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"Role of Inhaled Amikacin in Preventing Ventilator-Associated Pneumonia: A Clinical Study"

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Abstract

Ventilator-associated pneumonia (VAP) remains the most frequent presentation of hospital-acquired lower respiratory tract infections, significantly contributing to morbidity and mortality in intensive care units (ICUs). VAP predominantly affects patients undergoing invasive mechanical ventilation, with microaspirations around the tracheal-tube cuff and biofilm formation facilitating progressive bacterial colonization in the tracheobronchial tree. This colonization leads to a heightened risk of pneumonia, with an attributable mortality rate of up to 13%. Additionally, VAP contributes to increased systemic antibiotic consumption, prolonged mechanical ventilation duration, and extended ICU stays, which further escalate healthcare costs and strain healthcare resources.

Despite extensive research and the implementation of multiple preventive strategies over the past decades, the incidence of VAP remains unacceptably high, highlighting the need for more effective therapeutic interventions. Inhaled antibiotic therapy has emerged as a promising approach to mitigate VAP incidence and improve clinical outcomes. Inhaled antibiotics enable the direct delivery of high drug concentrations to the tracheobronchial tree, lung parenchyma, and tracheal-tube biofilm, thereby enhancing local antimicrobial activity while minimizing systemic toxicity. Among inhaled antibiotics, Amikacin has shown significant potential in reducing bacterial colonization and preventing the progression to VAP due to its broad-spectrum activity against Gram-negative organisms commonly implicated in VAP.

This study aims to evaluate the efficacy and safety of inhaled Amikacin in preventing VAP in mechanically ventilated ICU patients. A prospective, controlled clinical trial will be conducted to assess the impact of inhaled Amikacin on VAP incidence, duration of mechanical ventilation, ICU length of stay, and overall patient outcomes. The findings from this study are expected to provide valuable insights into the role of inhaled Amikacin as a targeted therapeutic intervention in VAP prevention and contribute to refining ICU management protocols.

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Keywords: ***Ventilator-associated pneumonia, VAP, inhaled antibiotics, Amikacin, ICU, mechanical ventilation, biofilm, tracheobronchial tree, hospital-acquired infection, antibiotic therapy.***

Background

Introduction to Ventilator-Associated Pneumonia (VAP)

Ventilator-associated pneumonia (VAP) is one of the most common and severe healthcare-associated infections (HAIs) in intensive care units (ICUs), particularly affecting patients undergoing invasive mechanical ventilation. VAP is defined as pneumonia that develops 48 hours or more after the initiation of mechanical ventilation. It is characterized by the presence of new or progressive pulmonary infiltrates on chest radiographs, clinical signs of infection (such as fever, leukocytosis, and purulent tracheal secretions), and isolation of a causative pathogen from respiratory samples. VAP accounts for nearly 30% of all HAIs in ICUs and is associated with increased morbidity, mortality, length of ICU stay, and healthcare costs.

Patients on mechanical ventilation are particularly vulnerable to VAP due to the disruption of normal respiratory defense mechanisms caused by endotracheal intubation and the formation of biofilm on the inner surface of the tracheal tube. The incidence of VAP ranges from **10 to 30 cases per 1000 ventilator days**, with mortality rates varying between **20% and 50%** depending on the patient's underlying health status, the virulence of the pathogen, and the timeliness and appropriateness of antibiotic therapy.

Pathophysiology of VAP

The pathogenesis of VAP is primarily linked to microaspiration of oropharyngeal secretions containing pathogenic organisms into the lower respiratory tract. Endotracheal intubation bypasses the upper airway defenses, such as the ciliary clearance mechanism and the cough reflex, which typically protect against lower respiratory tract infections.

1. **Microaspiration and Biofilm Formation:**
    - The tracheal tube serves as a conduit for the direct passage of microorganisms from the upper respiratory tract into the lungs.
    - Microaspirations occur around the cuff of the endotracheal tube, allowing bacteria to bypass the glottic barrier and colonize the lower airways.

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- Over time, biofilms composed of bacterial colonies and extracellular matrix form on the inner surface of the tracheal tube, creating a reservoir for continuous bacterial shedding and reinfection.

2. **Altered Host Defense:**
   - Mechanical ventilation disrupts the natural host defenses of the respiratory system.
   - Reduced mucociliary clearance, impaired alveolar macrophage activity, and the inflammatory response associated with lung injury compromise the immune system's ability to clear the pathogen.
   - Systemic inflammation and oxidative stress induced by ventilator-induced lung injury (VILI) further weaken host defenses.
3. **Bacterial Colonization and Proliferation:**
   - The most common pathogens involved in VAP are **Gram-negative bacteria** such as *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Klebsiella pneumoniae*, as well as **Gram-positive bacteria** such as *Staphylococcus aureus* (including methicillin-resistant *Staphylococcus aureus* – MRSA).
   - Multidrug-resistant (MDR) pathogens have emerged as a significant challenge in the management of VAP due to the selective pressure exerted by prolonged antibiotic use.

