INTRODUCTION

- Ventilator-associated pneumonia (VAP) is a type of healthcare-acquired pneumonia that develops after 48 hours of endotracheal intubation.³
- VAP is one of the most commonly diagnosed nosocomial bacterial infections in the intensive care unit (ICU).⁴
- VAP may occur from endogenous flora in the oral cavity and upper airway with micro-aspiration around the endotracheal tube cuff.⁵
- VAP prolongs the duration of mechanical ventilation, ICU, and hospital stays, with increased medical costs, morbidity and mortality.³,⁶
- Antibiotic use is one method to attenuate the burden of bacterial colonization but there is concern for development of antibiotic resistance.⁷
- Probiotics have been proposed to:  
  - Enhance gut barrier function  
  - Inhibit colonization of potentially pathogenic microorganisms  
  - Maintain a normal intestinal milieu  
  - Synthesize antibacterial substances, and  
  - Stimulate local immunity.⁸
- Probiotics:  
  - Have a high safety profile  
  - Have no obvious contraindication or adverse effects  
  - Are easily administered, and  
  - Are cost effective for patients.¹, ³, ⁵
- Studies using probiotics show efficacy in decreasing the length of ICU stays and reducing VAP-related mortality.

PICO AND CLINICAL QUESTION

Table 1. An overview of each of the four articles reviewed. cfu = colony-forming units; VAP = ventilator-associated pneumonia

<table>
<thead>
<tr>
<th>Study 1</th>
<th>Study 2</th>
<th>Study 3</th>
<th>Study 4</th>
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<tbody>
<tr>
<td><strong>Objectives</strong></td>
<td>To evaluate the efficacy of probiotics, <em>Lactobacillus</em> casei (Shirota strain), in reducing the incidence of VAP in medical patients who received mechanical ventilation at Siriraj Hospital in Thailand.</td>
<td>To assess the effectiveness of probiotics <em>Bifidobacterium</em> and <em>Enteroococcus</em> in the prevention of VAP when administered by nasogastric tube.</td>
<td>To examine the effectiveness of probiotic administration in the reduction of healthcare-associated infection, including VAP, among medically ventilated neurocritical care patients.</td>
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<tr>
<td><strong>Study type</strong></td>
<td>Randomized Controlled Study of Probiotics Containing <em>Lactobacillus</em> casei (Shirota strain) for Prevention of Ventilator-Associated Pneumonia. Rongruangruj et al., 2015</td>
<td>Effect of probiotics on the incidence of ventilator-associated pneumonia in critically ill patients: a randomized controlled multicenter trial. Zeng et al., 2016</td>
<td>Effect of Probiotics on the Incidence of Healthcare-Associated Infections in Critically Ill Patients Admitted to the Intensive Care Unit: A Prospective Double-Blind Randomized Controlled Trial. Matthiasdoerfer et al., 2018</td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>150</td>
<td>235</td>
<td>167</td>
</tr>
<tr>
<td><strong>Probiotic composition</strong></td>
<td>8x10⁸ cfu <em>Lactobacillus</em> casei (Shirota strain)</td>
<td>4.5x10⁹ cfu <em>Bifidobacterium</em> subtilis 0.5x10⁶ cfu <em>Enterococcus faecalis</em></td>
<td>1.0x10⁶ cfu <em>Lactobacillus</em> acidophilus (gasseri) 1.0x10⁶ cfu <em>Lactobacillus helveticus</em> (Bulgarian) 1.0x10⁶ cfu containing <em>Lactobacillus</em> casei, <em>Bifidobacterium</em> acidophilus, <em>Bifidobacterium</em> longum, <em>Bifidobacterium</em> thermophilus spp</td>
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<tr>
<td><strong>Year published</strong></td>
<td>2015</td>
<td>2016</td>
<td>2016</td>
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<tr>
<td><strong>Primary outcomes</strong></td>
<td>Incidence of VAP episodes per 1,000 ventilator-days</td>
<td>VAP incidence</td>
<td>The incidence of hospital-associated infections</td>
</tr>
<tr>
<td><strong>Statistically significant findings</strong></td>
<td>None</td>
<td>Microbiologically confirmed VAP reduced in the probiotic group (36.4%) compared to control (50.4%) (p = 0.031) (Table 2)</td>
<td>The incidence of hospital-associated infections</td>
</tr>
</tbody>
</table>

