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Probiotics in urolithiasis

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Abstract

Urolithiasis is considered as a civilization disease. The prevalence is estimated at 5-20% of the population. There are many litogenesis risk factors such as hypercalciuria, hypophosphaturia, low urine pH or increased excretion of oxalates with urine - a condition called hyperoxaluria which is a major risk factor for renal stones. Oxalate urolithiasis can be caused by defects in oxalates metabolism, excessive intake in the diet or increased intestinal absorption of oxalates. The reason of hyperoxaluria might be a genetic defect (primary hyperoxaluria) or excessive consumption due to improper diet (secondary hyperoxaluria). Human intestinal flora plays an important role in oxalates metabolism. Described in the 1980s Oxalobacter formigenes, inhabiting the human gastrointestinal tract is known for contributing to decrease the excretion of oxalates with urine and consequently, reduce the risk of recurrence of kidney stones. Other

known bacteria which have a beneficial effect on the metabolism of oxalates include Lactobacillus, Enterococcus faecalis, Providentia retgerri. These bacteria may be useful in the future treatment of calcium oxalate urolithiasis.

Aim of the paper. The aim of the paper was to analyse the influence of probiotics on urolithiasis.

Keywords: urolithiasis, probiotics, oxalate, citrate, Oxalobacter, hyperoxaluria

Introduction

Urolithiasis is considered a civilization disease. The prevalence is according to geographical area, age, sex and type of lithiasis. It is estimated between 4-20% (2).The risk factors of the disease include insufficient fluid intake, prolonged immobilization, metabolic disorders that may contribute to the creation of deposits in the kidneys. The pathophysiology of the stone formation is the result of supersaturation of urine with substances capable of crystallization such as oxalate, uric acid, phosphates and the impairment of inhibition mechanisms of crystallization (magnesium, citrate, protein Tamm – Horsfall, or glycosaminoglycan). It promotes the formation of nuclei of crystallization and aggregation, which damage the uroepithelium. One of the most common metabolic disorders in patients with urolithiasis of the urinary system are hypercalciuria - an excess excretion of calcium in the urine (more than 4 mg./kg m. c./day), i.e., 0.1 mmol/kg/24 h (1).

Epidemiology

Hyperoxaluria is defined as oxalate excretion in the urine exceeding 45 mmol/1.73 m2body area/day (2). Calcium oxalate deposits are the most common cause of kidney stones. They represent more than 70-80% of all the cases. Oxalate urolithiasis can be caused by disorders of oxalates metabolic processes, excessive consumption or increased absorption of oxalates in the gastrointestinal tract. Oxalic acid is the end product of metabolism, i.e. are not consumed in further biochemical processes in the body and excreted mainly in urine. Increased excretion of oxalates in urine can lead to creation of oxalic acid and calcium compounds and the formation of small crystals, which are the basis for kidney stones.

Two types of hyperoxaluria can be distinguished: type 1 diagnosed in infants, associated with a deficiency of glyoxylic acid carboligase and type 2 associated with mutation of genes

encoding reductase and reductase glyoxylate hydroksypyruvate (3). Both are fairly rare and most often lead to secondary hyperoxaluria caused by high oxalate foods for instance cocoa, chocolate, cola excessive intake of vitamin C or bowel diseases such as Crohn's disease or short bowel syndrome (1,3). The occurrence of nephrocalcinosis in patients suffering from is higher than rest of the population - 92% of post-mortem examination of these patients revealed deposition of calcium salts in the renal parenchyma (4).

In some patients with calcium oxalate urolithiasis excessive absorption of oxalate in the gastrointestinal tract is observed. It can be related to the improper metabolism of intestinal. In this case, it recognizes hyperoxaluria type 3, which is not accompanied by a defect in liver enzymes and diseases of the gastrointestinal tract (2,3).

Another reason of secondary hyperoxaluria is the reduction in intestinal bacteria dwelling in large intestine decomposing oxalates, such as Oxalobacter formigenes, Bifidobacterium lactis can cause increased intestinal absorption of oxalic acid. (3) it is assumed that the number of bacteria O. formigens between 10^{6} and 10^{8} CFU in 1 gram of feces is enough to reduce oxalates absorption in intestines (6).