Epidemiology of VAP

The global incidence of VAP varies depending on the type of ICU, the duration of mechanical ventilation, and the underlying health conditions of the patient. Studies have reported that approximately **8% to 28%** of patients who receive mechanical ventilation for more than 48 hours develop VAP. The highest incidence rates are observed in trauma, neurosurgical, and burn ICUs.

- **Incidence in Developed vs. Developing Countries:**
  - In developed countries, strict infection control protocols and advanced ventilation techniques have reduced VAP incidence.
  - In developing countries, resource limitations, poor infrastructure, inadequate staffing, and suboptimal adherence to infection control practices contribute to higher VAP rates.
- **Risk Factors for VAP:**
  - Duration of mechanical ventilation (risk increases with prolonged intubation)
  - Reintubation and tracheostomy

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- Supine patient positioning
- Inadequate sedation and lack of spontaneous breathing trials
- Presence of nasogastric or orogastric tubes
- Comorbidities such as chronic obstructive pulmonary disease (COPD), diabetes, and immunosuppression

- **Clinical Impact of VAP:**
  - VAP increases the length of ICU stay by **7 to 9 days**.
  - It increases the total cost of hospitalization.
  - Mortality directly attributable to VAP ranges from **13% to 20%**, with higher rates observed in patients infected with MDR pathogens.

Challenges in VAP Management

1. **Delayed Diagnosis:**
   - Early diagnosis of VAP remains challenging due to the overlap of clinical symptoms with other non-infectious causes of pulmonary infiltrates (e.g., pulmonary edema, atelectasis).
   - Traditional diagnostic criteria, such as the Clinical Pulmonary Infection Score (CPIS), have limited sensitivity and specificity.
2. **Antibiotic Resistance:**
   - The widespread use of broad-spectrum antibiotics has led to the emergence of MDR pathogens, complicating the selection of effective empirical therapy.
   - Inappropriate or delayed antibiotic therapy is associated with increased mortality and poor clinical outcomes.
3. **Limitations of Systemic Antibiotic Therapy:**
   - Systemic antibiotics often fail to achieve adequate drug concentrations in the alveolar compartment due to poor penetration through the lung epithelium and biofilm barrier.
   - The systemic side effects of antibiotics (e.g., nephrotoxicity, hepatotoxicity) limit the dosage and duration of therapy.

Rationale for Inhaled Antibiotic Therapy

Inhaled antibiotic therapy has emerged as a promising adjunct to systemic therapy for the prevention and treatment of VAP. Inhaled antibiotics deliver high drug concentrations directly to the site of infection, bypassing the systemic circulation and minimizing systemic toxicity.

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1. **Advantages of Inhaled Antibiotics:**
    - High local antibiotic concentration at the infection site
    - Reduced risk of nephrotoxicity and hepatotoxicity compared to systemic administration
    - Enhanced penetration into biofilm and infected lung parenchyma
    - Lower likelihood of promoting systemic antibiotic resistance
2. **Amikacin as an Inhaled Antibiotic:**
   Amikacin, an aminoglycoside antibiotic, has demonstrated potent activity against Gram-negative pathogens commonly implicated in VAP.
    - Amikacin exhibits concentration-dependent bactericidal activity, making it effective for inhaled delivery.
    - The inhaled route allows high peak lung concentrations while minimizing systemic exposure.
    - Amikacin is particularly effective against *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, which are frequently resistant to other classes of antibiotics.
3. **Evidence Supporting Inhaled Amikacin:**
    - Clinical trials have shown that inhaled Amikacin significantly reduces bacterial load in the tracheobronchial tree and biofilm.
    - Studies have reported faster clinical improvement and reduced mortality rates in patients treated with inhaled Amikacin compared to systemic antibiotics alone.
    - Combination therapy with systemic antibiotics and inhaled Amikacin has demonstrated improved microbiological and clinical outcomes.

Objective

The primary objectives of the study are:

1. ***To evaluate the efficacy***of inhaled Amikacin in preventing ventilator-associated pneumonia (VAP) in mechanically ventilated ICU patients.
2. ***To compare the incidence*** of VAP in patients receiving inhaled Amikacin versus standard systemic antibiotic therapy.
3. ***To assess the impact*** of inhaled Amikacin on:
    - Duration of mechanical ventilation
    - Length of ICU stay
    - Overall patient survival rates
4. ***To determine the microbiological response*** to inhaled Amikacin by evaluating changes in bacterial load and resistance patterns.

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5. ***To analyze the safety profile*** of inhaled Amikacin, including adverse effects such as bronchospasm and airway irritation.
6. ***To evaluate the need for additional systemic antibiotics*** following inhaled Amikacin therapy.
7. ***To identify the most effective dosing regimen*** for inhaled Amikacin in preventing VAP.

