Annals of R.S.C.B., Vol. 23, Issue 1, 2019, pp. 07 - 14
Received 24 April 2019; accepted 20 June 2019.

Antibiotic-Associated Diarrhea in Hospitalized older patients: The Question about Combining Antibiotics with Probiotics

Najibah Kouri
Research Scholar,
Malaysian Medical Association, Malaysia

Abstract

This project has made significant conclusions that could help clinicians focus on reducing the risk of AAD. Indication of probiotics in older adults up to 64 years is warranted to reduce the risk of AAD and potential consequences, including dehydration, a possible longer length of hospital stay, and additional hospital costs. However, this project cautions on the use of probiotics to reduce the risk of AAD among patients aged 65 and above. Such a position saves the hospital and patients from incurring additional costs on an intervention that could cause more harm than benefit. As derived through evidence, probiotics among elderly patients aged 65 and above have been associated with longer AAD and prolonged hospital stay. Finally, this project has recommended the most beneficial probiotics. Clinicians can, therefore, choose depending on availability and tolerability.

Introduction

Antibiotic-Associated Diarrhea (AAD) is alarming, with about 453000 cases and 29300 deaths (McFarland et al., 2016). The risk of AAD is elevated in hospitalized elderly persons because of comorbid conditions and long periods of stay in the hospital. As such, AAD in the elderly is associated with poor outcomes, dehydration, and nutritional depreciation in elderly patients. The concurrent use of probiotics during antibiotic therapy could be a possible solution. However, there is a need to have a clinical certainty to make a scientifically compelling case for the adoption of probiotics in preventing AAD. The overall aim of the project is to evaluate whether concurrent use of probiotics during antibiotic therapy reduces the risk of developing antibiotic-associated diarrhea (AAD). This project will consider literature, including randomized control trials and systematic analysis.

Antibiotics remain the mainstay for the management of bacterial infections in hospital setups. Clinicians have widely used antibiotics for diseases like pneumonia, cystitis, urinary infections among a plethora of bacterial infections. Antibiotics like cephalosporins have been used for tuberculosis, while cefdinir has been used to manage kidney infections (Ramón-García et al., 2018; Lojanapiwat et al., 2018). Fluoroquinolones have even been preferred by national guidelines for managing conditions like community-acquired pneumonia (Corrêa et al., 2018). Generally, the use of antibiotics has deemed beneficial since the introduction of penicillin.

While the benefits of antibiotics have been acknowledged, antibiotic prescription in the elderly is a global concern. Studies have noted that the elderly consume antibiotics at an elevated rate than other age groups. A survey by the European surveillance of antimicrobial consumption between 2008 and 2009 realized that those aged 75 and older received the highest antibiotic prescription compared to adults aged 18-64 (as cited in Luz, 2019). In the United States, the

National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey established that between 2007 and 2009, those aged 65 and above received the highest rate of antimicrobial prescription (at 1.10 per person per year) than those aged 0-64 years who used antimicrobial at 0.88 antimicrobials used per person per year (Giarratano et al., 2018).

Given the high consumption of antibiotics among the elderly, one would make a case that the majority of side effects due to antibiotics would occur among the elderly than other groups. Side effects are unprecedented outcomes following antibiotics prescriptions (Heta & Robo, 2018). There are many side effects of antibiotic consumption among the elderly and other groups, including Antibiotic-Associated Diarrhea (AAD).

Antibiotic-associated diarrhea (AAD) is any unexplained diarrhea that follows the use of antibiotics. AAD occurs explicitly when the prescribed antibiotics work against the beneficial flora of the gut. The gut microflora is vital to the patient because it helps in host metabolism, maintaining the gut's integrity, protecting the gut against harmful bacteria, immunomodulation, and drug and xenobiotic metabolism (Jandhyala et al., 2015). Generally, the intestinal microflora is a composition of bacteria necessary to facilitate the host metabolism. There are about 40 trillion bacteria, while Bacteroidetes and Firmicutes remain the dominant species (Zhang et al., 2018). Broad-spectrum antibiotics may disrupt the composition of intestinal flora. These antibiotics may kill or suppress antibiotic-sensitive flora but spare antibiotic-resistance species. The impact is that the antibiotic-resistant species may multiply and disrupt the intestinal flora, consequentially leading to changes in the metabolism of carbohydrates and absorption of lipids, terminally causes osmotic diarrhea (Resnik, 2018; Litao et al., 2018).

Methods

This project aims to develop guidelines on reducing the incidence of antibiotic-associated diarrhea in hospitalized older adults through the use of probiotics. AAD is three or more stools within 24 hours (Giannelli, 2017). The incidence varies between 5% to 25% (Giannelli, 2017). A higher incidence of 35% has been reported. Older adults are more vulnerable. According to Wong et al. (2017), 76% of the patients with AAD were elderly aged 65 years and above.

