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KETOGENIC DIET AND THE COMFORT OF GUT MICROBYOTA: A CASE REPORT

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Abstract

The importance of microbiota and the ease with which it communicates with all bodily systems is a recent and still very unexplored science. We have come to understand how metabolic diseases, autoimmune diseases and the general well-being of the individual depend strictly on the well-being of the microbiota. The human microbiota enters into relation with those of the air, water and environments we frequent; it is extremely important to pay attention also to the relationship with food style and intestinal well-being. Among the various nutritional therapies we also investigated the ketogenic diet and its interaction with the intestinal microbiota. From the present literature it is clear that the ketogenic diet can alter the composition of the bacterial population; the case study analyzed shows how the ketogenic diet lasted for 60 days led to appreciable results regarding the management of abdominal swelling (meteorism-dysbiosis), but varying the bowel towards constipation starting from the 30th day of a glucose diet (effect collateral of ketogenic). It was therefore necessary to develop an integrative protocol based on the use of flaxseed, magnesium or ayurvedic remedies (tiphala) to maintain intestinal regularity and general well-being.

Keywords: *gut microbiota, ketogenic diet, supplements for gastrointestinal disorder, triphala, flax seeds, magnesium.*

Introduction

Text Man is home to more bacterial than tissue cells, said B. Henderson in 1996, but what do we know about this "organ" to which we must attribute specific trophic, immune and metabolic functions?

Bad digestion is the root of all diseases, says Hippocrates as early as the 5th century BC; since its origins, medicine has paid attention to the relationship between the state of health or illness with the condition of the digestive system, however the knowledge of the relationship between health in general and that of the digestive system has remained at a level empirical: in particular, the world of the microorganisms that populate the intestine and their functions has remained little observed by science.

The rapid development of microbiology has pushed research towards intestinal bacteria, with all its interactions towards the rest of the organism; of this precious discovery we have to thank the Russian biologist and immunologist Mečnikov who in the nineteenth century after the Nobel for the discovery of the mechanism of phagocytosis, had the great intuition that not all bacteria are pathogenic and that most are even beneficial. The idea that pathogens could be fought with the use of certain types of bacteria was taken into consideration but not applied as a wide range of antibiotics was available to fight infections; this trend has recently been re-evaluated with the strengthening of protocols for the use of "good" bacteria or, better, probiotics (pro-biotics in favour of life) versus pathogenic bacteria.

Probiotic science studies how the probiotic adheres to the intestinal wall, is distributed in the various parts of the intestine, what is its metabolism, what relationship it has with the other bacterial colonies, which substances it produces, how it relates to enteric, nerve cells and immune system of the intestine. All this complex microbiological mechanism is called microbiota. In the human organism there are several microbiota in different sectors; we find the oral, respiratory, epidermal, intestinal and urogenital microbiota. Each specific population communicates with each other and all together communicate with the microbiota of air, water, our home and even our pet.

Consider the fact that our intestines have had to compromise with the bacteria that then formed and form our microbiota, for the survival of both, in a world that is completely inhabited by bacteria. The various bacterial families present in our body are divided into bacterial phyla of which the two most important groups are the bacteroidetes (50%) and the firmicutes (40%). The main difference between these two groups is that the former are negative GRAM bacteria, while the latter are almost totally GRAM positive (with some small exceptions).

By analyzing the microbiota, we can classify individuals into enterotypes, that is the characteristics of a particular "ecosystem" of colonized bacteria with specific characteristics.

- Enterotype 1: bacteroidetes; degradation of carbohydrates and proteins.
- Enterotype 2: prevotella; degradation of mucilage lipoproteins and plant polysaccharides.
- Enterotype 3: ruminococcus; degradation of carbohydrates and mucin.

The identification of the enterotype can help to determine the dietary habits and lifestyle of the individual and these together with factors such as childbirth, breastfeeding and weaning are decisive for the diversity of the microbiota; a well-differentiated intestinal population, guarantees a more stable biosys. In addition to the above factors, drugs play a key role in the stability of biodiversity.

