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Comparative Efficacy Of Metoclopramide And Azithromycin In The Prevention Of Ventilator-Associated Pneumonia (VAP)

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Abstract

Introduction and Background: Ventilator-associated pneumonia (VAP) poses a significant threat to critically ill patients in intensive care units (ICUs), contributing to increased morbidity, mortality, and healthcare costs. This study aims to compare the efficacy of two pharmacological interventions, metoclopramide, a prokinetic agent, and azithromycin, an antibiotic with anti-inflammatory properties, in preventing VAP in mechanically ventilated patients.
Objectives: The primary objective is to compare the incidence of VAP between patients receiving metoclopramide and those receiving azithromycin. Secondary objectives include evaluating safety profiles, assessing impact on gastric residual volumes and inflammation markers.
Study Design: A randomized, controlled, open-label trial conducted from June 2021 to December 2022 in the ICU of Chirayu Medical College & Hospital.
Participants: Adults (≥18 years) on mechanical ventilation for ≥48 hours were included, excluding those with allergies to study drugs, significant gastrointestinal motility disorders, or severe liver/kidney dysfunction.
Interventions: Patients received either intravenous metoclopramide (Group A) or azithromycin (Group B) for up to 14 days.
Outcome Measures: Primary outcome was the incidence of VAP within 14 days. Secondary outcomes included time to onset of VAP, gastric residual volumes, adverse events, length of ICU stay, and 28-day mortality.
Results: The study found no significant difference in VAP incidence between the two groups. Both drugs showed similar safety profiles and secondary outcomes.
Discussion: Lower-than-expected VAP rates may have impacted statistical power. Nonetheless, both interventions demonstrated comparable efficacy and safety, suggesting their potential utility in VAP prevention.
Conclusion: Both metoclopramide and azithromycin appear equally effective in preventing VAP in mechanically ventilated patients. Further research could explore combined drug regimens or alternative strategies for VAP prevention.
Potential Impact: Identifying effective pharmacological interventions for VAP prevention could improve patient outcomes and reduce healthcare-associated infections in ICUs, thus benefiting both patients and healthcare systems. Further research is warranted to confirm and extend these findings.

Introduction and Background

Ventilator-associated pneumonia (VAP) is a significant cause of morbidity and mortality among critically ill patients in intensive care units (ICUs). Preventing VAP is crucial to improving patient outcomes and reducing healthcare costs. Current strategies include strict infection control protocols, optimized mechanical ventilation settings, and pharmacological interventions. This study aims to compare the efficacy of metoclopramide, a prokinetic agent, and azithromycin, an antibiotic with anti-inflammatory properties, in preventing VAP in mechanically ventilated patients.

Objectives

Primary Objective

To compare the incidence of VAP in patients receiving metoclopramide versus those receiving azithromycin.

Secondary Objectives

- To evaluate the safety profile of metoclopramide and azithromycin.
- To assess the impact of these interventions on gastric residual volumes and markers of inflammation.

Hypotheses:
- **Null Hypothesis (H0):** There is no significant difference in the incidence of VAP between patients treated with metoclopramide and those treated with azithromycin.
- **Alternative Hypothesis (H1):** There is a significant difference in the incidence of VAP between patients treated with metoclopramide and those treated with azithromycin.

Study Design:
Type: Randomized, controlled, open-label trial.
Duration: June 2021 to December 2022.
Setting: Intensive Care Unit (ICU) of Chirayu Medical College & Hospital.

Participants
Inclusion Criteria
- Adults (≥18 years) requiring mechanical ventilation for ≥48 hours.
- Expected to remain on mechanical ventilation for ≥72 hours.
- Written informed consent from patient or legal representative.

Exclusion Criteria
- Known allergy to metoclopramide or azithromycin.
- Pre-existing significant gastrointestinal motility disorders.
- Severe liver or kidney dysfunction.
- Pregnancy or breastfeeding.

Interventions
- **Group A:** Patients received metoclopramide 10 mg intravenously every 6 hours.
- **Group B:** Patients received azithromycin 500 mg intravenously once daily.
- **Duration of Treatment:** Until the patient is weaned off mechanical ventilation or for a maximum of 14 days.

Outcome Measures:
Primary Outcome: Incidence of VAP, defined according to CDC criteria, within 14 days of mechanical ventilation.
Secondary Outcomes:
- Time to onset of VAP.
- Gastric residual volumes measured every 6 hours.
- Incidence of adverse events related to the study drugs.
- Length of ICU stay.
- 28-day mortality.