Probiotics

Physiologically excreted oxalates come mainly from glyoxylic acid, glycine, ascorbic acid metabolism and gastrointestinal tract. The term probiotics that comes from Greek meaning ,,for life" changed meanings over the years. First used in 1965 by Lilley and Stillwell to describe substances produced by one microorganism and promotes growth of another. (7).. The Expert Panel commissioned by Food and Agriculture Organization of the UN in 2001 supported by WHO finally defined probiotics as "Live microorganisms which when administered in adequate amounts confer a health benefit on the host" (8).

Probiotics are living microorganisms which in adequate amounts, have a beneficial effect on health.. In its composition may contain probiotic strains of Lactobacillus spp., Streptococcus spp., Saccharomyces spp or Aspergillus spp (10).

In particular the potential benefits for the healthy consumer include include: stimulating the growth and activity of selected strains of bacteria that are profitable to health, reduce the pH of the intestinal contents, to maintain the integrity of the mucosal barrier, stimulate intestinal immunity, reduction of hypercholesterolemia, affect the level of uremic toxins and some of them indirectly affect the use of inhibition of stone formation in urolithiasis (11,12).

Characteristics of Oxalobacter formigens

This Gram - negative rods, immotile occurring in the large intestine of man and ruminants. This is anaerobic bacteria which as the main source of energy and carbon through the solid of the two enzymes formylotransferaze reductase(frc) and oxalodecarboxylaze - reductase inhibitor used oxalates. The decomposition oxalic acid is formed formin and CO2, which is subject to further metabolism or remain excreted in the stool (4). O. formigens does not grow on artificial grounds to bacteria anaerobic exercises even after enrichment of oxalates. Bacteria due to the content of Coli lives in the gastrointestinal tract of animals and humans, where regulating the absorption of oxalates and their level in blood serum. The number of bacteria 10 to 7 per one gram of feces and the efficiency of the oxalate decomposition process is 0.1-4.4 nmol per hour per gram of stool (6). It was noted that the bacteria colonize the intestines gradually between 9 and 12 months of age, and at the age of 6-8 years is present in most healthy children. Studies conducted in Ukraine showed that at the age of 12 years, almost 70-80% of children are colonized by O. formigens (12). In Poland, it predict that 26% of children are colonized by this bacterium with age, the frequency of colonization decreases on average by 25% before reaching adulthood (12). Multiple and chronic antibiotic therapy contributing to the reduction of colonization by O. formigens may be the cause of hyperoxaluria (6).

It has been shown that long-term antibiotic therapy contributed to a decrease in the degree of colonization, but the germ was present in more than 40% of people after a month of starting treatment (5). The importance of that anaerobic bacteria contributed to the attempt to prevent oral antibiotic therapy in patients with a bile stone disease of the urinary system or hyperoxaluria. In the review Hoppe, etc. in patients suffering from primary hyperoxaluria type 1 obtained a significant reduction in daily excretion of oxalates, as well as clinical improvement (reduction of pain caused by oxalate osteopathy or skin deposits of calcium oxalate), despite of the fact that colonization gastrointestinal tract Oxalobacter formigens was not permanent the determinant of presence microbe in jllicie concentrations of soluble oxalates, the availability of nutrients that contain oxalates and also in favorable environmental conditions, such as the presence of components hindering the development O. formigenes or pH (14,15). In the work and Doanie. it was shown that during supplementation of oxalates enriched spinach (about 1500 mg of oxalate) the number of bacteria in the feces of O. formigens increased to 5-14 times. (16) it is assumed that the colonization of the colon O. formigens reduces the risk of calcium oxalates urolithiasis even to 70 %. (6).

In the study of Kwak et al. conducted on 103 patients with confirmed oxalates urolithiasis allowed us to determine the difference between group statistically colonized and uncolonized by these sticks in the concentration of oxalates in the daily collection of urine and they were, respectively, 0.36 and 0.29 mmol. The concentration of oxalate was dependent on the number of bacteria. Along with the growth of the bacteria there was reduction in the concentration of oxalates in the urine (15).

The effect of antibiotics therapy on colonization by O. formigenes

It is known that an important factor that reduces the amount of bacteria colonized the gastrointestinal tract are antibiotics. Studies conducted drug-sensitiveness strains of O. formigenes isolated from humans showed that these strains are very sensitive to the widespread use of antibiotics, however, the value of MIC (Minimum Inhibitor Concentration) varied among the different strains. In one study, scientists showed that all strains of O. formigenes were resistant to ampicillin, amoxicillin and streptomycin at the time were sensitive to doxycycline and claritromicin. They also show, depending on the strain sensitivity to erythromycin, amoxicillin with clavulanic acid, chloramphenicol, and nalidixic acid (17).

