change the bacterial composition in as little as 24 hours, and can quickly be restored if the diet changes were only temporary.[3] For example, a significant change in gut microbiota was detected in a 2011 study in humans who changed their diet from a high fat/ low-fiber diet to a low fat/high fiber diet n 24 hours.[3] The effects of KD on gut microbiome have been explored in mice and humans with some mixed results.

The Effects of Ketogenic Diet on Intestinal Microbiota

Animal studies:

The gastrointestinal tracts of humans and mice are composed of organs that are anatomically similar, which is why mice are often used to study gut microbiota.[12] While they do share important anatomical, physiological, and genetic characteristics, the authors point to key differences that could be shaped by different diets, eating behaviors, body size and metabolic requirements.[12] A 16 week study by Ma D., Wang AC., et al (2018) looked at effects of KD on gut microbiome composition and possible benefits on neurovascular functions in young healthy mice.[13] It found that KD increased beneficial gut microbiota, A. muciniphila, and Lactobacillus bacteria, which are capable of producing short chain fatty acids that help to protect the lining of the gut.[13] The diet reduced the potentially pro-inflammatory bacterial species, Desulfvibrio and Turibacter.[14] The KD did however decrease the overall microbial diversity, possibly due to the low carbohydrate intake, which decreases the polysaccharide content in the gut that many bacteria feed on.[14]

Another experiment in mice on a high fat and high sugar diet found the amount of Firmicutes increased and the amount of Bacteroidetes decreased compared to the mice who were fed a low fat and high sugar diet.[8] Reduced levels of Bacteroidetes and increase levels of Firmicutes are found in humans with irritable bowel syndrome (IBS), and are associated with obesity, type 2 diabetes, and altered blood glucose, compared to healthy individuals.[8,9] Gut microbiota also showed a decrease in diversity, as seen in other mice studies.[8] The types of dietary fat ingested have also been compared. A diet high in saturated fatty acid has been found to possibly affect gut microbiota composition, as seen in an 8-week study in mice comparing different proportions of dietary fatty acids.[8] The high saturated fatty acid diet increased the amount Firmicutes and decreased overall intestinal microbiota, compared to a low fat low sugar diet.[8]

Mouse models offer an important tool to study gut microbiota, especially in experiments that would be too invasive for human subjects, but it is important to note that the results are not always translatable to humans.[12]

Human studies:

Ketogenic diets and the effects on the microbiota in humans have shown some positive, as well as potentially negative results to overall health. Swidsinski A., et al (2017) analyzed the gut microbiota of 10 patients with multiple sclerosis (MS) on a KD for six months.[14] Results showed a dramatic decrease in bacterial diversity and concentrations, but after 12 weeks bacterial concentration began to recover back to baseline, and after 23-24 weeks it showed a significant increase in bacterial concentration above baseline.[14] Another study by Xie G., et al. (2017) compared KD on 14 pediatric patients with refractory epilepsy to 30 healthy aged matched infants.[15] Patients with epilepsy demonstrated an imbalance of gut microbiota prior to starting the KD, especially having higher amounts of pathogenic Proteobacteria (Escherichia, Salmonella ad Vibrio), which significantly decreased after KD treatment, and an increase of Bacterioidetes, mainly found in healthy infants, was also reported after treatment.[15] This experiment showed, that not only were symptoms of epilepsy mitigated, but also gut microbiota imbalances were corrected with KD.[15]

Research however, has also revealed some potential negative effects on the gut microbiota with subjects on a KD. A 2009 study by Brinkworth GD., et al. compared 91 overweight and obese subjects who were randomly assigned to either a hypo- caloric (30% deficit) iso-energetic low carbohydrate or high carbohydrate diet for 8 weeks.[16] The goal not only was to assess changes in body composition between the diets, but to also assess the effects on bowel health.[16] The low carbohydrate group was found to have a significant reduction in faecal output, defecation frequency, concentration of butyrate, the total number of short chain fatty acids, as well as bifidobacteria (a beneficial bacteria) for colon health.[16] Short chain fatty acids, like butyrate, generated by microbial fermentation, are the primary source of colonocytes (epithelial cells of the colon), which have been associated with colonic health, and protective against colorectal cancer.[16] Dietary fibers from plant based foods, are typically severely restricted on the very low carbohydrate diet, but contain a large number of resistant starches and non-digestible oligosaccharides that beneficial for gut health.[16]

To investigate how quickly the gut microbiome responds to short-term (5 days) macronutrient changes, David LA., Maurice CF., et al (2014) compared a diet entirely composed of animal products (meats, eggs, and cheeses) to diet entirely composed of plant foods (grains, fruits, legumes, vegetables) in 10 participants.[17] Researchers detected a significant increase in abundance of bile-tolerant microorganisms (Alistipes, Bilophila, Bacterioides) and a decrease in Firmicutes

(metabolize dietary plant polysaccharides) after one day on the animal based diet, which reverted back to its original baseline structure two days after study ended.[17] The animal based diet had a significant greater impact than the plant based diet on gut microbiota.[17] According to the authors, the increase abundance and activity of Bilophila can be connected to the increase in dietary fat, bile acids, and the outgrowth of microorganisms possibly causing inflammatory bowel disease.[17] Another bacteria group associated with exacerbating the inflammatory condition of the gut mucosa, Desulfovibrio spp, showed a substantial increase in a 3 -month KD diet study on 6 patients with drug resistant epilepsy and Glucose Transporter 1 Deficiency Syndrome (GLUT1 DS).[18] This study however, did not find any significant changes in Firmicutes and Bacteroidetes unlike David LA, Maurice CF study.[18]

Conclusion

In summary, the ketogenic diet has gained attention in the athletic population as a potential way to help increase performance and change body composition. There has been a growing interest in examining the effects of different diets on the gut microbiota. Diet has been shown to play a key role in influencing the overall bacterial composition and diversity. The effects of KD on gut microbiota have demonstrated mixed results with some showing beneficial results with balancing bacterial composition, while others reporting a decline in diversity and an increase in bacteria associated with inflammation. Future studies should focus on evaluating the long-term effects of a KD on microbiota in athletes. Chronic exercise training may mitigate the decrease in diversity, which could offset any possible negative health consequences related to low gut diversity.

Media-Friendly Summary

There are 10-100 trillion microbial cells residing in the human gut, which play a key role in human health and disease. Overall health is associated with higher gut bacterial composition and diversity; moreover, diet plays a crucial role in influencing both composition and diversity. The ketogenic diet may affect the gut microbiota; however, it is unclear what the long-term ramifications of this might be.

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