Data Collection and Analysis

Data Collection: Clinical data were collected daily from electronic medical records and bedside charts.

Statistical Analysis
- Incidence of VAP was compared using the chi-square test.
- Time-to-event data were analyzed using Kaplan-Meier curves and log-rank tests.
- Continuous variables (e.g., gastric residual volumes) were analyzed using t-tests or Mann-Whitney U tests as appropriate.
- Multivariate logistic regression was used to adjust for potential confounders.

Sample Size Calculation
Based on previous studies, assuming an incidence of VAP of 25% in the control group and aiming to detect a 10% absolute reduction in the intervention groups, with a power of 80% and a significance level of 0.05, a sample size of approximately 200 patients per group was required.

Ethical Considerations
Ethical Approval: The study protocol was reviewed and approved by the institutional review boards.

Informed Consent: Written informed consent was obtained from all participants or their legal representatives.

Confidentiality: Patient confidentiality was maintained throughout the study.

Timeline

- Month 1-3 (June 2021 - August 2021): Study preparation, staff training, and patient recruitment initiation.
- Month 4-15 (September 2021 - November 2022): Patient recruitment and data collection.
- Month 16-18 (December 2022): Data analysis and manuscript preparation.

Results

The study's findings are summarized in three tables. Table 1 outlines the baseline characteristics of the participants, divided into two groups: the Metoclopramide Group and the Azithromycin Group. It provides crucial demographic and clinical information such as age, gender distribution, APACHE II scores, and duration of ventilation. Table 2 delves into the primary outcome of the research, which is the incidence of ventilator-associated pneumonia (VAP) in each group. It compares the number and percentage of VAP cases between the Metoclopramide and Azithromycin Groups, accompanied by a p-value indicating the statistical significance. Lastly, Table 3 presents secondary outcomes, including the time to onset of VAP, gastric residual volumes, incidence of adverse events, length of ICU stay, and 28-day mortality rates for both groups. These tables collectively offer a comprehensive overview of the study's findings, shedding light on the effectiveness of Metoclopramide and Azithromycin in preventing VAP and their impact on various patient-related factors.

Table 1: Baseline Characteristics

Characteristic	**Metoclopramide Group (n=200)**	**Azithromycin Group (n=200)**	**p-value**
Age (mean ± SD)	55.4 ± 16.2	56.1 ± 15.8	0.62
Gender (Male/Female)	112/88	115/85	0.77
APACHE II Score (mean ± SD)	22.3 ± 5.4	21.9 ± 5.1	0.42
Duration of Ventilation (days) (mean ± SD)	9.8 ± 3.2	9.6 ± 3.4	0.58

Table 2: Primary Outcome

Outcome Measure	Metoclopramide Group (n=200)	Azithromycin Group (n=200)	p-value
Incidence of VAP (%)	18 (9%)	12 (6%)	0.26

Table 3: Secondary Outcomes

Outcome Measure	Metoclopramide Group (n=200)	Azithromycin Group (n=200)	p-value
Time to Onset of VAP (days) (mean ± SD)	5.2 ± 1.8	4.8 ± 1.6	0.18
Gastric Residual Volumes (mL) (mean ± SD)	102 ± 35	98 ± 33	0.33
Incidence of Adverse Events (%)	25 (12.5%)	18 (9%)	0.24
Length of ICU Stay (days) (mean ± SD)	15.3 ± 4.8	14.7 ± 5.1	0.22
28-day Mortality (%)	30 (15%)	26 (13%)	0.56

Discussion

This study found no significant difference in the incidence of VAP between patients treated with metoclopramide and those treated with azithromycin. Both drugs showed similar safety profiles, and there were no significant differences in secondary outcomes such as time to onset of VAP, gastric residual volumes, length of ICU stay, and 28-day mortality.
The observed VAP rates were lower than anticipated, which may have affected the study's power to detect a significant difference. Additionally, the similar efficacy and safety profiles suggest that either medication could be considered based on individual patient characteristics and clinical context.

Conclusion

The findings suggest that both metoclopramide and azithromycin are similarly effective in preventing VAP in mechanically ventilated patients. Future research could explore the combined use of both drugs or other pharmacological strategies to further reduce VAP incidence.

Potential Impact

The results of this study could significantly impact clinical practice by identifying two effective pharmacological interventions for VAP prevention. This could improve patient outcomes and reduce healthcare-associated infections in

ICUs. Further research may be warranted to confirm these findings and explore the long-term benefits and risks associated with these interventions.

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