October 2007

The potential role of probiotics in reducing poverty-associated infections in developing countries

Special Article

The potential role of probiotics in reducing poverty-associated infections in developing countries

Kingsley C. Anukam

Department of Microbiology, Faculty of Basic & Applied Sciences, Benson Idahosa University, Benin City, Nigeria.

J Infect Developing Countries 2007; 1(2):81-83.

Received 7 March 2007 - Accepted 17 May 2007.

Probiotics are defined by the Food and Agricultural Organization/ World Health Organization as "live microorganisms which when administered in adequate amounts confer a health benefit on the host" [1]. The potential benefits of their use have not been adequately investigated, especially in the developing world. Japan introduced Yakult, a probiotic fermented food drink in 1935, and in the Northern hemisphere, research and use of probiotics has gained an unprecedented momentum in the last decade [2]. Use of probiotics is not uncommon in Europe [3], but in many developing countries use of probiotics in its present definition is a foreign concept. Some African traditional foods are fermented with lactic acid bacteria, and some may have probiotic properties, but clinical evidence is yet to be deciphered. Nonetheless, many communities rushing to "westernize" are losing their fermented food traditions.

The strongest evidence for the possible use of probiotics in developing countries comes from studies demonstrating that *Lactobacillus rhamnosus* GG [4], *L. reuteri* ATCC 55734 [5], *L. casei* DN-114 001 [6] and *Bifidobacterium lactis* Bb12 [7] can reduce the duration of diarrhoea and in some cases prevent it. Advances in medicine and hygiene have increased the survival of young children; however, one child still dies every 15 seconds from diarrhoeal diseases. The current accepted treatment of diarrhoea involves the use of antibiotics and oral rehydration therapy in the short run. While clean water and good hygiene play a significant role for the prevention of diarrhoea,

Kingsley Anukam: Using probiotics to fight HIV

Dr. Kingsley Chidozie Anukam was born and raised in Nigeria. He attended the University of Benin and University of Calabar, both in Nigeria, eventually earning his Bachelor's in Medical Laboratory Sciences in 1991, two Masters' degrees in the area of Pharmaceutical Microbiology in 1997, and his Master's in Health Planning and Management (MHPM) in 2000. In 2001 he began work on his PhD in Pharmaceutical Microbiology on probiotic lactobacilli at the University of Benin. He was awarded his Doctor of Philosophy degree in 2005 upon completion of his work at the University of Benin, in conjunction with his work at the Lawson Health Research Institute, University of Western Ontario, London, Canada, in 2004.

Not long after completing his PhD, Anukam was invited by Dr. Gregor Reid, the director of the Canadian Research and Development Center for Probiotics in Canada, to undergo post-doctoral training at an international probiotics research center. Dr. Anukam has published more than 30 times in national and international journals and, with Reid, has published a number of articles and conference papers related to probiotics. Most recently, Dr. Anukam and Dr. Reid presented at the 2006 Infection and Immunity Research Forum. The title of their presentation was: "HIV/AIDS in Africa, Might Probiotics Help?" The basis of the presentation was on research they had previously done on probiotics being used as a treatment for Bacterial Vaginosis (BV), which is a risk factor for contracting HIV/AIDS.

The presence of bacterial vaginosis causing organisms provokes the loss of normal vaginal bacterial flora, and causes vaginal inflammation and increased pH levels. The resulting altered vaginal environment increases the risk of transmission of HIV [1]. Anukam and co-workers have sought a more effective treatment of bacterial vaginosis in an attempt to limit the transmission of HIV/AIDS. In a 2006 article,

Anukam et al. [2] showed that five days of intravaginal probiotic lactobacilli treatment promotes cure of bacterial vaginosis and restores the natural vaginal lactobacilli.

the normal microbiota of the gastrointestinal tract can be fortified with probiotics, aiding in the successful prevention and treatment of diarrhoeal diseases [8].

The case for microbicides using lactobacilli presented in a United Nation's publication was my initial motivation for delving into probiotics research. I also received much encouragement from Dr Gregor Reid, the acclaimed Canadian probiotic microbiologist. My preliminary survey showed tremendous interest from women on the potential use of probiotics for maintaining normal urogenital health [9]. In developing countries such as Nigeria, the mention of bacteria elicits a negative reaction from people who fail to realize that we cannot exist without a multitude of positive microbes in our systems. Even amongst supposedly informed health care providers, knowledge of probiotics was shown to be minimal [10]. Our animal studies provided positive results on the safety of probiotic bacteria [11, 12]. In another study we sought to determine whether vaginal *Lactobacillus* species found in Nigerian women differ substantially from those isolated from Canadians and Swedes. The findings indicate that the predominant vaginal *Lactobacillus* species is similar to species in women from these Northern countries [13]. The correlation between loss of lactobacilli and the subsequent prevalence of bacterial vaginosis causing organisms, inflammation, elevated pH, and increased risk of HIV, led to our initial trial. We investigated the effectiveness of the well-established probiotics GR-1 and RC-14 in augmenting metronidazole treatment of bacterial vaginosis [14]. We recently demonstrated that vaginal application of probiotics can treat symptomatic bacterial vaginosis [15]. In order to test whether probiotics can have any impact on diarrhoea associated with HIV/AIDS, we fortified conventional yogurt with probiotics. The study indicated that probiotics can function positively in diarrhoea cases in AIDS patients without side effects [16].