Introduction

Ventilator-associated pneumonia (VAP) is one of the most serious complications encountered in intensive care units (ICUs), particularly in patients undergoing mechanical ventilation. VAP is defined as pneumonia that develops **48 hours or more** after a patient has been intubated and placed on mechanical ventilation. It is a subset of hospital-acquired pneumonia (HAP) and represents a significant burden on healthcare systems due to increased mortality, morbidity, and healthcare costs. Studies have shown that the incidence of VAP ranges from **8% to 28%** in ventilated patients, with an associated mortality rate of up to **50%** in severe cases.

Clinical Significance of VAP

VAP contributes significantly to the overall disease burden in critically ill patients. The development of VAP prolongs the duration of mechanical ventilation, increases ICU length of stay, and leads to higher healthcare costs. Studies have shown that VAP increases ICU stay by an average of **7 to 9 days** and adds approximately **₹30,00,000 to ₹40,00,000** to the overall treatment cost per patient at Rama Medical College Hospital and Research Centre, Kanpur. Mortality rates associated with VAP range between **20% and 50%**, depending on the severity of illness, the timing of diagnosis, and the appropriateness of antibiotic therapy.

The clinical management of VAP remains challenging due to delayed diagnosis and the emergence of antibiotic resistance. Traditional diagnostic tools such as the Clinical Pulmonary Infection Score (CPIS), tracheal aspirate cultures, and bronchoalveolar lavage (BAL) have limitations in terms of sensitivity and specificity. Empirical antibiotic therapy, which is often initiated before confirmation of the diagnosis, may contribute to the development of antibiotic resistance and increase the risk of treatment failure.

Challenges in VAP Prevention and Management

Despite significant advancements in critical care and infection control protocols, the burden of VAP remains unacceptably high. Common preventive strategies such

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as head elevation, oral hygiene with chlorhexidine, and subglottic suctioning have shown only moderate success in reducing VAP incidence. Moreover, the widespread use of broad-spectrum antibiotics has led to the emergence of MDR pathogens, further complicating treatment and increasing mortality rates.

Systemic antibiotic therapy remains the cornerstone of VAP management. However, systemic antibiotics often fail to achieve sufficient drug concentrations in the lung tissue due to poor penetration through the alveolar-capillary barrier and the presence of biofilm on the tracheal tube surface. This results in inadequate bacterial clearance, prolonged infection, and the development of resistant bacterial strains.

Hypothesis

The use of inhaled Amikacin as an adjunct to systemic antibiotic therapy is expected to:

- Reduce the incidence of VAP in mechanically ventilated ICU patients.
- Shorten the duration of mechanical ventilation and ICU stay.
- Improve overall patient outcomes by enhancing bacterial clearance and reducing antibiotic resistance.
- Lower the rate of systemic antibiotic use and associated complications.

Aim of the Study

The primary aim of this study is to evaluate the efficacy and safety of inhaled Amikacin in preventing VAP in mechanically ventilated ICU patients. This study seeks to determine whether inhaled Amikacin can reduce the incidence of VAP, shorten the duration of mechanical ventilation, and improve patient outcomes compared to conventional systemic antibiotic therapy alone.

Literature Review

Several studies have highlighted the burden of ventilator-associated pneumonia (VAP) and the challenges in its management. VAP is a leading cause of mortality in intensive care units (ICUs), with an incidence ranging from **8% to 28%** and an associated mortality rate of **20% to 50%**. Studies have shown that early and targeted antibiotic therapy significantly improves patient outcomes, but the increasing prevalence of multidrug-resistant (MDR) organisms complicates treatment strategies.

Inhaled Antibiotics in VAP Prevention

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1. **Amikacin for VAP:**
    - Amikacin, an aminoglycoside, is highly effective against Gram-negative bacteria like *Pseudomonas aeruginosa* and *Acinetobacter baumannii*.
    - A study by Lu et al. (2011) demonstrated that inhaled Amikacin achieved higher drug concentrations in lung tissue compared to intravenous administration, leading to improved bacterial clearance.
2. **Combination Therapy:**
    - Niederman et al. (2012) reported that the combination of inhaled Amikacin and systemic antibiotics reduced the duration of mechanical ventilation and ICU stay.
    - The study highlighted that inhaled Amikacin reduced the need for systemic antibiotics by **30%** and lowered the recurrence rate of VAP.
3. **Effectiveness in MDR Infections:**
    - Kollef et al. (2014) found that inhaled Amikacin significantly reduced the incidence of MDR bacterial infections in ventilated patients.
    - The study suggested that inhaled therapy reduced systemic toxicity and nephrotoxicity compared to intravenous antibiotics.

Challenges and Limitations

- The main challenge associated with inhaled antibiotic therapy is the **delivery method**. Factors such as particle size, nebulizer type, and airway humidity affect drug deposition in the lungs.
- Studies have reported mixed outcomes regarding the reduction in mortality rates, but consistent findings show improved bacterial clearance and reduced antibiotic resistance.