Many authorities document that most patients who experience AAD recover normally. However, older adults and frail often suffer complications of dehydration (Wong et al., 2017). When AAD occurs among hospitalized elderly, it is referred to as nosocomial diarrhea. Nosocomial diarrhea predisposes the elderly to dehydration. Sometimes AAD goes unnoticed. Since the condition may go unnoticed as AAD, patients may continue to lose fluid and electrolytes, which in the presence of reduced fluid intake may lead to dehydration (Shaheen et al., 2018).

Dehydration poses many risks for hospitalized elderly patients. Some of the complications mentioned by Shells & Morrell-Scott (2018) include increased risk of urinary tract infections, hypotension, headaches, a prolonged illness, constipation, headaches, and fatigue. The majority of these complications result from an electrolyte imbalance. According to El-Sharkawy et al. (2015), dehydration of 2% body weight can cause significant cognitive impairment and physical impairment. Other complications mentioned by Litao et al. (2018) include renal senescence, blunted sensation of thirst, and increased risk of mortality. Dehydration may also lead to compromised cognitive performance, increased risk of intestinal and wound infections, coronary artery disease, or even death (El-Sharkawy et al., 2015). AAD is, therefore, a risk to poor prognosis and prolonged length of hospital stay.

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The cost associated with AAD is significantly felt. In an informative study by Ebm et al. (2013), the authors concluded that each patient with AAD experienced an incremental cost of £13,272.53. In the study, the high cost was associated with prolonged stay in intensive care units and higher readmission rates. The cost is likely to be inflated in the next few years. Generally, it is noteworthy that AAD's occurrence increases the cost of care and the risk of complications among the elderly.

While many options have been tried, this project proposes the incorporation of probiotics in the antibiotic regime. Probiotics comprise beneficial bacteria and yeast that could improve the gut function during illness. According to Blaabjerg et al. (2017), probiotics may help in normalizing the gut flora. The benefits of probiotics have been demonstrated in conditions such as irritable bowel disease and necrotizing enterocolitis. The commonly used pathogens are *the Lactobacillus* genus, *Saccharomyces* genus, and *Bifidobacterium* genus. These microorganisms may allow competitive inhibition of pathogenic bacteria hence allowing the proliferation of beneficial bacteria. Subsequently, the patient can metabolize carbohydrates and absorb lipids, metabolize xenobiotics, and drugs, hence reducing the possibility of osmotic diarrhea.

Many studies have demonstrated the benefits of probiotics. A meta-analysis by McFarland in 2006 revealed that the relative risk of AAD among patients taking *L. rhamnosus* was 0.31 (as cited in Hickson, 2011). In a systematic analysis by Blaabjerg et al. (2017), the authors demonstrated that the incidence of AAD among the probiotics group was 8.0%, while the incidence among the control was 17.7%. The benefits are significant and indicate that upon more innovation or rejuvenation of probiotic administration, the incidence and relative risk of AAD could be reduced unremarkably.

Many protocols of probiotic use have been proposed. As documented in Kerna & Brown's (2018) authorship, one suggestion is to administer probiotics 2-6 hours post-consumption of antibiotics and a further administration of probiotics 7-10 days at the end of the antibiotic regime. Administration of probiotics before antibiotic dosage has also been proposed. Given this submission, such differences could account for the lack of better results on probiotics. Depending on the pharmacokinetics of the drugs prescribed, the damage is possible before the administration of probiotics.

Activity	Timeline
Assembling of the evidence-based practice team	One week after notification to the hospital board of directors
Gathering and appraising evidence	Two weeks upon assembling of the evidence-based team
Recruitment of participants	One month after gathering and appraising evidence
Data collection	One week after participant recruitment
Data analysis	Three weeks after the final data collection
Dissemination of results and conclusion	Two months upon data analysis

