

Evidence Based Critically Appraised Topic

Probiotics in the Prevention of Antibiotic-Associated Diarrhea

Tracy Hylland, FNP-s

University of Mary

## Probiotics in the Prevention of Antibiotic-Associated Diarrhea

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### **Clinical Scenario**

A 66-year-old male presents to the clinic complaining of a hacking productive cough, respiratory congestion, pain in left ribs, and malaise. Rapid influenza test was negative and chest x-ray shows a medium sized infiltrate in the left lung indicating pneumonia. Patient underwent a course of antibiotics for an acute respiratory infection approximately a month ago. Will start him on Levofloxacin 750mg daily for 5 days. Patient is concerned about getting diarrhea as he has had diarrhea in the past when he was on antibiotics and wants to know if there's anything he can do to prevent it.

### **Clinical Question**

In adult patients taking antibiotics does the co-administration of probiotics, compared to those not on probiotics, reduce the incidence of antibiotic-associated diarrhea?

### **Articles**

Amita, A., & Miley, H., (2011). Probiotics for the prevention of antibiotic-associated diarrhea and clostridium difficile-associated disease in hospitalized adults – A meta-analysis. *American Academy of Nurse Practitioners*, 23: 269-274. doi: 10.1111/j.1745-7599.2011.00617.x

Ritchie, M.L., & Romanuk, T.N., (2012). A meta-analysis of probiotic efficacy for gastrointestinal diseases. *PLoS One*, 7(4): 1-11. doi: 10.1371/journal.pone.0034938

### **Summary and Appraisal of Key Evidence**

Study 1: Amita and Miley (2011) performed a meta-analysis of randomized control trials (RCTs) to determine what the effect of administering probiotics has in the prevention of antibiotic-associated diarrhea (AAD) and clostridium difficile-associated diarrhea (CDAD) in hospitalized adults. The meta-analysis looked at all available RCTs with inclusion criteria of publication since 1990, hospitalized patient populations older than 18 years of age, available in English language and full text, and only study patients with no pre-existing GI disorders or compromised immune systems. The investigators independently assessed each article for inclusion according to the specified inclusion criteria. The search yielded 37 abstracts, of which 27 were excluded as they were not conducted on hospitalized patients. In the end only 8 of the studies met inclusion criteria. The total number of participants across the 8 RCTs was 1220. AAD was defined in this meta-analysis as more than 2 liquid stools per day for 3 or more days in quantities in excess of normal for each patient. There were no adverse outcomes noted in this analysis. The Mantel-Haenszel relative risk (RR) ratio was 0.56, showing a protective effect of probiotics for AAD.

This meta-analysis is considered a Level 1, Grade A level of evidence based on the Strength of Recommendation Taxonomy (SORT) tool. The basis of this level of

evidence rating is that this meta-analysis was done using RCTs that included high-quality patient-oriented evidence and consistent findings (Ebell, et al., 2004).

Study 2: Ritchie and Romanuk (2012) performed a meta-analysis to determine if probiotics are effective in the treatment and prevention of 8 different gastrointestinal diseases across 11 species or species mixtures of probiotics. The authors conducted a literature search for randomized, controlled, efficacy trials. Inclusion criteria consisted of RCTs published in peer-reviewed journals, trials on humans with gastrointestinal disease, and studies that compared probiotic therapy with placebo or no therapy. There were a total of 84 trials that were utilized, spanning 10,351 patients, 11 probiotic species or mixtures, and 8 different diseases. The analysis included six different factors: the disease treated with probiotics (AAD is the only one of concern for this topic), the type of probiotic used, the dose of probiotic, the amount of time the probiotic was administered for, the age group of subjects receiving probiotics, and single versus multiple species of probiotics. In this meta-analysis AAD is defined as 3 loose stools per day for at least 2 days or 5 loose stools in 48 hours, within 2 months of antibiotic exposure. There were no adverse events that occurred in any of the trials. The relative risk (RR) ratio for AAD was 0.43, showing a significant effect across all eleven species of probiotics.

This meta-analysis is considered a Level 1, Grade A level of evidence based on the Strength of Recommendation Taxonomy (SORT) tool. This level of evidence rating for this meta-analysis is based on its review of RCTs that included high-quality, patient-oriented evidence, and consistent outcomes (Ebell, et al., 2004).

### Results

The results of the both of these reviews indicate that the administration of probiotics is effective in the prevention and treatment of AAD. There were several limitations in both studies, of which included heterogeneity, possible publication bias, and small sample size in some of the trials. Study 1 also only included eight trials, which is a relatively low number. Further research is currently needed in the area of specific species of probiotics on different diseases in order to determine which probiotic to advise based on the current or potential gastrointestinal disease.

### Clinical Bottom Line

According to these two studies the use of probiotics is an effective recommendation in the prevention and treatment of AAD. However, further research is needed to determine if specific species are more effective in the prevention and treatment of AAD. These studies are relevant today because there has been a marked increase in the past ten years. The U.S. hospital costs of *clostridium difficile* management in 2008 were estimated to be \$3.2 billion per year. As a result, providers need to be conscientious of ways to aid in the prevention of AAD and the development of *clostridium difficile* infections in order to protect our patients.

### Implications for Practice

As a result of this information I would definitely recommend the concomitant administration of probiotics with antibiotics. There are several different species of probiotics that are available, but the most commonly seen is *lactobacillus acidophilus*.

These studies showed *s. bouardii* and *lactobacillus acidophilus* to be the most effective against AAD when taken as directed for up to 49 days, generally paralleling the duration of antibiotics. More research on this topic would be extremely beneficial.

## References

- Amita, A., & Miley, H., (2011). Probiotics for the prevention of antibiotic-associated diarrhea and clostridium difficile-associated disease in hospitalized adults – A meta-analysis. *American Academy of Nurse Practitioners*, 23: 269-274. doi: 10.1111/j.1745-7599.2011.00617.x
- Ebell, M.H., Siwek, J., Weiss, B.D., Woolf, M.D, ...Bowman, M., (2004). Strength of recommendation taxonomy (SORT): A patient-centered approach to grading evidence in the medical literature. *American Family Physician*, 69(3): 548-556. Retrieved from: <http://www.aafp.org/afp/2004/0201/p548.html>
- Ritchie, M.L., & Romanuk, T.N., (2012). A meta-analysis of probiotic efficacy for gastrointestinal diseases. *PLoS One*, 7(4): 1-11. doi: 10.1371/journal.pone.0034938