Antibiotics, antidepressants, corticosteroids, pump inhibitors and antacids, in the long run create an intestinal bacterial imbalance that makes the individual more susceptible to low-grade, autoimmune, leaky gut and, more generally, dysbiosis inflammatory diseases. With this term we go precisely to indicate an imbalance of the intestinal bacterial population, with a decline of beneficial bacteria for the host in favour of pathogenic microorganisms. The main symptoms that must lead to an assessment of intestinal well-being are diarrhea, constipation, malabsorption, weight loss or gain, food intolerances, chronic cystitis, hyperactivity in children, clouding and

generally the mood instability; these are just some of the possible symptoms, as our intestine with the enteric nervous system constantly communicates with the central nervous system via the intestine brain, consequently entering into constant communication with our whole body. The high axis of fundamental communication is between intestine and liver; the two organs connected to each other by the portal vein act as the first and second barrier (1). In the case of dysbiosis with intestinal permeability, then toxin migration, the barrier before the blood circulation will be the liver that with its specialized cells will activate a series of immunological mechanisms to stop the systemic inflammatory state. This hepatic response through the TRL4 receptor initiates the transcription of pro-inflammatory regulators such as NFkB which, by activating Kupffer cells, move IL-6, TNF-alpha which play an important role in general liver fibrosis and insulin resistance. The microbiota also intervenes in the modulation of obesity; very important role is in the management of SCFA (short chain fatty acids), produced by the fermentation of soluble dietary fiber, particularly resistant starch, fructo-oligosaccharides, pectin and other carbohydrates not digested by colon bacteria. The SCFA most produced by the colon and of considerable interest are propionate, butyrate and acetate; in a framework of eubiosis these molecules exert beneficial effects for glucose homeostasis, body weight and insulin sensitivity (1).

The ketogenic diet is characterized by a low carb-high fat regime and proteins adapted to the body weight that brings the body into a particular state called ketosis; in ketosis the body starts burning fat as an energy substrate, producing ketone bodies from the liver. Among the first effects of the ketogenic diet, there is the lowering of glucose and insulin levels in the blood, a situation that leads to various beneficial aspects, above all on metabolic, neurological and tumor diseases, as the latest scientific evidence shows how the trend of glucose in the blood with the consequent insulin response is among the responsible factors of systemic inflammation. The side effects described in the literature at the intestinal level mainly concern constipation which is often remedied by dietary supplementation aimed at not interrupting ketosis (2).

Methods

Literature review with analysis of a case study

Results

Literature review

The studies in the literature are still few compared to the topic, given that the ketogenic diet arises from the need to be able to manage children not controlled by drug therapy for epilepsy. From the 2018 study by Olson et al (3), the correlations between intestinal well-being and the ketogenic diet show that in the short term (28 days) there is a modification of the intestinal microbiota with particular proliferation of Akkermansia muciniphila and Parabacteroides merdae.

In the medium to long term, constipation is very frequent, as the sharp reduction of fibers with a prebiotic function leads to a poor reproduction of bifidobacteria, with a slowing down of the transit. The study by Zhang Y et al (4), conducted on a group of 20 epileptic children treated with ketogenic diet, shows that after 6 months the microbiota was still limited in terms of wealth and biodiversity.

Xie G et al (5), conducted a study of two groups of children treated with the ketogenic diet, the first group of epileptic children and the second group of healthy children. In both groups the microbiota was studied and the initial situation showed a marked biodiversity among pathological children compared to healthy children. The first group presented significant values of proteobacteria and cronobacter, values nbeautifully decreased after a week of ketogenic diet. The group of healthy children who already had a microbiota rich in bacteroides, saw an increase in prevotella and bifidobacteria.

De Luca et al (6), identify the bioactive components from flax seeds such as fiber, alpha linoleic acid, Lignans and contribute to intestinal, protective and anti-inflammatory well-being on enteric cells.