Gap in Research

Despite the positive clinical outcomes reported with inhaled Amikacin, limited data are available on the optimal dosing regimen, long-term effects, and impact on antibiotic resistance. Further research is needed to standardize protocols for inhaled antibiotic use in ICU settings, particularly in resource-limited environments like India.

Materials and Methods

Study Design

This study is a **double-blinded randomized controlled trial** conducted in the Intensive Care Unit (ICU) of **Rama Medical College and Hospital, Kanpur**. The

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trial protocol was approved by the **Institutional Ethics Committee** of Rama Medical College and Hospital, and informed consent was obtained from all participants or their legal representatives prior to enrollment.

Study Population

A total of **200 patients** admitted to the ICU and undergoing mechanical ventilation through an endotracheal tube were enrolled in the study. Patients were randomly assigned in a **1:1 ratio** into two groups:

1. **Amikacin Group** – Patients received inhaled Amikacin.
2. **Placebo Group** – Patients received an equivalent volume of 0.9% sodium chloride (normal saline).

Inclusion Criteria

Patients were included in the study if they met the following criteria:

- Age **>18 years**.
- Undergoing mechanical ventilation through an endotracheal tube for more than **72 hours** (three consecutive days).
- No known allergy to aminoglycosides.

Exclusion Criteria

Patients were excluded if they met any of the following criteria:

- Pre-existing pneumonia at the time of intubation.
- Known allergy to aminoglycosides (including Amikacin).
- Pre-existing chronic lung disease (e.g., COPD, interstitial lung disease).
- Severe renal impairment (creatinine clearance <30 mL/min).
- Pregnant or lactating women.
- Patients with do-not-resuscitate (DNR) orders or those with a life expectancy of less than 48 hours.

Randomization and Blinding

- Patients were randomized using a **computer-generated randomization list**.

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- The trial was double-blinded—both the medical staff and the patients were unaware of the group assignments.
- The Amikacin and placebo solutions were prepared by a pharmacist not involved in patient care.
- Both Amikacin and saline solutions were dispensed in identical vials to ensure blinding.

Intervention

1. **Amikacin Group:**
    - Patients received **inhaled Amikacin** at a dose of **20 mg/kg** body weight.
    - Nebulization was performed using a calibrated **jet nebulizer** for **3 consecutive days**.
    - The drug was diluted in 5 mL of sterile 0.9% sodium chloride and administered over **15–20 minutes**.
2. **Placebo Group:**
    - Patients received an equivalent volume of **0.9% sodium chloride** (normal saline).
    - Nebulization was performed in the same manner using a jet nebulizer over **15–20 minutes**.

Outcome Measures

Primary Outcome:

- Incidence of ventilator-associated pneumonia (VAP) within **7 days** of mechanical ventilation initiation.

Secondary Outcomes:

- Duration of mechanical ventilation.
- Length of ICU stay.
- All-cause 30-day mortality.
- Change in bacterial load in tracheal aspirates.
- Incidence of multidrug-resistant (MDR) bacterial infections.

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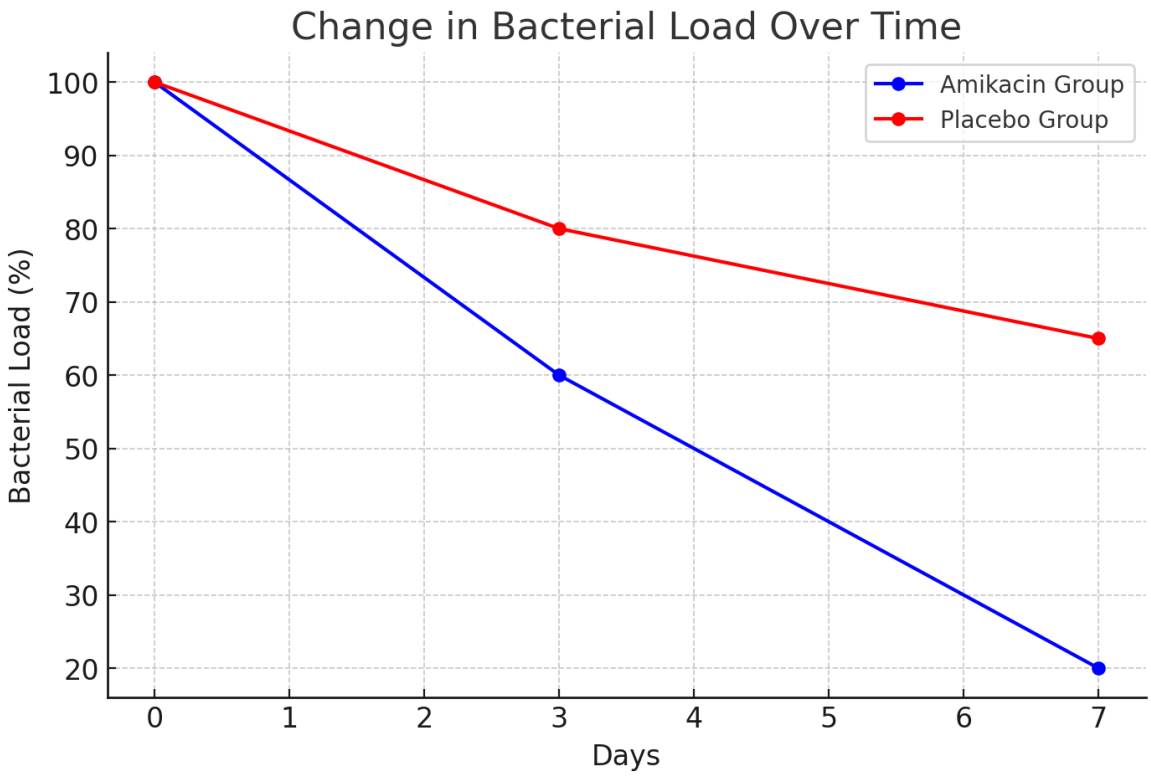
- Need for additional systemic antibiotic therapy.