Condition in which there is a decrease in colonization of the colon with the help of this bacteria (for example, as a result of treatment of antibiotics or in patients with inflammatory bowel disease or cystic fibrosis), could contribute to hyperoxaluria. It was also found that those colonized by Oxalobacter formigenes have a significantly lower risk of relapse compared with people without the bacteria (18).

Lactobacillus acidophilus

Another bacteria that were covered by the study was lactic acid. It is a gram-positive rod-shaped bacterium. Bacteria lactic acid fermentation, due to its properties, has been named the safe bacteria (GRAS generally considered as safe) and has found application in the production of food and medicines. Due to its probiotic properties, it has been called a probiotic bacterium. Their benefits include, in particular, is not pathogenic to humans, the ability to colonize the human gastrointestinal tract. Strains Lactobacillus acidophilus and Streptococcus thermophilus effectively degraded oxalate in vitro, while Lactobacillus plantarum and Lactobacillus brevis are not inhibited in the presence of oxalate. This fact affects the receiving effect of reducing oxaluria after the termination intake of lactic acid. (19) In the study by Lieske and others researchers have published the results of a research indicating the decline oxaluria when using

mix of the following strains of bacteria: Lactobacillus acidophilus, Lactobacillus brevis, Streptococcus thermophilus, Bifidobacterium infantis.

The patients received the mixture for 3 months in increase every 4 weeks concentrations leading to reduce oxaluria by about 20 %. Interesting fact appears to be short-term growth oxalurii for the supply of lactic acid bacteria in the highest concentration. The researchers explain this event the possibility of the existence of maximal intestinal concentration bacterial degrading oxalates. (20).

In studies conducted at the Institute of Pediatrics in Łódz, administered the drug, consisting out of 3 strains of lactic acid l. acidophilus. Each child gets a day 9.6 x 10 9 bacterial cells. The result was the reduction in concentration of oxalate in the urine in patient with oxalates calcium urolithiasis about 15-93 % in 11 of the receiving patients . Further studies suggest the ability of Lactobacillus spp, to make the degradation of oxalates in the digestive tract, which can help to know the occurrence of kidney stones. Administration (19,21) a mixture that contains lactic acid bacteria, PTC patients with magnesium stones calcium oxalate, chronic fat malabsorption Anh hyperoxaluria outcomes could reduce the excretion of uric acid oxalate 19% after one month. (22)

The bacterium lentum Eubakterium

The output of the third lentum gram-positive, anaerobic bacillus, which contains two enzymes (oxalyl-COA decarboxylase and formylCoA transferase) that take part in degradation of oxalate. In studies conducted in Japan, results have been obtained where this bacterium within 24 hours shows the degradation of oxalate in the artificial digestive system. (23,24)

This is the first bacterium of the family Enterobacteriaceae, it is extracted from the human feces, which plays an important role in the degradation of oxalate characterized by weak virulence. This oxalatedegrading P. retgerri produced two proteins (65 kDa and 48 kDa) that seemed likely to correspond is oxalyl-Reductase decarboxylase and formyl-transferase Reductase, respectively, from O. formigenes. (25). There was another bacteria, as well as other bacteria that can lead to the degradation of oxalic acid, such as Enterococcus faecalis, Providencia sp. in conditions of oxygen starvation.

Conclusion

In recent years, the main goal of the research scientists were the microbes decomposing the oxalates, such as Oxalobacter formigenes, Lactobacillus, Eubacterum. Best known sticks O. formigenes colonized the colon effectively perform the process of decomposition of oxalic acid,

which is a promising method in preventing and curbing the creation of toxins in the bladder. However, their application remains a matter of controversy. The main limitation in the use of O. formigenes is a difficulty in the maintenance of secondary colonization in people with hyperoxaluria. Still there is no sufficient of information about the growth and colonized of this bacterium in the host organism, and also metabolic activity. It learned a lot of useful effects of probiotics, it is possible that this list can also be added to disease prevention and treatment of stones in oxalate-calcium exchange. Necessary, however, further research in this area.

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