

Probiotics and Antibiotics - Should they be Given Together?



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The use of antibiotics in clinical treatment of various infections is often essential in patients. However, it is now well recognised that antibiotics (particularly broad spectrum antibiotics) can adversely affect the balance of the resident gut microflora resulting in a dysbiosis, or microflora imbalance, of the gastrointestinal (GI) tract and can therefore act as an immune suppressor.

There are over 500 different species of microorganisms residing in the GI tract¹. When antibiotics are administered, a proportion of the beneficial microorganisms resident in the gut become disrupted. The consequent reduction in colonisation and disease resistance is manifested by an increased vulnerability to pathogenic bacteria colonisation of the gut, which leads to dysbiosis and often an increased risk of developing an intestinal infection; the main symptom being diarrhoea.

The World Health Organisation defines antibiotic-associated diarrhoea (AAD) as three or more abnormally loose bowel movements per 24 hours while on antibiotics. Antibiotics that act on anaerobes, such as aminopenicillins, cephalosporins and clindamycins, are most associated with diarrhoea². Twenty percent of people who take a course of antibiotics suffer from diarrhoea. As well as being an unpleasant side effect, it can in some cases, lead to chronic or persistent diarrhoea. It is estimated that 25% of cases of AAD are caused by *Clostridium difficile*. Infection with this pathogen can lead to colitis and is a common complication of antibiotic therapy becoming increasingly prevalent in hospital inpatients, particularly the elderly.

The incidence of diarrhoea in children receiving broad spectrum antibiotics has been reported in the range of 11-40%³. Young children (under three years of age) are more susceptible to clinical consequences of infectious diarrhoea and may have the most to gain from probiotic treatment.

Probiotics, known widely as beneficial bacteria and yeasts, assist in restoring the normal population levels of beneficial microorganisms in the GI tract. This is one of the principle indications for their use in both human and veterinary medicine. Whilst the restoration of the gut microflora, when antibiotic therapy has finished, is an obvious application for probiotics, there is also scientific support for the administration of probiotics alongside antibiotic treatment.

In recent human research, studies have looked at the role of probiotics in augmenting the use of antibiotics in the management of various infections (for example *C. difficile*) and also in the prevention of AAD⁴⁻⁸.

The mechanisms of action have been studied and one method is thought to be due to the probiotic bacteria interfering with the invasion and adhesion of pathogens⁹. In addition to stopping bacteria infecting cells already exposed, probiotic bacteria may help to protect the gut epithelium from further invasion. *Lactobacillus rhamnosus* has been shown to have beneficial effects on intestinal immunity, by increasing the numbers of cells that secrete immunoglobulins in the intestinal mucosa and stimulating the local release of interferon¹⁰. *L. rhamnosus* has also been shown to produce an antimicrobial substance that inhibits the growth of *Escherichia coli*, *Streptococci* spp, *C. difficile*, *Bacteroides fragilis* and *Salmonella* spp¹¹.



To summarise the following mechanisms of action have been documented for probiotics:

Immunomodulation

- Increases the number of intestinal mucosa cells secreting immunoglobulins
- Facilitates antigen transport to underlying lymphoid cells ensuring a faster immune reaction to disease causing bacteria.

Antibacterial action

- Production of antibacterial substances (such as bacteriocins)
- Action against common pathogens including *E. coli*, *C. difficile* and *Salmonella* spp.

Competitive Exclusion

- Good adhesion to the gut wall, preventing pathogens binding
- Colonisation of the gut with beneficial bacteria.

Johnston and team³ undertook a review of randomised controlled trials (RCTs) of probiotics in children taking antibiotics. The probiotics were co-administered with the antibiotics, and the review examined whether the probiotics prevented the development of AAD. Ten RCTs were identified, involving a total of 1,986 children. Six of the ten RCTs used lactic acid bacteria probiotics. The review found an average risk reduction of 51% (against placebo).

Probiotics have been shown to prevent *C. difficile* infection after the use of antibiotics. The probiotic strain *L. rhamnosus* has been used in the prevention of relapsing *C. difficile* diarrhoea, associated with antibiotic use. In a trial, elderly patients receiving antibiotics were also given either a placebo or a probiotic containing *Lactobacillus* and *Bifidobacterium*¹². Stool samples from all patients were analysed for *C. difficile* toxins, which were found in 78% of the control group and 46% of the probiotic group. This means that the probiotic was reducing the pathogen numbers and the production of toxins. It is these toxins which cause inflammation within the gut, leading to colitis.

It is also worth remembering that with various GI tract disorders, the immune system plays a central role in the

pathogenesis of many of these disorders, as does the enteric microflora. In fact the importance of the GI tract's immune function becomes more apparent when we consider that 70% of the body's immune cells reside in the gut.

Conclusion

The use of probiotics in conjunction with antibiotics, will act to reduce the effects of the dysbiosis caused by the antibiotics, and maximise the benefits of the probiotic directly in the gut on competitive exclusion and immune stimulation. It is advisable however to stagger the administration of the antibiotic and probiotic such that the probiotic is administered at least three hours after the antibiotic dose, where possible, otherwise the antibiotic may reduce the efficacy of the probiotic microorganisms. It is important to note that the reverse is not true: probiotics will not cause a reduction in efficacy or effectiveness of the antibiotic. The administration of the probiotic for at least one week following the completion of the antibiotic course.



Whilst the spectrum of many antibiotics means they are compatible with Protexin® probiotics, staggering the administration of the probiotic so that it is administered at least 3 hours after the antibiotic dose is recommended.

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About the author

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Aileen graduated with her degree in Animal Science from the University of Wales, Aberystwyth in 1996 and attained her masters, which focused on the benefits of probiotics in poultry, at the University of Liverpool whilst working in industry as a nutritionalist. Aileen joined Probiotics International Ltd in 2000 working initially as the Technical Manager before being promoted to Technical Director in 2003. She is currently the Research, Development and Quality Director.

Probiotics International Ltd is one of the largest manufacturers and suppliers of probiotic supplements for the healthcare, veterinary and animal health industry. Products are marketed under the brand name of Protexin.

As published in:

2010. *The Clinical Use of Probiotics*. Ed Barlow J. Probiotics International Ltd, United Kingdom.

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