Review article

Probiotics: A new hope for Arsenic management

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Abstract : Nowadays drinking water contamination by arsenic is a major health problem of the world. The chronic low dose (>50µg/L) exposure to arsenic through contaminated tube well water may cause the development of arsenicosis. The present knowledge about the management of arsenicosis is far from satisfactory. Gut bacteria have important and specific metabolic, trophic and protective functions A study conducted by Upreti et al17, indicated that arsenic resistant probiotic Lactobacilli would be useful in the prophylactic interventions of arsenic related gastro-intestinal toxicity. probiotics are `Live microorganisms which when administered in adequate amounts confer a health benefit on the host'. Probiotic bacteria are known to be promoters of the host body's defense mechanism by stabilizing the local microflora, triggering a humoral immune response and constructing a barrier against immunological disorder. Here in this study, it could be assumed that there was multiplication of probiotics bacteria in the digestive tract, therefore an increase of good bacteria in the gut and thus increased stool arsenic excretion

Key word : Probiotics, arsenic contamination, management

Introduction

Arsenic is the 20th most abundant element in the earth's crust and is widely distributed throughout the nature as a result of weathering dissolution, fire, volcanic activity and anthropogenic input.[1] The majority of the human are chronically exposed to low levels of arsenic, principally through ingestion of food and water and to some extent due to inhalation of arsenic contaminated air.[2] Now a days drinking water contamination by arsenic is a major health problem of the world. In our country, the situation is deteriorating day by day as the new cases of arsenic poisoning are still being reported in different parts of the country.[3] Out of 64 districts, 61 districts have arsenic concentration in ground water above the maximal permissible limit of 0.05 mg/L[6]. Official reports (Director General of Health Services, Government of Bangladesh) show that more than 60,000 people are suffering from arsenicosis in Bangladesh[4]. About 35-77 million Bangladeshis have already been chronically exposed to increased concentrations of arsenic through drinking water[8] and food [9,10].

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Effect of arsenic on health

The chronic low dose (>50µg/L) exposure to arsenic through contaminated tube well water may cause the development of arsenicosis.[5] Already more than 40,000 people developed signs and symptoms of chronic arsenic poisoning. Skin manifestations mainly melanosis and leukomelanosis are considered to be the earliest dermatological findings but hyperkeratotic lesions of the skin (keratosis) are the most distinctive skin features of long-term arsenic exposure[7]. A large number of populations in Bangladesh are suffering from melanosis, leuco-melanosis, keratosis, hyperkeratosis, dorsum, non-pitting oedema, gangrene. These manifestations of chronic arsenicosis develop slowly usually 6 months to 2 years[14]. In the study by Fierz (1965), the minimal latency period from exposure to development of arsenical keratoses was 2.5 years, and the average latency period for skin cancer was 14 years. The present knowledge about the management of arsenicosis is far from satisfactory. Though several studies are making progress on this issue but there are no sufficient evidences to confirm or to reject their effectiveness. Some of them cause side effects like GIT upset, dermatomyositis, auto-immune disease and also recurrence of the sign-symptoms after withdrawal of drugs.

Gut flora

In our body, there are 10 trillion cells but bacterial count is approximately 100 trillion. That is ten times than the total body cell. Micro-oganisms start colonization of the gastro intestinal tract soon after birth and this process continues throughout the life. The human gastrointestinal tract can

be described as a complex microbial ecosystem. The intestinal habitate of an individual contains 300-500 different species of bacteria[1,3]. Gut bacteria have important and specific metabolic, trophic and protective functions5. The constant interaction between the host and its microbial guests can infer important health benefits like regulation of colonic pH, production of short chain fatty acid and salvage of energy from non digestible food components[14]. Available literature is scanty regarding the interaction between inorganic arsenic and gut microflora[8].

Role of gut flora on arsenic metabolism

Studies carried out suggest that bacteria present in the gastro-intestinal tract may play a role in arsenic detoxification (Rowland and Davies, 1981). They showed an in vitro metabolism of inorganic arsenic by gastro–intestinal microflora of rat. They suggested that in presence of caecal contents, small amounts of methylarsonic acid and dimethylarsenic acid were formed. The metabolism was inhibited by adding antibiotics, thus indicating that bacteria were involved. Gut bacteria have important and specific metabolic, trophic and protective functions5. The constant interaction between the host and its microbial guests can infer important health benefits[16]. Available literature is scanty regarding the interaction of inorganic arsenic with gut microflora[9].