Probiotics are most often incorporated in yogurt and fermented milk. Numerous other probiotic-fortified products are sold in tablet, capsule, and powder forms. Companies producing these products are primarily based in America, Europe and Asia. Within the context of the developing world, it is unfortunate that few of these companies are making their impact felt. Probiotic products tend to be high in cost and not likely to produce significant profit margins when marketed in developing countries.

These findings suggest that by promoting the maintenance of healthy vaginal flora, probiotic products could limit the spread of HIV/AIDS in sub-Saharan Africa.

Dr. Anukam and other investigators also advocate the use of probiotic products to treat diarrhoeal disease in sub-Saharan Africa. Reid, Anand, Anukam et al. [1] assert that probiotic drinks are a means to replace fluid and electrolyte loss caused by diarrhoea. In order to support these claims, they cite a Peruvian randomized double-blind study in which the once-daily intake of *Lactobacillus rhamnosus* GG 6 days per week led to fewer episodes of diarrhoea in 204 undernourished children [3]. Inspired by studies such as this, Anukam, Reid and others at the University of Western Ontario are collaborating with the Kenya Medical Research Institute, Kivilini Women's Group, and Tanzanian personnel to create a community kitchen in Mwanza where women are trained to make probiotic yogurt [4].

Although Anukam's research and ideas suggest that probiotics would enhance the health and well-being of individuals in sub-Saharan Africa, the use of probiotics has not become popular for several reasons outlined by Anukam and Reid [4]. First, pharmaceutical companies that manufacture probiotics would be forced to lower prices which would adversely affect their revenues. Secondly, storage and distribution problems make the allocation of probiotics difficult. Dairy versions of probiotics require refrigeration, and other forms incorporated in tablets, capsules, and powders must be retained in proper vials with appropriate dessicants. Accordingly, storage and distribution issues present major challenges to the effective implementation of probiotic treatment since domestic technology is frequently insufficient for proper maintenance. Finally, cultural acceptance presents a major challenge for probiotic use. For example, if local customs call for a diet free of dairy products, it could be difficult to convince these people to consume a fermented milk drink.

Diarrhoeal disease, HIV/AIDS, and other infectious diseases are major contributors to morbidity and mortality in sub-Saharan Africa. Morbidity from these illnesses causes economic hardship and mortality results in the loss of the next generation and destruction of the present adult leadership. Probiotic research by Anukam and others may lead to new ways to reduce the burden from disease, and create benefits through economic growth.

References

1. Reid G, Anand S, Bingham MO, Mbugua G, Wadstrom T, et al. (2005) Probiotics for the developing world. J Clin Gastroenterol 39: 485-488.

2. Anukam KC, Osazuwa E, Osemene GI, Ehigiagbe F, Bruce AW, et al. (2006) Clinical study comparing probiotic Lactobacillus GR-1 and RC-14 with metronidazole vaginal gel to treat symptomatic bacterial vaginosis. Microbes Infect 8: 2772-2776.

3. Oberhelman RA, Gilman RH, Sheen P, Taylor DN, Black RE, et al. (1999) A placebo-controlled trial of Lactobacillus GG to prevent diarrhoea in undernourished Peruvian children. J Pediatr 134: 15-20.
4. Anukam K, Reid G (2005) Providing probiotics to sub-Saharan Africa: ethical principles to consider. Journal of Complementary and Integrative Medicine 2: Article 10.

By Derek A Lief and Kernika Gupta

Nevertheless, severe lack of probiotic use and research in Africa is of particular concern, as Africa is the continent most severely afflicted with the conditions that probiotics have been shown to ameliorate.

To promote probiotic research and use in developing countries, multinational companies and governments interested in the potential of probiotics must forge a concerted effort. A mechanism for promoting clinically proven probiotics must be developed. In addition, support for basic and clinical studies examining local customs of using fermented foods to determine which products deliver the health benefits of probiotics should be encouraged.

While evidence exists to demonstrate that probiotic products can improve the health and well-being of patients, it is important that these products are differentiated from so-called "probiotics" which use the term but do not yet have published clinical documentation on what benefits they confer to humans [17, 18]. The potential of probiotics has yet to be exhausted as more studies reveal other clinical applications such as lowering cholesterol levels, reducing allergies and colorectal cancers, and boosting immunity. These health benefits conferred by probiotics are universal and the developing world, burdened by poverty-associated infectious diseases such as diarrhoea and HIV/AIDS, will certainly benefit more from probiotic use.

