Original Article

Role of Probiotic to Reduce the Incidence of Ventilator Associated Pneumonia in Neuro-Critical Care Patients

Benzir Shofi[1], Hasan Al Banna[2], Md. Harun Ur Rashid[3], Muhammad Farhan Sajid[4], A K M Ferdous Rahman[5]

DOI: https://doi.org/10.3329/bccj.v14i1.88325

Abstract:

Background: *Critical illness is characterized by a loss of commensal flora and an overgrowth of potentially pathogenic bacteria, leading to a high susceptibility to infection. Ventilator associated pneumonia (VAP) remains a common hazardous complication in patients who are mechanically ventilated and associated with increased cost, adverse outcome. The use of probiotics has been accepted as a strategy to prevent VAP offering a effective combination of safety, simplicity and cost-effectiveness.*

Objective: *To evaluate the role of probiotics in reducing the incidence VAP in neuro-critical care patients who received mechanical ventilation for at least 48 hours.*

Methodology: *This randomized controlled trial was conducted in the ICU of Dhaka Medical College Hospital at Department of Anaesthesia, Pain, Palliative & Intensive Care over a period of 20 months without interrupting standard care practiced in the department. A total of 135 neuro-critical patients admitted in ICU, who needful mechanical ventilation for at least 48 hours were enumerated qualified for inclusion. Participants were randomly allocated into two groups using a simple lottery method in a 1:1 ratio. The intervention group received probiotic supplementation and control group received placebo. The Clinical Pulmonary Infection Score (CPIS) criteria was used for diagnosis of VAP in all patients. Data were analyzed using SPSS version 26.0 with statistically significant p-value <0.05.*

Results: *The mean ± SD age of patients in the intervention group was 41.1 ± 11.86 years and in the control group was 43.2 ± 9.92 years, without any significant difference between groups (p>0.05). There was no statistically significant difference in baseline characteristics including age, sex, comorbidities and smoking status. The incidence of VAP was significantly lower in the intervention group compared to the control group (5.7% vs 25.3% , p= 0.002).*

Conclusion: *Probiotic administration was associated with a significant reduction in the incidence of ventilator associated pneumonia in the neurocritical patients.*

Keywords: *Clinical pulmonary infection score (CPIS), Mechanical ventilation (MV), Neurocritical care, Ventilator Associated Pneumonia (VAP).*

Introduction:

Patients receiving invasive mechanical ventilation are at risk for numerous complications. One of the most widespread and serious complications of mechanical ventilation in critically ill patients especially in neuro-critical care is Ventilator-associated pneumonia (VAP). VAP is a common nosocomial infection. Because of decreased immune function and increased permeability of the digestive tract, ICU patients are at increased risk of VAP. Specifically, brain-injured patients have T-helper cell inhibition that can put them at aggravated risk of infection[1]. It occurs in 9-27% of patients maintained on mechanical ventilation for more than 48hrs[2].

Patients with VAP have increased morbidity, mortality, hospital costs as well as prolonged intensive care unit and hospital length of stay, and increased costs. Risk factors are thought to contribute to increased bacterial colonization of the aerodigestive tract and facilitate the entry of pathogenic bacteria into the lower respiratory tract[3]. Endogenous flora in the oral cavity and upper airway of the patients play an important role in the development of VAP and abnormal colonization and translocation of potentially pathogenic microorganisms in the oral cavity and upper airway are believed to be the main pathogenesis of VAP [4]. Also, the airways can be colonized by pathogens, due to broad-spectrum antibiotic use, reduction in gastric pH as part of the stress ulcer prophylaxis, and the impairment of mucosal defense mechanisms due to trauma- induced by indwelling endotracheal or nasogastric tubes[5]. Micro-aspiration of oropharyngeal secretions contaminated with endogenous flora around the endotracheal tube cuff is the major route for microbial invasion[4]. Fragments of biofilm from the endotracheal tube are also responsible for causing VAP. The formation of such biofilm can be delayed but not prevented by the use of tubes with special coatings [6]. Because the pathogenesis of VAP is so complex, there are several pharmacological and non-pharmacological interventions for its prevention, such as antibiotics, semi-recumbent position, selective gut decontamination, endotracheal tube equipped with subglottic secretion drainage, and chlorhexidine mouth wash [7].