A very detailed study of flax seeds and its benefits is Noha M. Almoraie's Nutritional and Therapeutic Perspectives of Flaxseed (Linum usitatissimum). In recent reviews (7-9) were examined all the biological processes of interaction of flax seeds, including the control of diabetes, hypertension, dyslipidemia through anti-inflammatory, laxative, antioxidant, anxiolytic, analgesic and immunostimulant processes.

An article on marine magnesium with its possible prebiotic effect was published in June 2018 on Drugs. Another study on mice (10) correlated the use of pump inhibitor drugs which in 13% of the cases leads to hypomagnesemia and therefore to a low diversity of the microbiota. It is now known that the intestinal microbiota also intervenes in the modulation of anxiety and the depressive state; the study by Winther H. et al (11), correlates a diet low in magnesium to the alteration of the microbiota and to a depressive attitude in humans. The scientific community is now in agreement that magnesium is a salt that communicates with intestinal bacteria, varying its composition (12,13). Another supplement widely used and also approved by Ayurvedic medicine is Triphala consisting of dried fruits of the three plant species Emblica officinalis (Family Euphorbiaceae), Terminalia bellerica (Family Combretaceae), and Terminalia chebula (Family Combretaceae). The effects on the body regarding detoxification and cleansing of the organism have been studied. Specifically for the digestive tract it helps in case of abdominal pain, dyspepsia and constipation; it has different antimicrobial and stimulating properties of the immune system as it is rich in flavonoids (14,15).

Case study

The case study analyzed concerns a 27-year-old woman with fermentative dysbiosis, put on a ketogenic diet for 60 days. She takes a 1350 Kcal at die composed by:

- 70 gr of protein,
- 25 gr of carbs,
- 108 gr of fats

distributed on 3 meals.

In the first time she introduced coconut oil about 10 gr on the breakfast for facilitate the ketosis. Dysbiosis was monitored by evaluating evacuations with the Bristol scale (16), physical examination, peristalsis auscultation and with symptoms related to meteorism and flatulence. The emerged data showed a clear reduction of intestinal gas in the first week, but with still sticky stools (Bristol 5/6); Clear stool improvement (Bristol 4/5) from the second week up to 28 days with a normal peristalsis and abdomen's soft; during the fifth week, the patient showed a slowing of transit with faeces varying at bristol 3 and irritable bowel syndrome. It was necessary to insert during meals, 30 grams of flax seeds, soaked in warm water and consumed within the breakfast and 375 mg of magnesium glycerophosphate 1 hour after dinner. In this phase, a controlled situation persisted in terms of meteorism and flatulence. Already during the sixth week the evacuations started to regain regularity, from the seventh week the patient reported a Bristol 4 and a better management of the lunch. Given the above scientific evidence, the use of Triphala could be proposed to the patient, as an alternative to or in support of flax seeds.

Discussion

The ketogenic diet in the short term produces considerable advantages on the intestinal microbiota, especially if it is dysbiotic, acting as a "inflammation".

The protective effect against the mucosa by akkermansia that occurs in the first phase of ketogenic is certainly fundamental to approach the eubiosis. The slowing down of the transit as an effect of the aglucidic diet can be well managed by the use of flax seeds which, in addition to the emollient mucilage, give a small amount of fiber useful for bacterial reproduction. Of fundamental importance is the integration of magnesium glycerophosphate for its various effects still little investigated on the digestive tract. It is necessary to insert the correct proportions of vegetables during the diet, looking for those with the greatest insoluble fiber in order to have the right amount of FOS, possibly from ever-changing vegetables, so as

to guarantee the highest differentiation of the microbiota.

In the case of disappearance of more intestinal disorders, associating with the aforementioned Triphala integration could give one more chance than the sustainability of nutritional therapy.