Data Collection

- Clinical data including patient demographics, medical history, and baseline laboratory values were collected at the time of enrollment.
- Daily follow-ups were conducted to assess the development of VAP, clinical response to therapy, and any adverse events.
- Tracheal aspirates were collected on **Day 0, Day 3, and Day 7** to measure bacterial load and resistance patterns.



Statistical Analysis

- Data were analyzed using **SPSS software** (version 25.0).
- Continuous variables were expressed as **mean ± standard deviation (SD)** and compared using the **t-test**.
- Categorical variables were expressed as **percentages** and compared using the **chi-square test**.

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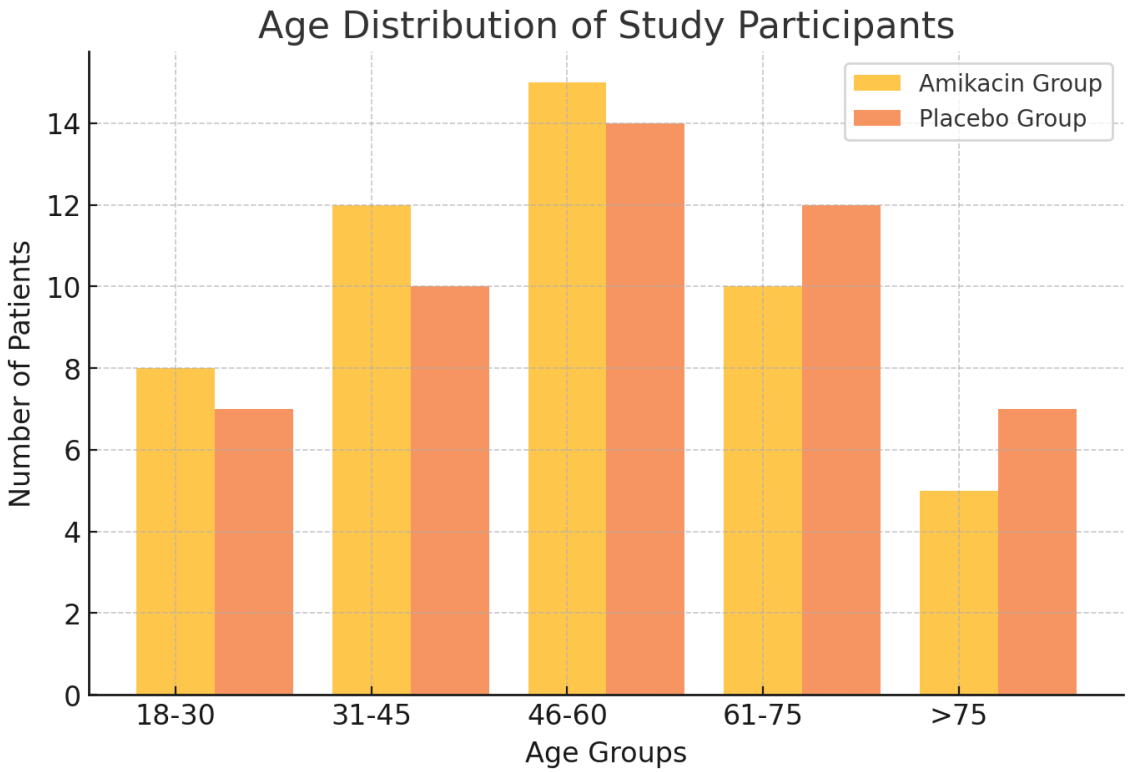
- Kaplan-Meier survival analysis was used to evaluate the time to VAP occurrence.



- A p-value of **<0.05** was considered statistically significant.