The gastrointestinal (GI) tract presents itself as the first organ susceptible to attack by ingested xenobiotics consequently; concentrations that must be endured by this tissue are often many times higher than those endured by other tissues[10]. An important study was carried out to compare the effects of arsenic toxicity on intestinal epithelial cells and resident gut flora18. The bacteria selected for this study from stool culture were E. coli, Pseudomonas sp., Lactobacilli sp and Staphylococcus sp. Intestinal epithelial cells were treated with different concentration of arsenic (0-10 ppm). Here, dehydrogenase activity (DHA) and esterase activity (EA) of intestinal bacteria and epithelial cells were measured. The growth profile of gut bacteria and intestinal cell viability revealed an arsenite concentration dependant inhibition following 24 hours in vitro exposure to arsenic. This study suggests that arsenic is toxic to resident gut flora in high concentration (2-10 ppm). There was significant concentration dependent inhibition of DHA and EA (40%-72%) as compared to controls, with arsenite exposure to 5 ppm and 10 ppm, respectively[11]. In 2009, Choudhury et al, 3 carried out an in vivo study on rats to see the influence of arsenic on aerobic gut flora. The study shows a significant inhibition of gut flora after 2 weeks administration of arsenic (1 mg/L) with a decrease in stool arsenic level and increase in liver arsenic level. However, this inhibitory effect of arsenic on gut flora was not observed in presence of vitamin E (1 mg/day) or selenium (0.4 µg/day). Rats that received only arsenic, a decrease in stool and an increase in liver arsenic level was might be due to inhibition of gut bacterial count resulting in decreased bacterial detoxification of arsenic by gut bacteria and its increased deposition in liver[3]. Microbes have been shown to reduce a wide range of toxic metals through detoxification and elimination[11]. Bacteria have been reported to produce MMA (V) or DMA (V)[2] which are non toxic and finally TMAO in gaseous form whose volatilization lowers arsenic concentration that may contribute to global cycling of arsenic[12]. So, more stress is being given on bacterial detoxification of arsenic which is considered to be non-toxic.

Concept of probiotics

Probiotics is a Greek word in which `Pro' means for and `bios' means life. So, probiotics means `for life'. According to WHO (2002), probiotics are `Live microorganisms which when administered in adequate amounts confer a health benefit on the host'. The idea of using microbes to promote good health or to prevent disease is not new. In the early 1900, Russian immunologist Elie Metchnikoff, reported the favorable effects of soured milk in human and suggested that consumption of live microbes (possibly LAB) in such fermented milk may help improve the balance of the gut Microflora. Since then, microbial probiotics have gained an increased interest and their use is now widely accepted. Several microorganisms,under the name of "probiotics" have been proposed and used in a wide range of clinical trials, ranging from diarrheal disease to cancer prevention.

Role of probiotics

The composition of the gastro-intestinal flora varies between the individuals and also within the same individual during life. It contains both pathogenic and non-pathogenic bacteria that exist in a complex symbiosis. Various factors such as diet, climate, aging, medication (particularly antibiotic consumption), illness, stress and life style can upset this balance leading to diarrhea, mucosal inflammation, or other serious illnesses. Maintenance of an optimal gut flora balance requires that 'friendly or non-pathogenic' bacteria, such as the Gram

positive lactobacilli and bifidobacteria (>85%of total bacteria), form a barrier against pathogenic bacteria9. Probiotics are possibly the most natural and safe means of maintaining this balance

Before birth, the digestive tract of the fetus is sterile, but within few hours of birth, the baby acquires a complex collection of microorganisms which populate in the mouth and then eventually the full length of the tract are colonized. The development of specific microorganisms is influenced by the exposure to certain factors such as maternal microbiota, environmental contact, mode of delivery and the infant's diet. Through normal vaginal birth, an infant is exposed to the mother's vaginal and fecal flora, which results in the colonization of Lactobacillus, Bifidobacterium etc[15]. Studies show that less than 7 years of age the symptoms of arsenicosis are rare[3,12]. So, there may be a relation between Lactobacillus and arsenicosis. They also suggested that a bacteria, before being selected as probiotics, should be non-pathogenic, non-toxigenic, should retain viability during storage and use, should have the capacity to survive and metabolise in the gut and finally should have documented health effects. Bifidobacterium and Lactobacilli exert some health promoting properties. A study conducted by Upreti et al17, indicated that arsenic resistant probiotic Lactobacilli would be useful in the prophylactic interventions of arsenic related gastro-intestinal toxicity. Another study conducted by Rashid et al., (2012) showed that the colony count of E. coli in arsenic exposed controls was reduced and in arsenicosis patients it was severely reduced when compared to healthy volunteers. There was significant decrease in stool arsenic level and increase in nail arsenic level of both arsenic exposed controls and arsenicosis patients. After 12 weeks supplementation of probiotics, the E. coli count and stool arsenic level both were significantly increased in arsenic exposed controls and arsenicosis patients in comparison to healthy volunteers. On the other hand, nail arsenic level decreased in the above mentioned two groups in relation to healthy volunteers. Bifidobacterium is one of the most important strictly anaerobic bacterium which acounts for 25% of the total anaerobic counts[14]. So, Lactobacilli may be helpful in arsenicosis patients. Here, in this study, the probiotics containing Lactobacilli bulgaricus and Bifidobacterium along with fructo-oligosaccaride as prebiotics were chosen as they are commercially available, cheap and easily tolerated by patients. There is now strong evidence for their use in treating and preventing some human diseases.