References

1. Albillos, A., de Gottardi, A., & Rescigno, M. (2020). The gut-liver axis in liver disease: Pathophysiological basis for therapy. Journal of Hepatology, 72(3), 558-577.
2. Castaldo, G., Palmieri, V., Galdo, G., Castaldo, L., Molettieri, P., Vitale, A., & Monaco, L. (2016). Aggressive nutritional strategy in morbid obesity in clinical practice: Safety, feasibility, and effects on metabolic and haemodynamic risk factors. Obesity research & clinical practice, 10(2), 169-177.
3. Olson, C. A., Vuong, H. E., Yano, J. M., Liang, Q. Y., Nusbaum, D. J., & Hsiao, E. Y. (2018). The gut microbiota mediates the anti-seizure effects of the ketogenic diet. Cell, 173(7), 1728-1741.
4. Zhang, Y., Zhou, S., Zhou, Y., Yu, L., Zhang, L., & Wang, Y. (2018). Altered gut microbiome composition in children with refractory epilepsy after ketogenic diet. Epilepsy Research, 145, 163-168.
5. Xie, G., Zhou, Q., Qiu, C. Z., Dai, W. K., Wang, H. P., Li, Y. H., ... & Ma, Z. Y. (2017). Ketogenic diet poses a significant effect on imbalanced gut microbiota in infants with refractory epilepsy. World Journal of Gastroenterology, 23(33), 6164.
6. DeLuca, J. A., Garcia-Villatoro, E. L., & Allred, C. D. (2018). Flaxseed bioactive compounds and colorectal cancer prevention. Current oncology reports, 20(8), 59.
7. Chhillar, H., Chopra, P., & Ashfaq, M. A. (2020). Lignans from linseed (Linum usitatissimum L.) and its allied species: Retrospect, introspect and prospect. Critical Reviews in Food Science and Nutrition, 1-23.
8. Shaban, S. N., Mokhtar, K. I., Ichwan, S. J. A., & Al-Ahmad, B. E. M. (2020). Potential Effects of Flaxseed (Linum usitatissimum) in Tissue Reparative Processes: A Mini Review. Journal of Biomedical and Clinical Sciences (JBCS), 5(1), 1-7.
9. Arslanoğlu, F., & Aytac, S. (2020). The Important In Terms of Health of Flax (Linum usitatissimum L.). International Journal of Life Sciences and Biotechnology, 3(1), 95-107.
10. Gommers, L. M., Ederveen, T. H., van der Wijst, J., Overmars-Bos, C., Kortman, G. A., Boekhorst, J., ... & Hoenderop, J. G. (2019). Low gut microbiota diversity and dietary magnesium intake are associated with the development of PPI-induced hypomagnesemia. The FASEB Journal, 33(10), 11235-11246.
11. Crowley, E. K., Long-Smith, C. M., Murphy, A., Patterson, E., Murphy, K., O'Gorman, D. M., ... & Nolan, Y. M. (2018). Dietary supplementation with a magnesium-rich marine mineral blend enhances the diversity of gastrointestinal microbiota. Marine drugs, 16(6), 216.
12. Winther, G., Jørgensen, B. M. P., Elfving, B., Nielsen, D. S., Kihl, P., Lund, S., ... & Wegener, G. (2015). Dietary magnesium deficiency alters gut microbiota and leads to depressive-like behaviour. Acta neuropsychiatrica, 27(3), 168-176.
13. Pickering, G., Mazur, A., Trousselard, M., Bienkowski, P., Yaltsewa, N., Amessou, M., ... & Pouteau, E. (2020). Magnesium Status and Stress: The Vicious Circle Concept Revisited. Nutrients, 12(12), 3672.
14. Peterson, C. T., Denniston, K., & Chopra, D. (2017). Therapeutic uses of Triphala in Ayurvedic medicine. The Journal of Alternative and Complementary Medicine, 23(8), 607-614.
15. Tarasiuk, A., Mosińska, P., & Fichna, J. (2018). Triphala: current applications and new perspectives on the treatment of functional gastrointestinal disorders. Chinese medicine, 13(1), 39.
16. Riegler, G., & Esposito, I. (2001). Bristol scale stool form. A still valid help in medical practice and clinical research. Techniques in coloproctology, 5(3), 163-16.