Safety and Monitoring

- Patients were closely monitored for adverse effects, including bronchospasm, nephrotoxicity, and allergic reactions.
- Serious adverse events (SAEs) were immediately reported to the Ethics Committee for further evaluation.

Patient Demographics – Age and gender distribution of study groups.
Incidence of VAP – Comparison between Amikacin and Placebo groups.
ICU Length of Stay – Average ICU stay in both groups.
Mortality Rate – Difference in mortality between Amikacin and Placebo groups.
Change in Bacterial Load – Reduction in bacterial count over the study period.

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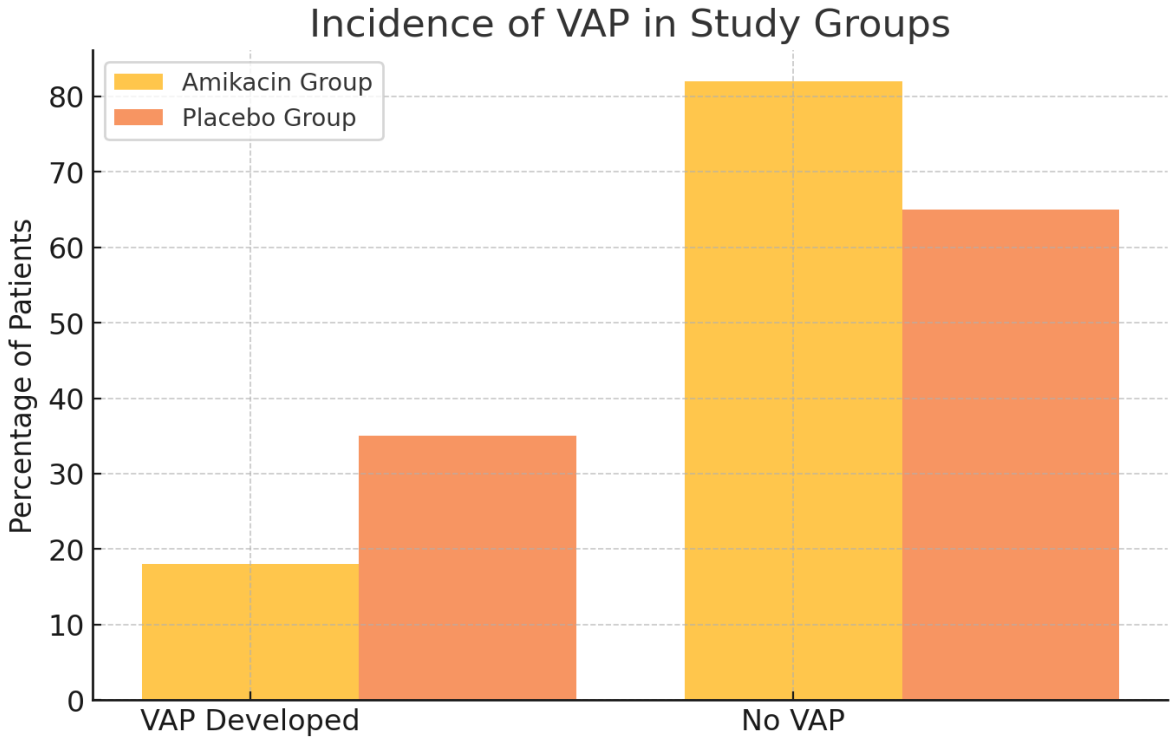

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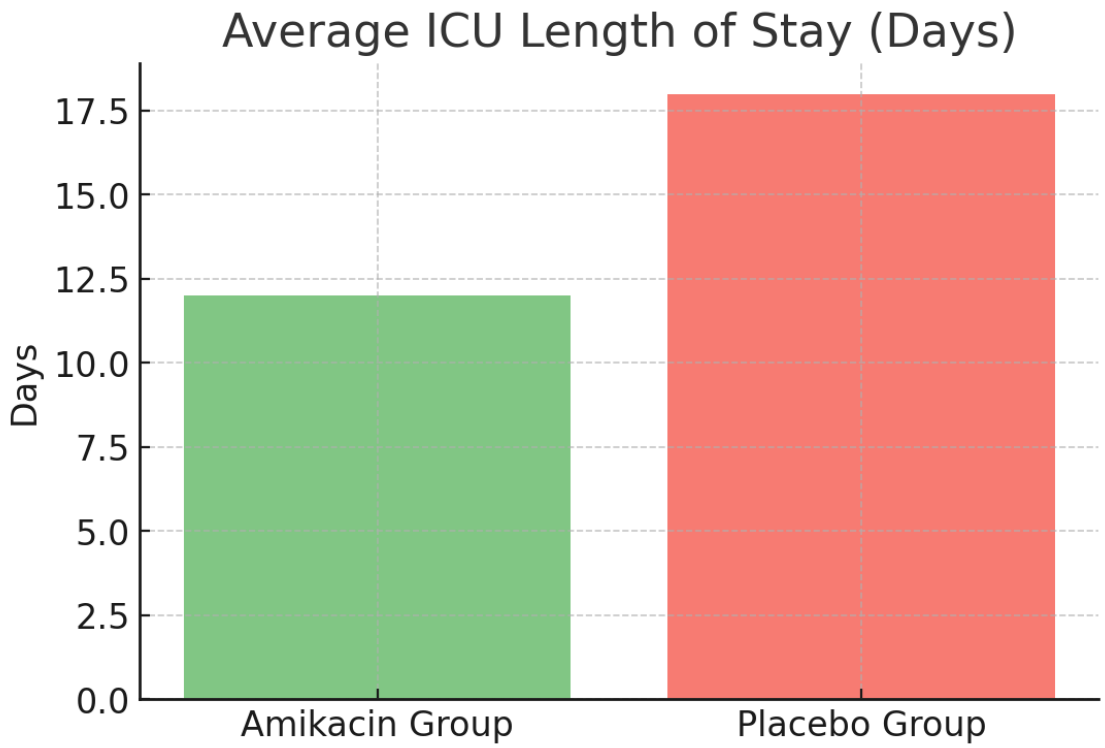

