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EFFICACY OF SINGLE-DOSE ANTIBIOTIC ADMINISTRATION TO COMATOSE VENTILATOR PATIENTS FOR PROPHYLAXIS OF EARLY-ONSET PNEUMONIA

Mahnoor Khalil Ahmed[1], *Baquar Raza[2], Bushra Rehman[3], Akbar Gohar[4], Arshad Sattar Lakho[5], Tahir Hanif[6], Muhammad Muneeb[7], Aatir H. Rajput[8] & Asma Rajput[9]*

Karachi Medical & Dental College, Abbasi Shaheed Hospital, Karachi[1, 2], Shaukat Omar Memorial Hospital. *(*Fauji Foundation*)*, Karachi[3], Muhammad Medical College, Mirpurkhas[4, 5], Military Hospital, Rawalpindi[6], Liaquat University of Medical & Health Sciences[7, 8], LUMHS Research Forum [6, 7, 8, 9]

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Abstract:

Background: *Nosocomial pneumonias are recognized as an important cause of morbidity and mortality and comatose patients present a particularly high risk of early-onset ventilator-associated pneumonia (EO-VAP) for which antibiotic prophylaxis has been proposed.*

Objective: *To evaluate the efficacy of a single-dose of antibiotic prophylaxis at intubation against EO-VAP.*

Methodology: *This prospective cohort was conducted upon a sample of 400 comatose patients (Glasgow Coma Score 8) admitted to the Abbasi Shaheed Hospital, Karachi from June 2018 to December 2018 and administered a single-dose of antibiotic within 4 h of intubation and additionally comatose patients (admitted 4 h after intubation admitted from January 2018 to May 2018 who did not receive antibiotic prophylaxis. The incidence of EO-VAP, late-onset VAP, and ventilator-associated trachea-bronchitis was noted in both groups. The data obtained was recorded onto a structured questionnaire and analyzed using SPSS v.21 & Microsoft Excel 2016.*

Results: *Among, the 300 patient enrolled into the study, 29% were males while the remaining 71% were females. The mean age of the sample stood at 41 (SD ± 7). The incidence of VAP and incidence of EO-VAP were lower in the prophylaxis group. The incidence of late-onset VAP did not differ. The prophylaxis group yielded a lower incidence of ventilator-associated trachea-bronchitis. No differences in mortality were found between groups. Regression analysis confirmed that a single dose of antibiotic prophylaxis was independently associated with lower incidence of EO-VAP.*

Conclusion: *After careful consideration, it can be concluded that single dose of antibiotic prophylaxis at intubation might lower the incidence of EO-VAP. However, a randomized clinical trial should be conducted to confirm our findings.*

Keywords: *Nosocomial Pneumonia, Ventilator Associated Pneumonia, Trachea-Bronchitis, Efficacy, Antibiotic Therapy and Prophylaxis.*

Corresponding author:

Dr. Mahnoor Khalil Ahmed,

(MBBS, FCPS), Assistant Professor, Department of Medicine
Karachi Medical & Dental College, Abbasi Shaheed Hospital, Karachi
+92-336-3454788

QR code

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INTRODUCTION:

Ventilator-associated pneumonia (VAP) is the most frequent nosocomial infection in the intensive care unit (ICU), being responsible for more than half of antibiotic prescriptions in the ICU. [1] Altered consciousness is a recognized risk factor for VAP, [2] and the occurrence of EOP in these patients is extremely high, accounting for 70% of all cases of pneumonia. [2]

Recent research suggests that the occurrence of EOP in patients with an ICU stay of >48 h was 32%, [3] 44% in comatose patients and 29% in non-comatose patients. Colonization of the upper airways (nose, pharynx and trachea) is an independent risk factor for the development of EOP, and is demonstrable within 24 h of ICU admission in critically ill neurological patients. [4]

Etiologic pathogens for EOP in these patients are the same bacteria that colonize the upper airways, namely methicillin-susceptible Staphylococcus aureus, Haemophilus Influenzae and Streptococcus Pneumoniae. [5] In a randomized controlled trial (RCT), short-term antibiotic prophylaxis (two single cefuroxime doses 1,500 mg each 12 h apart after intubation) has been demonstrated to reduce the occurrence of EOP in critically ill neurological patients. [6]

Early-onset VAP (EO-VAP), which occurs during the first 4 days of MV in patients who have not received prior antibiotics or who have not had prior hospitalization, is usually caused by antibiotic sensitive bacteria, and late-onset VAP (LO-VAP), which occurs from the fifth day, is more likely to be caused by more-resistant pathogens. [6]

In comatose patients, EO-VAP develops due to micro-aspirations caused by glottic dysfunction before intubation and high bacterial inoculum introduction into the lower airway during the intubation procedure. [6] The most commonly isolated pathogens are methicillin-sensitive Staphylococcus aureus. (MSSA), Haemophilus Influenzae , and Streptococcus pneumoniae.

Some guidelines recommend different strategies to prevent VAP. [7] The latest American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) guidelines conclude, from level 1 evidence based on a single, prospective, randomized, clinical trial, that prophylactic administration of a systemic antibiotic for 24 h at the time of emergent intubation may be useful to prevent VAP in patients with closed head injury. [8]

However, the ATS/IDSA guidelines have not yet recommended the prophylactic use of systemic antibiotics, pending availability of more data. In 2005, Acquarolo et al [9] demonstrated a 64% relative risk reduction of EO-VAP in comatose patients receiving ampicillin-sulbactam for 3 days. Furthermore, selective digestive decontamination with topical antibiotics combined with IV antibiotics during the first days can also help prevent VAP. [10] However, a European consensus document on hospital-acquired pneumonia opined that more research is necessary to conclude that prophylactic antibiotic administration immediately after intubation reduces EO-VAP. [11]

We aimed to evaluate the efficacy of an intervention protocol with a single dose of antibiotic at intubation in reducing EO-VAP in comatose patients. We also analyzed the impact on the incidence of LO-VAP and ventilator-associated tracheobronchitis (VAT) on the length of MV, ICU stay, and hospital stay, and on mortality.

