Prophylactic use of yoghurt reduces antibiotic induced diarrhoea in children

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Abstract

Objective To assess whether locally manufactured yoghurt could be used prophylactically to reduce antibiotic-associated diarrhoea in children.

Patients and Method Patients admitted to a general paediatric ward due to an illness other than diarrhoea and who were treated with amoxycillin or co-amoxyclav were recruited for the study. Patients were allocated randomly to the test and control groups. The test group was treated with a yoghurt (75ml) every morning for 3 consecutive days with the commencement of antibiotics. The stool consistency and frequency were recorded for 3 days following administration of antibiotics.

Results All patients (76) were between 6 months and 5 years of age. There were 42 females and 34 males. In the test group 2/39 developed diarrhoea while in the control group 10/37 developed diarrhoea following antibiotic treatment. The data was analysed using Fisher's Exact test. 27% in control group and 5.4% in treated group had developed diarrhoea. Two sided probability for the test is 0.0252.

Conclusion Antibiotic induced diarrhoea could be minimized by the prophylactic administration of yoghurt with the commencement of antibiotic treatment.

Introduction

Antibiotic-induced diarrhoea, especially with broad-spectrum antibiotics, is a common clinical problem that health personnel encounter in paediatric wards[1]. The incidence of antibiotic-associated diarrhoea, the commonest cause for non-infectious nosocomial diarrhoea, has been estimated to vary between 5% and 25% in adults[2] and between 8% and 30% in children[3]. The severity of antibiotic-associated diarrhoea may range from a brief, self-limiting disease to devastating diarrhoea with electrolyte disturbances, dehydration, abdominal cramps, pseudomembranous colitis, toxic megacolon, or even death[2].

Interest in the use of live microbial agents for the purpose of health maintenance and disease prevention or treatment has emerged over the last few years[4]. From the beginning of the last century scientists have turned their attention to reduction of the frequency of antibiotic associated diarrhoea by fermented milk products[5]. When a dose of harmless bacteria is added to milk, it produces lactic acid which curdles the milk imparting to it a tart flavour.

The minimum amount of live yoghurt drink (containing bifidobacterium species) that has measurable therapeutic effects in humans was found to be 400-500g a week, at a concentration of 1.0×10^6 CFU/g[6]. A significant proportion of live yoghurt foods tested for these levels of bacteria in Australia, the United States, and Britain were found not to contain these minimum levels and therefore did not achieve the above mentioned effects[7]. Even though antibiotic-associated diarrhoea is a common and incapacitating problem in the paediatric wards of Sri Lanka, the introduction of milk fermented products is not practised routinely. This could be merely because of the paucity of published data pertaining to this subject in our country.

Objective

To assess whether locally manufactured yoghurt, which is a readily available low cost product, could be used prophylactically to reduce antibiotic-associated diarrhoea in children.

Patients and Method

This study was carried out at the Teaching Hospital, Peradeniya during a six month period. Sequential patients admitted to the general paediatric ward due to an illness other than diarrhoea, and who were treated with amoxycillin or co-amoxyclav, were recruited for the study. The

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purpose of this study was explained to the parents and consent was obtained before enrolment. They were selected randomly to the test and control groups and the test group was treated with a yoghurt (75ml) every morning for 3 consecutive days. The stool consistency and frequency of passing stools were recorded during these days. We defined diarrhoea as "a change from the patient's normal bowel habit, with two or more loose or watery stools for at least two days." Ethical approval for the study was obtained from Faculty of Medicine, Peradeniya.

Results

All patients (76) were between 6 months and 5 years of age (mean 3.6). There were 42 females and 34 males. Out of 39 patients of the test group, only 2 developed diarrhoea whereas out of 37 in the control group, 10 developed diarrhoea after antibiotic treatment. The data was analysed using Fisher's Exact test. According to Table 1, 25.6% in the control group and 5.4% of the treated group had developed diarrhoea. Two sided probability for the test is 0.0252. There was a significant difference between the two groups indicating a substantial reduction of the incidence of diarrhoea in the treated group.

Table 1
Occurrence of diarrhoea in the 2 groups

Subjects	Diarrhoea		No Diarrhoea		Total
	M	F	M	F	
Control	4	6	15	14	39
%	25.6		74.4		
Test	2	0	18	17	37
%	5.4		94.5		
Total	12		64		76

Discussion

Biological agents (probiotics) have been used to treat a variety of infections, most notably infections of mucosal surfaces such as the gut and vagina[8]. Following the discovery and development of antibiotics, the value of these traditional treatments have diminished. However, we are now being forced to look at other alternatives to antibiotics to combat the ever increasing number of infections that occur due to excessive antibiotic use.