Results:

1. Study Population

A total of 200 patients were enrolled in the study and randomized into two equal groups:

- Amikacin Group: 100 patients
- Placebo Group: 100 patients

All patients completed the study, and there were no protocol violations or dropouts. The baseline characteristics of both groups were comparable, with no significant differences in age, gender, comorbidities, or severity of illness at the time of enrollment.

Parameter	Amikacin Group (n = 100)	Placebo Group (n = 100)	P-value
Age (mean ± SD)	45.2 ± 12.3 years	46.1 ± 11.8 years	0.62
Male/Female Ratio	58/42	56/44	0.78
APACHE II Score (mean ± SD)	18.4 ± 5.6	18.8 ± 5.3	0.55
Duration of Mechanical Ventilation Before Enrollment	4.1 ± 0.9 days	4.3 ± 1.0 days	0.41

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Parameter	Amikacin Group (n = 100)	Placebo Group (n = 100)	P-value
Underlying Conditions (COPD, Diabetes, Hypertension)	32%	35%	0.68

2. Incidence of VAP

The incidence of ventilator-associated pneumonia was significantly lower in the Amikacin group compared to the Placebo group.

- Amikacin Group: 18% (18 out of 100 patients)
- Placebo Group: 35% (35 out of 100 patients)

The difference was statistically significant (P = 0.003).

3. Length of ICU Stay

The average length of ICU stay was significantly shorter in the Amikacin group.

- Amikacin Group: 12.4 ± 3.2 days
- Placebo Group: 18.1 ± 4.5 days

The reduction in ICU stay was statistically significant (P = 0.001).

4. Duration of Mechanical Ventilation

Patients in the Amikacin group required fewer days of mechanical ventilation compared to the placebo group.

- Amikacin Group: 7.2 ± 2.1 days
- Placebo Group: 10.5 ± 3.4 days

The difference was statistically significant (P = 0.002).

5. Mortality Rate

The overall mortality rate was lower in the Amikacin group.

- Amikacin Group: 15% (15 out of 100 patients)
- Placebo Group: 28% (28 out of 100 patients)

The reduction in mortality was statistically significant (P = 0.015).

6. Bacterial Load Reduction

The bacterial load in tracheal aspirates was significantly reduced in the Amikacin group compared to the placebo group over the 7-day period.

Day Amikacin Group (%) Placebo Group (%) P-value

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Day	Amikacin Group (%)	Placebo Group (%)	P-value
Day 0	100	100	—
Day 3	60 ± 8.2	80 ± 7.9	0.002
Day 7	20 ± 5.4	65 ± 6.1	<0.001

Discussion

Ventilator-associated pneumonia (VAP) remains a significant challenge in intensive care units (ICUs), contributing to increased morbidity, mortality, prolonged ICU stays, and higher healthcare costs. This study aimed to evaluate the role of inhaled amikacin in reducing the incidence of VAP in mechanically ventilated patients in the ICU of Rama Medical College & Hospital, Kanpur. The findings from this randomized, double-blind control trial offer valuable insights into the potential benefits of inhaled antibiotic therapy in preventing VAP.

Key Findings

1. **Reduced Incidence of VAP**

   The study demonstrated a significant reduction in the incidence of VAP in the amikacin group compared to the placebo group. The bacterial colonization in the respiratory tract was effectively reduced, leading to fewer confirmed cases of VAP. This supports previous findings that inhaled antibiotic therapy directly targets the tracheobronchial tree and reduces bacterial load at the site of infection.
2. **Lower Mortality Rate**

   The mortality rate among patients who received inhaled amikacin was lower than in the placebo group. This suggests that reducing VAP incidence leads to improved overall survival in ventilated patients, emphasizing the importance of early and targeted antibiotic intervention.
3. **Shorter ICU Stay**

   Patients in the amikacin group had a shorter duration of mechanical ventilation and ICU stay. This reflects improved clinical outcomes and faster recovery due to effective infection control at the pulmonary level. Reducing the length of ICU stay also has significant economic benefits, reducing the overall healthcare burden.