Received : November 23, 2025; Accepted : February 20, 2026

Current effective VAP prevention strategies target modifiable risk factors for colonization and aspiration, including elevation of the head of the bed, silver-coated endotracheal tubes, intensive oral care, and minimizing the duration of mechanical ventilation through regular use of sedation vacations and weaning protocols [8]. In view of these events central to the pathogenesis of VAP, probiotic therapy is an interesting option as a non-antibiotic strategy for maintenance of the host' aerodigestive microbial balance and VAP prevention [9].

Probiotics are defined by the World Health Organization as living microbial agents of human origin that are to tolerate the hostile gastrointestinal environment (acid and bile) such that they ultimately persist in the lower alimentary tract to confer health benefits to the host. These bacteria do not contain any virulence properties or antibiotic resistance cassettes. They create an unfavorable environment for pathogens by mechanisms including promotion of the integrity of the guts defense barrier by modification of gut flora by including host cell antimicrobial peptides, the release of antimicrobial factor, anti-oxidative activity, inhibition of epithelial cell nuclear factor kappa B activation, normalizing intestinal permeability, modulation of intestinal secretory immunoglobulin function, control of intestinal inflammatory responses and by balancing the release of cytokines[2]. Probiotics maintain normal microecology of the gastrointestinal flora and antimicrobial effects mediated by nutrient competition, alteration of local pH, production of bacteriocins, modification of pathogen-derived toxins, and stimulation of epithelial mucin production [10]. Since probiotics are staying only transiently in the gut they have to be ingested every day [2]. This is crucial as most antibiotic treatments will kill the probiotic bacteria [11]. Probiotics can be regarded as safe according to a report of the Central Public Health Laboratory, London (now the Health Protection Agency Centre for Infections) [12].

Effects of probiotics on the prevention of VAP still remain inconclusive. In fact, its effect depends on the patient population and the probiotic strain studied. Despite the outcome benefits of probiotic therapy, recent guidelines have been unable to make a definitive recommendation for the routine use of probiotics in ICU patients [13]. Many studies have shown positive results of the administration of probiotics in critically ill patients toward decreasing VAP [14]. This manuscript describes the rationale behind probiotic strategies in neuro-critical patients. This is followed by a review dealing with the beneficial effects, risks, and routine of prophylactic probiotic therapy [15]a life-threatening complication. Proposed preventive measures against VAP include, but are not restricted to, selective decontamination of the digestive tract (SDD. Due to their availability, few side effects and easy to administer, fascinating to use probiotics further. The objective of this study to evaluate efficacy of probiotic in reducing VAP in mechanically ventilated neuro- critical patient in a tertiary care facility.

VAP is still an important issue in mechanically ventilated patients. Though the pathogenesis of VAP is so complex there are several methods for its prevention. With the increasing incidence of antimicrobial resistance in ICU and the lack of new antibiotics, strategies that target non antibiotic interventions need to be developed. Therefore a simple, inexpensive and safe prevention strategy will contribute to decreasing the VAP occurrence rate and corresponding burden. Probiotic administration is considered a non antibiotic option for the prevention of VAP through a local and systemic mechanism that minimizes the colonization of virulent species or modulate host immune defense. Although probiotic prophylaxis for VAP, does not eradicate the pathogenic microorganism, it can delay the time of bacterial colonization. To date, there is a minimal study regarding the use of probiotics in decreasing the incidence of VAP. The result of this study might help the intensivist use of probiotics as a beneficial effect in decreasing the rate of VAP and assess the advantages as well as risks.

Materials and Methods:

This randomized controlled trial was conducted in the ICU of Dhaka Medical College Hospital (DMCH), Department of Anesthesia, Pain, Palliative & Intensive Care, from March 2020 to October 2021 after receiving approval from the Ethical Review Committee of DMC [ERC-DMC/ECC/2020/71]. Neurocritical patients requiring mechanical ventilation for at least 48 hours were considered for inclusion. Using consecutive sampling, eligible patients were selected based on predefined inclusion and exclusion criteria after obtaining informed written consent from their guardians.