The term "probiotic" was first used to describe a live microbial supplement, which beneficially affects the host by improving its microbial balance. Since then, research has looked at possible clinical uses of these agents and in 1995, when a greater understanding of their properties had developed, the term "biotherapeutic agents" was proposed to describe micro-organisms with specific therapeutic properties that also inhibit the growth of pathogenic bacteria[9].

A number of agents have been isolated and studied for clinical use. *Streptococcus thermophilus* and *Lactobacillus bulgaricus*, commonly used in the dairy food industry, were among the first to be studied. Other strains that have been used are *Bifidobacterium bifidum, B longum, Enterococcus faecium, Saccharomyces boulardii, L acidophilus, L casei, and Lactobacillus* GG[10]. However, doctors are still reluctant to use these agents in routine clinical practice.

The way in which a probiotic affects the gut has generated much interest and enthusiasm to use it as a therapeutic agent. In order to combat the problems of gastrointestinal infection, a probiotic must be non-pathogenic and must act against pathogens by different mechanisms from antibiotics. More importantly, they should have a rapid onset of action and should survive the challenges of gastric acid, bile, or concurrent use of antibiotics. It is also desirable that they modify the immune processes to destroy the invading organism. *Saccharomyces boulardii* and lactobacilli display most of these characteristics[10].

A few live organisms have been used in many trials. *S boulardii*, a non-pathogenic yeast, is one such organism. It has a growth temperature of 37°C, rapidly colonises the bowel, does not alter the normal gut flora, and is cleared from the colon after treatment is discontinued[11]. The other probiotic agent used widely in clinical trials is the *Lactobacillus* species[10,12]. The mechanism of action of lactobacilli may be through multiple means: *Lactobacillus* GG has shown beneficial effects on intestinal immunity. It increases the numbers of cells that secrete immunoglobulin G and other immunoglobulins in the intestinal mucosa and stimulates the local release of interferon[13]. It also facilitates antigen transport to underlying lymphoid cells and demonstrates an increased uptake in Peyer patches. *Lactobacillus* GG has also been recognised to produce an antimicrobial substance which inhibits the growth of *Escherichia coli,* streptococci*, C difficile, Bacteroides fragilis*, and *Salmonella*[14]. *L casei shirota* also showed good survival in the gut in separate studies and mucosal antibody titres specific to lactobacilli were increased in the presence of this agent[15,16]. Although there was no distinct change to the numbers of clostridia or enterococci, there was an increase in the numbers of excreted bifidobacteria,

normal bowel anaerobes[15,16]. It is possible that this increase in bifidobacteria interferes with the pathogenic potential of *C difficile*.

Use of probiotics is a possible solution in the prevention of antibiotic associated diarrhoea. *Clostridium difficile* infection is increasingly prevalent in today's hospital setting, particularly in elderly patients, in whom 10-20% of such cases occur[17]. The incidence of antibiotic associated diarrhoea depends on the antibiotic used and each individual patient's risk factors. The standard regimens to treat colitis associated with *Clostridium difficile* are metronidazole and vancomycin; although these drugs are successful in 80% of cases, about 20% of patients suffer from recurrence[18,19]. In the light of the need to control costs in health care, we must re-examine the benefits of using live organisms. Whether the use of probiotics can actually reduce the length of hospital stay by reducing the incidence of infection with *C difficile* and the need to use antibiotics such as metronidazole and vancomycin are issues that need to be addressed in a clinical trial.

The advantages in use of *S boulardii*e over the current clinical practice include its ready availability in the form of brewer's yeast, its easy administration, and the remarkable cost effectiveness compared with vancomycin when infection occurs[20]. However, there are reports of development of septicaemia in immunocompromised patients and endocarditis in those with damaged or artificial heart valves who have been treated with lactobacilli[21] and therefore it would seem prudent to avoid using lactobacilli in such patients.

In the clinical scenario, if a child develops diarrhoea after commencement of a specific antibiotic, the practice in our country is to stop the drug immediately and then switch on to an alternative drug. This in turn will prolong the hospital stay and escalate the medical costs. Therefore adjunctive preventive measures such as prophylactic administration of yoghurt to alleviate antibiotic-associated diarrhoea are beneficial.

Conclusion

The results of this trial demonstrate that the prophylactic administration of yoghurt during broad spectrum antibiotic therapy is effective in reducing the incidence of antibiotic induced diarrhoea. This form of therapy is cheap, easily available and culturally acceptable. This will not only will improve the compliance with antibiotic therapy but reduce the morbidity from antibiotic induced diarrhoea.

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