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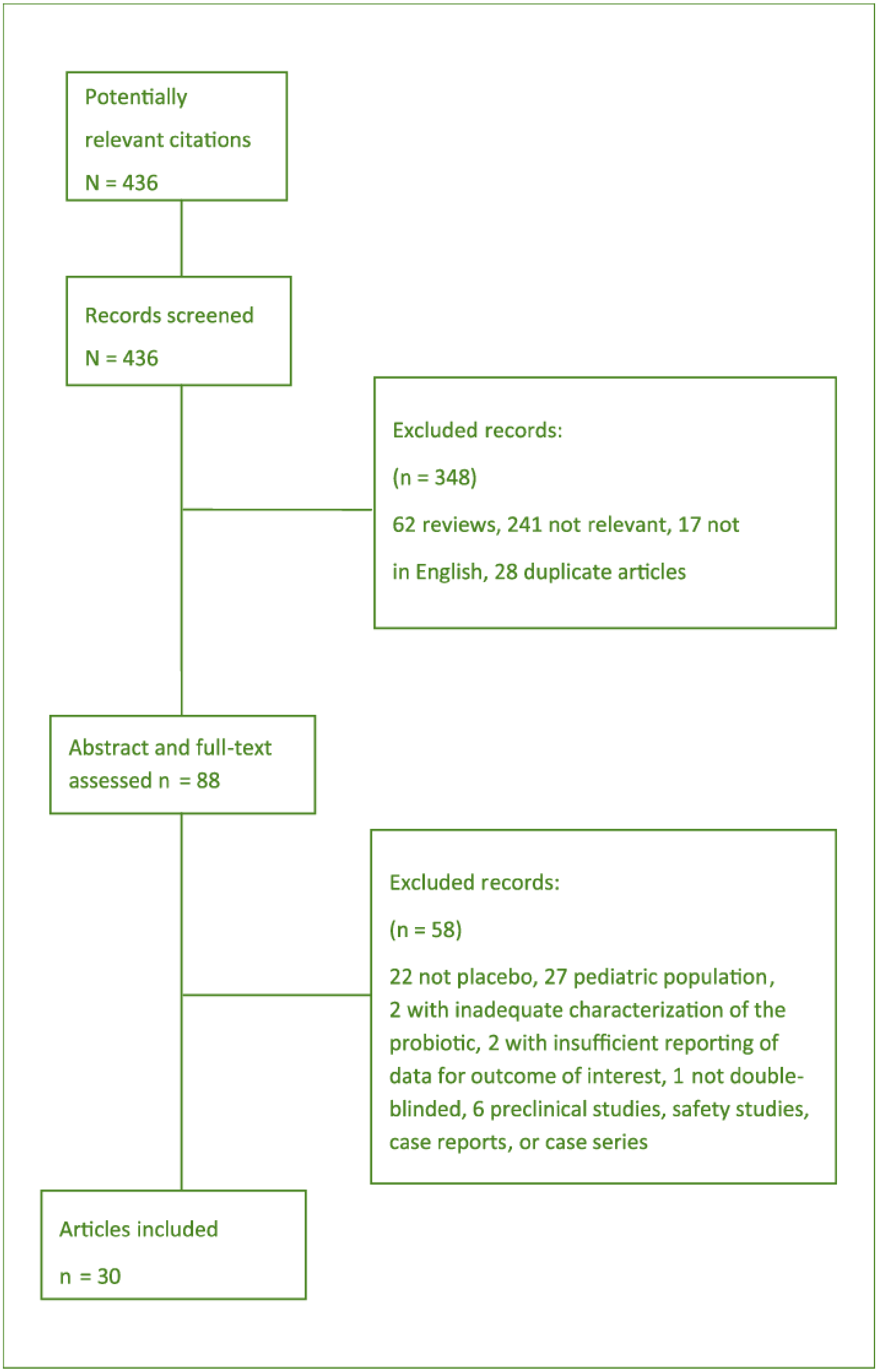
Results



Given the background of information and significance demonstrated above, the PICOT question for this project would be: In hospitalized older adults, does the concurrent use of probiotics with antibiotic therapy reduce the risk of antibiotic-associated diarrhea compared to placebo during the period of hospitalization?

Article #1

The first study appraised in this project is "Probiotics Reduce the Risk of Antibiotic-Associated Diarrhea in Adults (18–64 Years) but Not the Elderly (> 65 Years)" by Jafarnejad et al. (2016). The study is a meta-analysis hence offers a level I evidence, high-quality evidence. The study included an analysis of thirty randomized controlled trials (RCTs) with consistent results. Jafarnejad et al. (2016) provides an appropriate classification of the age groups and analyze results according to each group. Also, the study topic and bearing are in tandem with the current research's PICOT question. The validity, reliability, and applicability of the study are, therefore, unremarkable. One weakness noted in this study is that Jafarnejad et al. (2016) included only five RCTs that target elderly patients.

The study offers credible insights on the use of probiotics to prevent AAD. Jafarnejad et al. (2016) noted that in adults aged 18-64 years, adjunct administration of probiotics reduced the risk of AAD. However, in adults above 65, there is no statistical significance in the risk of AAD upon probiotics administration. Jafarnejad et al. (2016) open a gap for further studies to analyze the particular probiotics suitable for those aged 65 and above since the few RCTs involving the elderly cannot be used to conclude that probiotics are not effective in preventing AAD among the elderly.

Article #2

The second article appraised is “Comparative efficacy and tolerability of probiotics for antibiotic-associated diarrhea” by Cai, J., Zhao, C., Du, Y., Zhang, Y., Zhao, M., & Zhao, Q. (2018). This study is a systematic review of RCTs hence offers a level I evidence—the results of the RCTs are consistent and reliable. Also, the results can be generalized. The mean age for the participants was 43 years. The study has an elaborate topic that is consistent with the current PICOT questions. The purpose and goals are well-defined. There are, however, no study questions.