Patients aged 18-60 years, admitted in ICU with a neurological diagnosis[16] like ischemic stroke, intracerebral hemorrhage, traumatic head injury, GBS, myasthenia gravis, brain tumor, SAH, status epilepticus, or CNS infection who needed mechanical ventilation support for more than 48 hours were included in the study. Mechanically ventilated patients were those patients, who were given artificial ventilation to assist or replace spontaneous breathing, for reversible causes of respiratory failure for the duration of > 24 hours [17]. VAP was diagnosed if CPIS score 6 or more than 6 after 48hours of intubation and mechanical ventilation[18]. Patients were

1. Assistant Registrar, Intensive Care Unit, National Institute of Traumatology & Orthopaedic Rehabilitation, Sher-E-Bangla Nagar, Dhaka.
2. Indoor Medical Officer, Medicine, Dhaka Medical College, Dhaka.
3. Assistant Professor, Intensive Care Unit, National Institute of Traumatology & Orthopaedic Rehabilitation, Sher-E-Bangla Nagar, Dhaka.
4. FCPS part 2 trainee, Cardiology, Dhaka Medical College, Dhaka.
5. Associate Professor, Critical Care Medicine, Dhaka Medical College, Dhaka.

Corresponding Author:

Dr Benzir Shofi
Assistant Registrar
Intensive Care Unit
National Institute of Traumatology & Orthopaedic Rehabilitation
Email: benzirshofi@gmail.com

excluded if they had pre-existing pneumonia, primary diagnosis of severe acute pancreatitis, Pregnancy, Immunosuppression (AIDS), malignancy, neutrophil count less than 500/cumm, or cardiac arrest survivors.

Patients were randomly allocated in a 1:1 ratio into two groups using a simple lottery method. To ensure allocation concealment, identical allocation slips were placed inside sequentially numbered, opaque, sealed envelops prepared by an independent person not involved in patient recruitment. After enrollment, each patient's attendant drew an envelope to determine group assignment. Intervention group received probiotics and control group received placebo.

Diagnosis of VAP was made using the Clinically pulmonary infection score (CPIS). All relevant demographic, clinical and laboratory data were recorded in a structured data collection sheet. Data were compiled, coded and analyzed using SPSS version 26. A p-value<0.05 was considered statistically significant.

During the screening period, 140 patients were assessed; five died prior to group allocation. Remaining 135 patients were enrolled using consecutive sampling. Participants were randomized into two groups by the lottery method. Sixty-eight patients were allocated to the probiotic group (Intervention Group) and sixty-seven to the placebo group (Control Group). The study was double-blinded. The probiotic and placebo preparations were identical in appearance and packaging. Patients, treating physicians, and outcome assessors were blinded to group allocation; only the principal investigator was aware of the allocation sequence. Intervention group received probiotic capsules twice daily (every 12 hours) for 7 days. Each capsule contained Lactobacillus acidophilus (2×10^9 CFU), Lactobacillus bulgaricus (1×10^9 CFU), Bifidobacterium bifidum (1×10^9 CFU), and fructo-oligosaccharides (100 mg). The capsule contents were dissolved in 20 mL sterile water and administered via nasogastric tube. Control group conducted a placebo containing sterile maize starch powder, prepared and administered in an identical manner.

Patients were assessed on days 0, 4, and 7 for the development of ventilator-associated pneumonia using the CPIS. A CPIS ≥ 6 was considered diagnostic of VAP. Tracheal aspirates were collected on the same days for microbiological culture and analysis in the Department of Microbiology, DMCH. Relevant data were recorded from medical records, bedside flow sheet and report of microbiological studies of the patients. Patients were followed up total 14 days.

Statistical Analysis: Following data collection, all data were edited, coded, and entered into the Statistical Package for the Social Sciences (SPSS) version 26.0 for analysis. Data were entered as variables according to the predefined analysis plan. Descriptive statistics were expressed as frequency and percentage (%) for categorical variables. Quantitative data were expressed as mean ± standard deviation (SD). Continuous variables were compared between the two groups using Student's t-test, while categorical variables were analyzed using the Chi-square test to determine the significance of association between variables. A p-value of<0.05 was considered statistically significant.

Results

This randomized control trial was conducted in the Department of Anesthesia, Pain, Palliative & Intensive care, Dhaka Medical College Hospital. A total of 135 patients were allocated into two groups. Majority patients aged 40 to 55 years. The results are presented in the following tables & figures.