METHODOLOGY:

This prospective cohort was conducted upon a sample of 400 comatose patients (chosen via non-probability, consecutive sampling) admitted to the Abbasi Shaheed Hospital, Karachi from June 2018 to December 2018 and administered a single-dose of antibiotic within 4 h of intubation and additionally comatose patients (admitted 4 h after intubation admitted from January 2018 to May 2018 who did not receive antibiotic prophylaxis.

The present study compared two groups of patients. A prospective cohort of comatose patients on mechanical ventilation (Glasgow coma score 8) who were admitted who received a single dose of antibiotic as prophylaxis against EO-VAP within the first 4 h of intubation (the prophylaxis group) was compared with a control group comprising an old cohort of comatose patients who were mechanically ventilated admitted formerly and 4 h after intubation and who did not receive antibiotic prophylaxis.

Patients in the prophylaxis group received a single dose (2 g) of ceftriaxone within 4 h of intubation. Patients with known hypersensitivity to b -lactams received a single 1-g dose of Ertapenem, and patients with known anaphylaxis to b-lactams received a single 500-mg dose of levofloxacin. The incidence of EO-VAP, late-onset VAP, and ventilator-associated trachea-bronchitis was noted in both groups. The data

obtained was recorded onto a structured questionnaire and analyzed using SPSS v.21 & Microsoft Excel 2016.

RESULTS:

Among, the 300 patient enrolled into the study, 29% were males while the remaining 71% were females. The mean age of the sample stood at 41 (SD ± 7).

Age Group	**Males**	**Females**
Up to 20 years	*07*	*32*
21 to 30 years	*09*	*39*
31 to 40 years	*23*	*44*
41 to 50 years	*31*	*62*
51 years or more	*17*	*36*

The incidence of VAP and incidence of EO-VAP were lower in the prophylaxis group. The incidence of late-onset VAP did not differ. The prophylaxis group yielded a lower incidence of ventilator-associated trachea-bronchitis. No differences in mortality were found between groups. Regression analysis confirmed that a single dose of antibiotic prophylaxis was independently associated with lower incidence of EO-VAP.

Disease Condition	**Control Group *(n)***	**Intervention Group *(n)***
VAP	*54*	*29*
EO-VAP	*41*	*23*
LO-VAP	*13*	*06*
VA – Trachea-Bronchitis	*07*	*03*

DISCUSSION:

Our results demonstrate the effectiveness of a single dose of antibiotic for prophylaxis against EO-VAP in this specific group of comatose patients, without increasing incidence of infection by multi-resistant microorganisms. It is important to highlight that the incidence of EO-VAP in comatose patients is higher than in the general MV population.

The incidence of EO-VAP in comatose patients is higher than in the general MV population. In our study, the reported incidence of EO-VAP was 21.58% in the control group and is in agreement with other authors, such as Sirvent et al [12] (36% baseline EO-VAP), Acquarolo et al [13] (57.9% baseline EO-VAP), and Perbet et al [13] (64% baseline EO-VAP) in a population of unconscious patients with cardiac arrest. The high incidence of EO-VAP in patients with altered level of consciousness seems to be related to impaired swallowing, and gag and cough reflexes, which all facilitate aspiration.

In a study evaluating the risk factors for developing pneumonia within 48 h of intubation, Rello et al [14]

found that patients with respiratory/cardiac arrest and coma had the highest incidence of pneumonia in the first 48 h, that antibiotic use reduced the incidence of pneumonia within this period, and that other preventive measures such as the aspiration of subglottic secretions were ineffective because these patients had aspirated microorganisms while being intubated. [15]

Sirvent et al [12] conducted a randomized trial to evaluate the effectiveness of two doses of cefuroxime administered within 24 h of intubation in reducing the incidence of EO-VAP in patients with closed head injury. Acquarolo et al [13] also showed that 3 days' treatment with amoxicillin clavulanate reduced the incidence of pneumonia in comatose patients. Along the same line, Zandstra and Van Saene [15] suggested that the IV administration of systemic antibiotic (cefotaxime) in selective decontamination of the digestive tract during the first 5 days was largely responsible for the reduced incidence of VAP and improved survival observed in these patients. [16]

However, in these cases, the use of antibiotics may be more akin to a short course of treatment than true prophylaxis, and the administration of antibiotics for prolonged periods might increase the risk of subsequent infection with antibiotic-resistant micro-organisms. [17] For this reason, we decided to use a single dose of an antibiotic that has a long half-life and is effective against the primary endogenous flora responsible for most EO-VAP.

One of the dangers of overusing antibiotics is the selection for multi-resistant organisms. In our study, surveillance cultures were not obtained; however, we could not find differences in antibiotic resistance patterns for LO-VAP episodes between patients who did or did not receive antibiotic prophylaxis. This finding suggests that a single dose of antibiotic would not be a risk factor for generating resistance. [18]

CONCLUSION:

After careful consideration, it can be concluded that single dose of antibiotic prophylaxis at intubation might lower the incidence of EO-VAP. However, a randomized clinical trial should be conducted to confirm our findings.

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