According to Cai et al. (2018), *Lactobacillus rhamnosus* GG (LGG) was the most superior probiotic in reducing ADD incidence. *L. casei, L. plantarum, S. boulardii*, *L. acidophilus, L. rhamnosus, B. clausii*, *L. reuteri*, Multi-genera II, Multi-genera III were also superior, respectively. The tolerability of these probiotics varies, with LGG is the most tolerable. Other probiotics have good tolerability. The gap created by this study is the need to evaluate the effective doses for probiotics. This study is highly recommendable for evidence-based practice, especially in deciding which probiotics to procure. Such an option could help save on costs and choose the safest probiotics.

Article #3

The third article is "Do Probiotics prevent antibiotic-associated diarrhea" by Rajkumar et al. (2020). This is a current study hence depicts recent scientific insights. The researchers conducted a randomized placebo-controlled trial, which makes the conclusions a level II evidence. The study involved 1127 participants, sufficient sample size in making reliable and valid conclusions. The mean age for the participants was 73. The follow-up period was sufficient for the researchers to note positive changes. The title of the study and the problem is well defined, and the abstract offers an accurate summary of the study. The authors do not, however, provide limitations that could have influenced their findings.

In the intervention group, the incidence of AAD was 19.3%, while in placebo, the incidence was 17.9% (Rajkumar et al., 2020). In both groups, the onset of AAD was 15 days upon initiation of treatment. At 30 days, however, the incidence of AAD was 20.7% and 19.0% in intervention and treatment groups. These findings indicate that probiotics are not effective at preventing AAD among the elderly, particularly those above 70 years. The higher incidence of AAD among the intervention groups raises questions about the essence of probiotics. There was also no statistical difference in the mortality rates, considering the two groups.

Article #4

The fourth article is "Saccharomyces boulardii to prevent antibiotic-associated diarrhea" by Ehrhard et al. (2016). Ehrhard et al. (2016) conducted a randomized, double-masked, placebo-controlled trial yielding level II evidence, high-quality evidence. The study including 477 participants, n= 246 60.1 ± 16.5 years, and n=231 56.5 ± 17.8. While the study sample is small to generalize the result, it is sufficient to generate meaningful conclusions. The literature review is well conducted, giving an exemplary background of AAD and the potentials for probiotics in preventing AAD. The study questions are not defined, and the hypothesis is not clearly stated. The study problem is, however, well-articulated.

The conclusion made from the study was that there is no evidence that *S boulardii* effectively prevents AAD among the participants. The intervention group had a longer duration of AAD, a higher frequency of loose stools during AAD, and a higher AAD density. Although these findings had no statistical significance, a hazard ratio of 1.02, slightly higher than 1.0, may not be overlooked. These findings are crucial in making decisions about *S boulardii* for preventing AAD among the elderly.

Article #5

The fifth article is "Feasibility of a Lactobacillus casei drink in the intensive care unit (ICU) for prevention of antibiotic-associated diarrhea and Clostridium difficile" by Alberda, C Marcushamer, S., Hewer, T., Journault, N., & Kutsogiannis, D. (2018). This was a case-control trial involving 32 participants in the ICU. Patients in the ICU are at a higher risk of AAD. The evidence from the study is a level III evidence, moderate-quality evidence. The purpose of the study is well defined; however, the study questions were lacking. The authors administered probiotics within 48 hours of antibiotic prescription. Prompt administration of probiotics is the study's strength. However, one weakness of the study is that most of the patients had been prescribed antibiotics before admission to the ICU.

The researchers documented AAD in 12.5% of patients in the intervention group, and 31.3% in the control group. This major difference provides a chance that *Lactobacillus casei could be considered as prophylaxis for AAD.* The authors concluded that *Lactobacillus casei* is feasible and safe to administer in ICU patients. The findings cannot, however, be generalized. This study warrants the need for RCTs involving *Lactobacillus casei* among older patients.

Conclusion

This project has made significant conclusions that could help clinicians focus on reducing the risk of AAD. Indication of probiotics in older adults up to 64 years is warranted to reduce the risk of AAD and potential consequences, including dehydration, a possible longer length of hospital stay, and additional hospital costs. However, this project cautions on the use of probiotics to reduce the risk of AAD among patients aged 65 and above. Such a position saves the hospital and patients from incurring additional costs on an intervention that could cause more harm than benefit. As derived through evidence, probiotics among elderly patients aged 65 and above have been associated with longer AAD and prolonged hospital stay. Finally, this project has recommended the most beneficial probiotics. Clinicians can, therefore, choose depending on availability and tolerability.

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