Table-I: Demographic characteristics of the study subjects in two groups (N=135)

Variables	Intervention Group (n=68)	Control Group (n=67)	p-value
Age (years)			
Mean±SD	41.1±11.86	43.2±9.92	0.248
Male	43	44	0.948
Female	25	23	
H/O smoking habits			
Yes	18(26.5%)	24(35.8%)	0.240
No	50(73.5%)	43(64.2%)	
Clinical diagnosis			*p*-value
Traumatic brain injury	15(22.1%)	17(25.4%)	0.801
Intracerebral haemorrhage	12(17.6%)	15(22.4%)	0.491
Subarachnoid haemorrhage	4(5.9%)	2(3.0%)	0.414
Ischemic stroke	16(23.5%)	17(25.4%)	0.803
Status of epilepticus	2(2.9%)	2(3.0%)	1.000
Guillain-Barre syndrome	8(11.8%)	9(13.4%)	0.770
Myasthenia gravis	4(5.9%)	2(3.0%)	0.414
Motor neuron disease	5(7.4%)	2(3.0%)	0.252
Encephalitis	1(1.5%)	1(1.5%)	1.000
Brain tumor	1(1.5%)	0(0.0%)	0.319

Data were expressed as frequency and percentage and mean ±SD . p-value<0.05 considered as a level of significance

Table-II: Co-morbidities between two groups (N=135)

Comorbid disease	Intervention Group (n=68)	Control Group (n=67)	*p*-value
HTN	8(11.8%)	6(13.43%)	0.529
DM	24(35.3%)	30(44.8%)	0.261
IHD	2(2.9%)	4(5.9%)	0.393

Figures in the parentheses indicate the corresponding percentage; Chi-squared Test (χ^2) was done to analyze the data**.**

p<0.05 considered as a level of significance

Table-III: Comparison of PaO2/FiO2 ratio between two groups (N=135)

Variable	Intervention Group (n=68)	Placebo Group (n=67)	*p*-value
PaO2/FiO2(Day 0)	476.3±150.7	468.6±167.2	0.418
PaO2/FiO2(Day 4)	415.1±141.8	395.8±162.9	0.104
PaO2/FiO2(Day 7)	401.3±135.1	384.6±139.4	0.079
Variables			
MAP (mmHg)	85.34±11.24	83.21±7.58	0.191
HR (beats/min)	86.96±13.63	88.92±12.25	0.353
Temp. (ºC)	37.16±0.18	37.12±0.17	0.179
RR	16.2 ±4.25	18.11 ± 4.28	0.267
GCS	9.11±1.13	9.14±1.11	0.874
WBCs×109/L	9.81±1.57	9.73±1.92	0.788

Table-IV: Comparison of clinical and laboratory parameters between two groups throughout study (N=135)

Variables	Intervention Group (n=68)	Control Group (n=67)	*p*-value
MAP (mmHg)	85.34±11.24	83.21±7.58	0.191
HR (beats/min)	86.96±13.63	88.92±12.25	0.353
Temp. (ºC)	37.16±0.18	37.12±0.17	0.179
RR	16.2 ±4.25	18.11 ± 4.28	0.267
GCS	9.11±1.13	9.14±1.11	0.874
WBCs×10^9/L	9.81±1.57	9.73±1.92	0.788

Data were expressed as mean ±SD

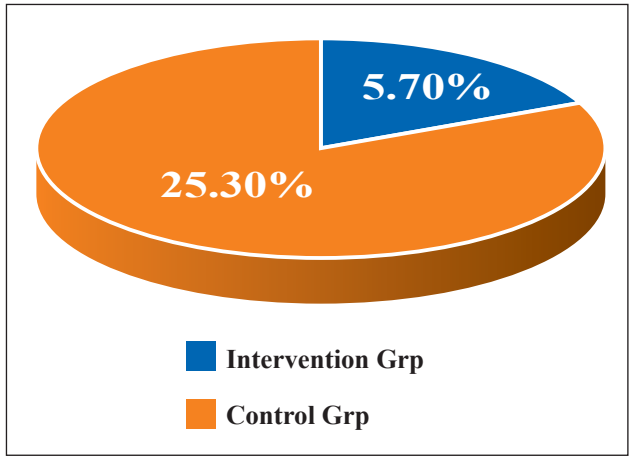

Figure 1: Incidence of VAP

On the evaluation of outcome, the present study shows the incidence of VAP in Intervention group was 5.7% and in Control group was 25.3% which was statistically significant as p =0.002 (fig 1).