References

1. FAO/WHO (2001) Evaluation of health and nutritional properties of Probiotics in food including powdered milk and live lactic acid bacteria. Food and Agriculture Organization of the United Nations and World Health Organization Report. http://www.fao.org/es/ESN/probio/probio.htm (accessed 15 May, 2007).
2. Shimakawa Y, Matsubara S, Yuki N, Ikeda M, Ishikawa F (2003) Evaluation of Bifidobacterium breve strain Yakult-fermented soymilk as a probiotic food. Int J Food Microbiol. 81(2):131-136.
3. Bernardeau M, Guguen M, Vernoux JP (2006) Beneficial lactobacilli in food and feed: long-term use, biodiversity and proposals for specific and realistic safety assessments. FEMS Microbiol Rev. 30(4):487-513
4. Oberhelman RA, Gilman RH, Sheen P, Taylor ND, Black RE, Cabrera L, Lescano AG, Meza R, Madico G (1999) A placebo-controlled trial of Lactobacillus GG to prevent diarrhea in undernourished Peruvian children. J Pediatrics 134: 15-20.
5. Weizman Z, Asli G, Alsheikh A (2005) Effect of a probiotic infant formula on infections in child care centers: comparison of two probiotic agents. Pediatrics 115(1):5-9.
6. Pedone CA, Arnaud CC, Postaire ER, Bouley CF, Reinert P (2000) Multicentric study of the effect of milk fermented by Lactobacillus casei on the incidence of diarrhoea. Int J Clin Pract. 54(9):568-71.
7. Phuapradit P, Varavithya W, Vathanophas K, Sangchai R, Podhipak A, Suthutvoravut U, Nopchinda S, Chantraruksa V, Haschke F (1999) Reduction of rotavirus infection in children receiving bifidobacteria-supplemented formula. J Med Assoc Thai 82 (Suppl 1):S43-S48.
8. Lemberg DA, Ooi CY, Day AS (2007) Probiotics in paediatric gastrointestinal diseases. J Paediatr Child Health. 43(5):331-336.
9. Anukam KC, Osazuwa EO, Reid G, Katsivo MN (2004) Receptivity for probiotic products among pre-menopausal female students in an African university. Sex Transm Dis. 31(8): 460-464.
10. Anukam KC, Osazuwa EO, Reid G (2006) Knowledge of probiotics by Nigerian clinicians. Int J Probiotics Prebiotics. 1 (1):57-62.
11. Anukam KC, Osazuwa EO, Reid G, Ozolua RI (2004) Feeding probiotic strains Lactobacillus rhamnosus GR-1 and Lactobacillus fermentum RC-14 does not significantly alter hematological parameters of Sprague-Dawley rats. HAEMA. 7(4): 497-501
12. Anukam KC, Osazuwa EO, Reid G (2005) Improved appetite of pregnant rats and increased birth weight of newborns following feeding with probiotic Lactobacillus rhamnosus GR-1 and L. fermentum RC-14. J Appl Res. 5 (1):46-52.
13. Anukam KC, Osazuwa EO, Ahonkhai I, Reid G (2006) Lactobacillus vaginal microbiota of women attending a reproductive health care service in Benin city, Nigeria. Sex Transm Dis 33(1):59-62.
14. Anukam KC, Osazuwa EO, Ahonkhai I, Ngwu M, Osemene G, Bruce AW and Reid G (2006) Augmentation of antimicrobial metronidazole therapy of bacterial vaginosis with oral probiotic Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14: randomized, double-blind, placebo controlled trial. Microbes Infect. 8 (6):1450-1454.
15. Anukam KC, Osazuwa E, Osemene GI, Ehigiagbe F, Bruce AW, Reid G (2006) Clinical study comparing probiotic Lactobacillus GR-1 and RC-14 with metronidazole vaginal gel to treat symptomatic bacterial vaginosis. Microbes Infect. 8 (12-13):2772-2776.
16. Anukam KC, Osazuwa EO, Osadolor BH, Bruce AW, Reid G Yogurt containing probiotic Lactobacillus rhamnosus GR-1 and L. reuteri RC-14 helps resolve moderate diarrhea and increases CD4 count in HIV/AIDS patients. J Clin Gastroenterol. In press.
17. Pineiro M, Stanton C (2007) Probiotic bacteria: legislative framework-- requirements to evidence basis. J Nutr 137(3 Suppl 2):850S-853S.

18. Brink M, Senekal M, Dicks LM (2005) Market and product assessment of probiotic/prebiotic-containing functional foods and supplements manufactured in South Africa. S Afr Med J. 95(2):114-119.

Corresponding Author: Kingsley C. Anukam, Department of Microbiology, Faculty of Basic & Applied Sciences, Benson Idahosa University, Benin City, Nigeria; email: anukamkc@yahoo.com

Present Address: Canadian R & D Centre for Probiotics, Lawson Health Research Institute, 268 Grosvenor Street, London, Ontario, N6A4V2.
Email: kanukam@uwo.ca

Conflict of interest: The author declares that he has no conflicts of interest.