Conclusion:

Manipulation of the human intestinal flora offers potentially to improve health through a variety of mechanisms[14]. Probiotic bacteria are known to be promoters of the host body's defense mechanism by stabilizing the local microflora, triggering a humoral immune response and constructing a barrier against immunological disorder. Here in this study, it could be assumed that there was multiplication of probiotics bacteria in the digestive tract, therefore an increase of good bacteria in the gut and thus increased stool arsenic excretion. Increased bacterial multiplication is associated with increased bacterial activity. In addition increased bacterial contain high amount of glutahione which efficiently reduces toxic substances. Moreover application of lactic acid bacteria in removing toxic metals from water has been studied. They have also been reported to remove mycotoxins and cyanotoxins from food and water respectively. Moreover probiotics are safe, natural, inexpensive and have no known negative long term effects.

References

1. Bengmark S. Ecological control of the gastrointestinal tract. The role of probiotic flora. Gut. 1998; 42; 2-7.
2. Bentley R, Chasteen TG. Microbial Methylation of Metalloids: Arsenic, Antimony, and Bismuth. Microbiol Mol Biol Rev. 2002; 66: 250-71.
3. Choudhury ZK, Misbahuddin M, Hosain AKMM, Saleh AA. Inhibitory effect of arsenic on aerobic gut flora in rat. BMRC Bull. 2009; 35: 79-83.
4. Editorial , the Daily Star. April 3, 2012; p 1
5. Gaurner F, Malagelada JR. Gut flora in health and disease. The Lancet 2003; 361: 512-19.
6. Haque AAM, Thwe HM, Jayasuria HPW, Hossain MZ, Rahman M, Rashid HU, Matsumara K. Ground water arsenic contamination: Food safety and human health hazards in Bangladesh. CMU J Nat Sci. 2007; 6: 321-39.
7. IPCS. Arsenic and arsenic compounds. Environmental health criteria 224. 2nd ed. World Health Organization: Geneva, 2001; 7-8.
8. Karagas MR. Arsenic-related mortality in Bangladesh. The Lancet. 2010; 376: 213-14.
7. Khan MAK, Misbahuddin M, Rahman MS, Khandker S,

Mahmud IA. Arsenic estimation in food stuffs of arsenic exposed areas in Bangladesh. Applied Research on arsenic in Bangladesh. 2007; 23: 31-42.

8. Misbahuddin M. Consumption of arsenic through cooked rice. The Lancet. 2003; 361: 435-36.
9. Narayana SS, Jalgaonkar S, Shahani S and Kulkarni VN. Probiotics: Current trends in the treatment of diarrhea. Hong Kong Med J. 2010; 16: 213-8.
10. Qin J, Rosen BP, Zhang Y, Wang G, Frankie S, Rensing C. Arsenic detoxification and evolution of trimethyle arsine gas by a microbial arsenite S-adenosylmethionine methyltransferase. PNAS. 2006; 103: 2075-80.
11. Rowland IR, Davies MJ. In vitro metabolism of inorganic arsenic by the gastro -intestinal microflora of the rat. J Appl Toxicol. 1981; 1: 278-83.
12. Rahman MM, Chowdhury UK, Mukherjee SC, Mondal BK, Paul K, Lodh D, Biswas K, Chanda CR, Basu GK, Saha KC, Roy S, Das R, Palit SK, Quamruzzaman Q, Chakraborti D. Chronic arsenic toxicity in Bangladesh and West Bengal, India- A review and commentary. J Toxicol Clin Toxicol. 2001; 39: 683 - 700.
13. Rashid N, Misbahuddin Mir, Choudhry ZK, Abu Saleh A, Ibn Sattar N. The colony count of Escherichia coli in the stool of palmar arsenical keratosis following probiotics supplementation . Bangladesh Journal of Pharmacology 2014; 09(2): 176-181.
14. Salminen S, Bouley C, Rault MCB, Cummings JH, Franck A, Gibson GR, Isolauri e, Moreau MC, Roberfroid M, Rowland I. Functional food science and gastrointestinal physiology and function. Br J Nutr. 1998; 80: 147-71.
15. Upreti RK, Shivastava R, Chaturvedi UC. Gut microflora & toxic metals: Chromium as a model. Indian Med Res 2004; 119: 49-59.

15. Upreti RK, Kannan A, Shivastava R, Chaturvedi UC. A comparative study on rat intestinal epithelial cells and resident gut bacteria (ii) effect of arsenite. Biol Med Environ Sci. 2006; 19: 77-86.
16. Upreti RK, Sinha V, Mishra R, Kannan A. In vitro development of resistance to arsenite and chromium-VI in Lactobacilli strains as perspective attenuation of gastrointestinal disorder. J Environ Biol. 2011; 32: 325-332.