Table- V: Pulmonary infiltration findings from chest X-ray between two groups at day 0, 4, 7 (N=135)

Pulmonary infiltration	Intervention Group (n=68)	Control Group (n=67)	*p*-value
Day 0			
Not infiltrate	00(0%)	00(0%)	
Day 4			
Not infiltrate	64(94.1%)	52(77.6%)	
Diffuse	1(1.47%)	4(5.97%)	0.04
Localized	3(4.41%)	11(16.4%)	
Total	68(100.0%)	67(100.0%)	
Day 7			
Not infiltrate	59(86.7%)	46(68.6%)	
Diffuse	2(2.94%)	6(8.95%)	0.006
Localized	7(10.29%)	15(22.3%)	
Total	68(100.0%)	67(100.0%)	

Table VI: Incidence of VAP according to CPIS score (N=135)

Variable	Intervention Group (n=68)	Control Group (n=67)	*p*-value
CPIS score ≥6	4(5.7%)	17(25.3%)	0.002

Figures in the percentheses indicate the corresponding percentage.

Discussion:

Ventilator-associated pneumonia (VAP) remains a significant cause of morbidity among mechanically ventilated ICU patients. The present study evaluated the incidence of VAP in neuro-critical care patients receiving probiotic therapy.

The baseline characteristics of both groups were comparable. The mean age of patients in intervention group was 41.1 ± 11.86 years and in control group was 43.2 ± 9.92 years. Male predominance was observed in both groups (63.2% vs 63.2%), with no statistically significant difference in gender distribution. Similar demographic findings were reported by Joseph et al [1].

No significant difference was observed between the groups regarding smoking status (p = 0.360). Mirtalaei et al.[2] also reported no statistically significant difference in smoking prevalence between intervention and control groups. However, Xie et al [3]. demonstrated that smoking is a strong predictor of VAP development, with smokers having a 4.37-fold higher risk compared to non-smokers or those who had ceased smoking. The increased susceptibility may be attributed to impaired pulmonary macrophage function and reduced bacterial clearance associated with chronic smoking.

The majority of patients in the present study were admitted with ischemic stroke, traumatic brain injury (TBI), and

intracranial hemorrhage (ICH). These findings are consistent with Kenna et al[4]. who reported similar admission diagnoses among neuro-critical patients.

Regarding comorbidities, diabetes mellitus (DM) was the most common, followed by hypertension (HTN) and ischemic heart disease (IHD). Although numerically higher in some categories, the differences between groups were not statistically significant. Similar findings were observed by Mahmoodpoor et al[5]. who reported that comorbid conditions such as DM and HTN are common among ICU patients with pneumonia.

Arterial blood gas parameters, particularly the PaO_2/FiO_2 ratio, were comparable between the two groups and did not show a statistically significant difference. These findings are consistent with Farouk et al [6]. who also reported no significant difference in oxygenation indices between probiotic and control groups.

However, purulent tracheal secretion was significantly lower in the probiotic group (13.2%) compared to the placebo group (29.9%) ($p<0.018$). Farouk et al [6] .similarly observed a higher incidence of purulent tracheal secretion in the control group compared to the probiotic group.

Limitations

The findings should be explained in light of diverse limitations. VAP diagnosis was primarily based on CPIS criteria without quantitative microbiological confirmation may have affected diagnostic accuracy. Furthermore, single-center design and modest sample size may limit the applicability of the findings to wide population. Finally, important long-term outcomes, including ICU mortality prevents a comprehensive evaluation of the clinical impact of the intervention.

Conclusion

Our study suggested that probiotic administration was associated with a statistically significant reduction in the incidence of VAP in neurocritical patients. They appear to be a safe, low cost intervention that may improve clinical outcome. So, Probiotic can be used to reduce ventilator associated pneumonia in neurocritical care patients.