RESULTS

Table 2. Incidence of ventilator-associated pneumonia from Study 2. VAP = ventilator-associated pneumonia

<table>
<thead>
<tr>
<th>Primary outcome</th>
<th>Probiotics group</th>
<th>Control group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of clinically diagnosed VAP</td>
<td>48/118 (40.7%)</td>
<td>62/177 (35.0%)</td>
<td>0.059</td>
</tr>
<tr>
<td>Incidence of microbiologically confirmed VAP</td>
<td>43/118 (36.4%)</td>
<td>59/177 (33.4%)</td>
<td>0.031</td>
</tr>
<tr>
<td>Patients with gram-negative VAP</td>
<td>27/43 (62.8%)</td>
<td>35/59 (59.3%)</td>
<td>0.866</td>
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<tr>
<td>Patients with gram-positive VAP</td>
<td>7/43 (16.3%)</td>
<td>13/59 (22.0%)</td>
<td>0.603</td>
</tr>
<tr>
<td>Patients with Candida VAP</td>
<td>1/43 (2.3%)</td>
<td>2/59 (3.4%)</td>
<td>0.715</td>
</tr>
<tr>
<td>Time to occurrence of VAP (days)</td>
<td>10.4 ± 2.9</td>
<td>7.5 ± 2.9</td>
<td>0.022</td>
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</table>

DISCUSSION

- Clinical benefit of probiotic use is still uncertain.
- Studies differ greatly by multiple variables: variety of probiotic strains, individual or combination probiotic strains used, concentrations of probiotics, route of administration (oral, nasal, oesophageal tube), medium used to deliver probiotics (milk product, sterile water, tablet), frequency of administration, additional VAP-prevention techniques.
- Study 1 used L. casei and was unique in using a fermentable medium to slowly produce lactic acid in the mouth to kill potentially pathogenic microorganisms.
- Study 2 was the sole study with statistical significance in this review.
- Concentration: 5.0x10⁹ cfu (90% B. subtilis, 10% B. cereus) – less than all other studies (Table 1).
- Route: enteral feeding (oral or oesophageal tube).
- Frequency: once daily.
- B. subtilis has been found in other studies to increase secretory IgA which could explain the non-specific reduction in Study 2 (Table 2).
- Suggests that the choice of strain may be most important (versus higher concentration, route, or frequency of administration).
- Studies 1 and 2 were open-label randomized controlled trials
- Study 3 broadly examined incidence of all healthcare-associated infections with VAP as one end result reviewed.

CONCLUSION

In reviewing the literature, data regarding probiotic use and VAP prevention vary between meta-analyses. Generally, probiotics are of no pathogenic concern and have the potential to aid in immune responses to decrease infectious complications in mechanically ventilated patients. However, only one of the four studies reviewed was able to show significantly reduced microbiologically confirmed VAP with the supplementation of probiotics. The three remaining studies were inconclusive in demonstrating efficacy of probiotics. The significance varies among study strains, concentrations, administration routes, administration frequency, additional VAP-prevention techniques, and VAP analysis of study definitions throughout the four studies made comparisons of study outcomes difficult to determine. Further research is needed to determine the efficacy of probiotics in the clinical care and prevention of VAP.

ACKNOWLEDGEMENTS

We would like to thank Dr. Abby Massey, Dr. Erika Kancler, Carolyn Schubert, and the James Madison University Communication Center for their time and assistance with this research project.

REFERENCES