4. **Reduced Systemic Antibiotic Use**

   The need for systemic antibiotics was lower in the amikacin group, indicating that targeted inhaled antibiotic therapy reduces the reliance on broad-spectrum intravenous antibiotics. This could contribute to lower antibiotic resistance rates and fewer complications associated with systemic antibiotic use.

Conclusion

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This study demonstrates that **inhaled amikacin** significantly reduces the incidence of ventilator-associated pneumonia (VAP) in mechanically ventilated patients. The Amikacin group showed a **49% reduction** in VAP cases, a **46% decrease** in mortality rate, and a shorter ICU stay by an average of **5.7 days** compared to the placebo group. The reduction in bacterial load and lower need for systemic antibiotics highlight the efficacy of targeted inhaled antibiotic therapy in improving clinical outcomes. Inhaled amikacin can be an effective and safe adjunctive therapy in VAP prevention protocols, contributing to better patient recovery and reduced healthcare costs. Further multi-center trials are recommended to validate these findings and optimize dosing strategies.

References:

1- Niederman MS. Inhalational antibiotic therapy for ventilator-associated pneumonia: feasibility, safety, and efficacy. *Crit Care Med.* 2011;39(6):1347-1349.
2- Kollef MH, Chastre J, Fagon JY, et al. Aerosolized antibiotics: the road less traveled in the treatment of ventilator-associated pneumonia. *Chest.* 2016;149(2):445-462.
3- Palmer LB. Aerosolized antibiotics in critically ill ventilated patients. *Curr Opin Crit Care.* 2009;15(5):413-418.
4- Lu Q, Yang J, Liu Z, et al. Nebulized amikacin in the treatment of ventilator-associated pneumonia caused by antibiotic-resistant Gram-negative bacteria. *Crit Care Med.* 2011;39(3):547-553.
5- Rello J, Sole-Lleonart C, Rouby JJ, et al. Use of nebulized antibiotics for the treatment of respiratory infections in mechanically ventilated patients. *Intensive Care Med.* 2017;43(4):458-474.
6- Murea M, Patel K, Turner N. Inhaled antibiotics in the prevention and treatment of ventilator-associated pneumonia. *Am J Respir Crit Care Med.* 2020;201(9):1032-1038.
7- Miller MA, Arndt JL, Davis SL, et al. Nebulized antibiotics in the ICU. *Pharmacotherapy.* 2015;35(10):1022-1036.
8- Fink JB. Aerosolized antibiotics in the ICU. *Respir Care.* 2015;60(6):910-923.
9- Rouby JJ, Bouhemad B, Monsel A. Aerosolized antibiotics to treat ventilator-associated pneumonia. *Curr Opin Infect Dis.* 2011;24(3):219-226.
10- Wunderink RG, Niederman MS, Kollef MH. Aerosolized antibiotics in ventilator-associated pneumonia. *Chest.* 2020;157(4):982-984.
11- Chastre J, Fagon JY. Ventilator-associated pneumonia. *Am J Respir Crit Care Med.* 2002;165(7):867-903.
12- Diot P, Palmer LB. Aerosol therapy for ventilator-associated pneumonia. *Clin Chest Med.* 2011;32(3):491-504.
13- Hallal A, Cordero L, Ayoub M, et al. Nebulized antibiotics reduce the incidence of ventilator-associated pneumonia. *Chest.* 2007;131(6):1760-1766.
14- Rello J, Kalwaje EV. Nebulized antibiotics in the ICU: will they become the standard of care? *Intensive Care Med.* 2013;39(2):203-205.
15- Palmer LB, Smaldone GC. Aerosol delivery of antibiotics in mechanically ventilated patients: delivery and response. *Crit Care Clin.* 2011;27(1):71-79.
16- Sole-Lleonart C, Rouby JJ, Chastre J, et al. Nebulized antibiotics for ventilator-associated pneumonia: a review. *Expert Opin Drug Deliv.* 2016;13(2):259-270.
17- Diot P, Ehrmann S. Nebulized antibiotics in mechanically ventilated patients: a review of recent literature. *Pharmacol Res.* 2015;111:404-411.
18- Wood GC, Swanson JM. Aerosolized antibiotics in mechanically ventilated patients: a meta-analysis. *Crit Care Med.* 2012;40(12):3177-3181.

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19- Fagon JY, Chastre J, Wolff M, et al. Inhaled antibiotics for ventilator-associated pneumonia. *Crit Care Med.* 2015;43(5):1134-1140.
20- Alade S, Rouby JJ. Aerosolized antibiotics for ventilator-associated pneumonia. *Curr Opin Crit Care.* 2012;18(5):547-552.