Conflict of interest

The authors have no conflict of interest to declare.

References:

1. Tan M, Zhu JC, Du J, Zhang LM, Yin HH. Effects of probiotics on serum levels of Th1/Th2 cytokine and clinical outcomes in severe traumatic brain-injured patients: a prospective randomized pilot study. Crit Care. 2011 Dec 2;15(6):R290.
2. Jacobi CA, Schulz C, Malfertheiner P. Treating critically ill patients with probiotics: Beneficial or dangerous? Gut Pathog. 2011 Feb;3(1):2.
3. Estes RJ, Meduri GU. The pathogenesis of ventilator-associated pneumonia: I. Mechanisms of bacterial transcolonization and airway inoculation. Intensive Care Med. 1995 Apr;21(4):365–83.
4. Rongrungruang Y, Krajangwittaya D, Pholtawornkulchai K, Tiengrim S, Thamlikitkul V. Randomized controlled study of probiotics containing Lactobacillus casei (Shirota strain) for prevention of ventilator-associated pneumonia. J Med Assoc Thai. 2015;98(3):253–9.
5. Chastre J, Fagon J. State of the art ventilator-associated pneumonia. Am J Respir Crit Care Med. 1997;10.
6. Hayakawa M, Asahara T, Ishitani T, Okamura A, Nomoto K, Gando S. Synbiotic Therapy Reduces the Pathological Gram-Negative Rods Caused by an Increased Acetic Acid Concentration in the Gut. Dig Dis Sci. 2012 Oct;57(10):2642–9.
7. Klarin B, Molin G, Jeppsson B, Larsson A. Use of the probiotic Lactobacillus plantarum 299 to reduce pathogenic bacteria in the oropharynx of intubated patients: a randomised controlled open pilot study. Crit Care. 2008 Nov 6;12(6):R136.
8. Lorente L, Blot S, Rello J. Evidence on measures for the prevention of ventilator-associated pneumonia. Eur Respir J. 2007;30(6):1193–207.
9. Dodek P, Keenan S, Cook D, Heyland D, Jacka M, Hand L, et al. Evidence-Based Clinical Practice Guideline for the Prevention of Ventilator-Associated Pneumonia. Ann Intern Med. 2004 Aug 17;141(4):305–13.
10. Morrow LE, Kollef MH, Casale TB. Probiotic Prophylaxis of Ventilator-associated Pneumonia: A Blinded, Randomized, Controlled Trial. Am J Respir Crit Care Med. 2010 Oct 15;182(8):1058–64.
11. McNabb B, Isakow W. Probiotics for the prevention of nosocomial pneumonia: current evidence and opinions. Curr Opin Pulm Med. 2008;14(3):168–75.
12. Madsen K. Probiotics in critically ill patients. J Clin Gastroenterol. 2008;42:S116–8.
13. Borchert D, Sheridan L, Papatsoris A, Faruquz Z, Barua JM, Junaid I, et al. Prevention and treatment of urinary tract infection with probiotics: review and research perspective. Indian J Urol. 2008;24(2):139–44.
14. Boyle RJ, Robins-Browne RM, Tang ML. Probiotic use in clinical practice: what are the risks? Am J Clin Nutr. 2006;83(6):1256–64.
15. Manzanares W, Lemieux M, Langlois PL, Wischmeyer PE. Probiotic and synbiotic therapy in critical illness: a systematic review and meta-analysis. Crit Care. 2016 Dec;20(1):262.
16. Weng H, Li JG, Mao Z, Feng Y, Wang CY, Ren XQ, et al. Probiotics for preventing ventilator-associated pneumonia in mechanically ventilated patients: a meta-analysis with trial sequential analysis. Front Pharmacol. 2017;8:717.
17. Xie J, Yang Y, Huang Y, Kang Y, Xu Y, Ma X, et al. The current epidemiological landscape of ventilator-associated pneumonia in the intensive care unit: a multicenter prospective observational study in China. Clin Infect Dis. 2018;67(suppl_2):S153–61.
18. Harde Y, Rao SM, Sahoo J, Bharuka A, Swetha B, Saritha P. Detection of ventilator associated pneumonia, using clinical pulmonary infection score (CPIS) in critically ill neurological patients. MORTALITY. 1926;84:0–96.