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Effect of Nebulized Amikacin to Systemic Antibiotics to Prevent Ventilator Associated Pneumonia

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Abstract: Background: Ventilator associated pneumonia is an intractable problem in critically ill intubated patients in the ICU where the respiratory infections persist despite treatment with potent systemic antibiotics. Objective: The purpose of this study is to determine the effect of antibiotics administered as a prophylactic via the respiratory tract which achieve a high drug concentration in the target organ in the prevention of ventilator associated pneumonia (VAP). Methods: 40 patients were studied in two groups, each group of 20 patients, in the intensive care unit of GHAZI-AL HARIRI general hospital in BAGHDAD MEDICAL CITY from (May 2019 to November 2019). Critically ill intubated patients were randomized above 18 years of age, from both gender, intubated at least for 3 days and expected to survive for more than one week. The 1st group (A) treated with amikacin via the respiratory tract by the nebulizer in addition to the systemic antibiotics, the 2nd group (B) treated with systemic antibiotics only. Results: From the 40 patients who were studied, 2 patients from group (A) who received amikacin nebulizer in addition to the systemic antibiotics were developed ventilator associated pneumonia while 18 patients not developed signs and symptoms or radiological features suggesting a diagnosis of pneumonia. From the other group (B) who received just the systemic antibiotics 9 patients were developed ventilator associated pneumonia and the other 11 patients didn't develop VAP. Conclusion: Our study showed that the use of amikacin via the respiratory tract by a nebulizer can have a role in the prevention of ventilator associated pneumonia in critically ill intubated patients.

Keywords: ventilator associated pneumonia, amikacin, prevention.

INTRODUCTION

Critically ill patients in the intensive care unit (ICU) who undergo invasive mechanical ventilation (MV) by an endotracheal tube (ETT) or tracheostomy have high risk to develop Ventilator associated pneumonia (VAP) and it is an important cause of morbidity and mortality. Early diagnosis and practices known to prevent VAP can reduce mortality and decrease the development of multidrug–resistant organisms.

VAP is a type of hospital-acquired pneumonia that occurs more than 48 hours after endotracheal intubation. This can be further classified into early onset (within the first 96 hours of MV) and late onset (more than 96 hours after the initiation of MV), which is more commonly attributable to multidrug–resistant pathogens. (Hunter, J. D, 2006)

VAP is responsible for about half of all antibiotics given to patients in ICUs.(Vincent, J. L. *et al*., 1995) the overall rate of VAP is 13.6 per 1000 ventilator days.3 However, the individual rate varies according to patient group, risk factors, and hospital setting. The average time taken to develop VAP from the initiation of MV is around 5 to 7 days, with a mortality rate quoted as between 24% and 76%.(Charles, P. *et al*., 2014)

Antibiotic-sensitive community-acquired bacteria such as *Hemophilus* and *Streptococcus* are the usual cause of Early-onset VAP, occurring within the first four days of MV. VAP developing more than 5 days after initiation of MV is usually caused by multidrug–resistant bacteria such as Pseudomonas aeruginosa.(Charles, P. *et al*., 2014)

The common risk factors for the development of a multidrug resistant pathogen:

- Intravenous antibiotics within 90 days before admission.
- Septic shock at the time of VAP.
- Respiratory distress syndrome preceding the development of VAP.
- > 5 days of hospitalization prior to the development of VAP.
- Patient requiring renal replacement therapy prior to VAP.

First of all, the treatment of VAP depends on the knowledge of the common pathogens, previous micropathology specimens, and patients risk factors like (underlying respiratory conditions and immunosuppression).

Antibiotics used in the treatments of VAP as an empirical treatment should have the cover against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and gram-negative bacilli. (1)

Failing to select the suitable antibiotic and the delay in the treatment has been shown to increase the rate of mortality.

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Aerosolized amikacin is a current option in the treatment of VAP, as the aerosolized amikacin can increased the local concentration of the drug at the alveoli without increasing the systemic toxicity.

PATIENTS AND METHODS

Randomized clinical trial in which 40 patients were studied in two groups, each group of 20 patients. The study was supplemented in the intensive care unit of GHAZI AL-HARIRI for surgical specialties hospital in Baghdad medical city from May 2019 to November 2019.

We used amikacin because of its action against multidrug–resistant bacteria such as *Pseudomonas aeruginosa* which is the most common cause of VAP developing more than 5 days after initiation of MV and gram-negative Bactria, in addition to its ability to be nebulized during ventilator support.

The study has been approved by Scientific council of Anesthesia and Intensive care-Iraqi board.

Inclusion criteria
Critically ill intubated patients were randomized above 18 year of age, from both genders, intubated at least for 3 days and expected to survive for more than one week.

The Exclusion Criteria

- Pediatric age group.
- Pregnancy.
- History of allergy or adverse effect to amikacin or aerosolized therapy.
- Acute or chronic renal insufficiency.
- Immunosuppression.

The first group of 20 patients was treated with amikacin via the nebulizer in the ICU in addition to the IV systemic antibiotics. the nebulization started in the first 48hr of admission after checking the exclusion criteria and daily data collection done for the patients which is consist of:

The name of the patient, Age of the patient, Gender, Date of admission, Temp, PR, RR, Spo2, Bp, P/F ratio, confusion, purulent discharge, x-ray changes of VAP (new infiltration, patchy infiltration) white blood cells, s. procalcitonin, CRP, figure (1).

Any procedures done for the patient later like: Cv line, double lumen, CRRT, bronchoscopy, tracheostomy, others.

Number of organ dysfunction
Apache 2 score.

We calculate the predicted body weight of the patient and The dose of amikacin given was 25mg/kg/day (29), every 2ml of the total dose diluted in 5ml of distil water and start the nebulization for 3 days only in addition to the dose of systemic antibiotics given to the patient first as an empirical therapy and then deescalated according to the culture taken in advanced.

The second group of 20 patients treated only with IV systemic antibiotics and the same data collection was note from the first 48 hr. of admission.

The clinical findings (fever, elevated WBC) and the x-ray findings was monitored daily for the development of VAP in addition to the microbiological examination which is done for all patient.

Criteria used for diagnosing VAP and according to the clinical pulmonary infection score (CPIS):
1-Signs and symptoms (fever, elevated WBC, purulent discharge)
2-X-ray changes. (patchy)
3-Culture result.
4-P/f ratio.

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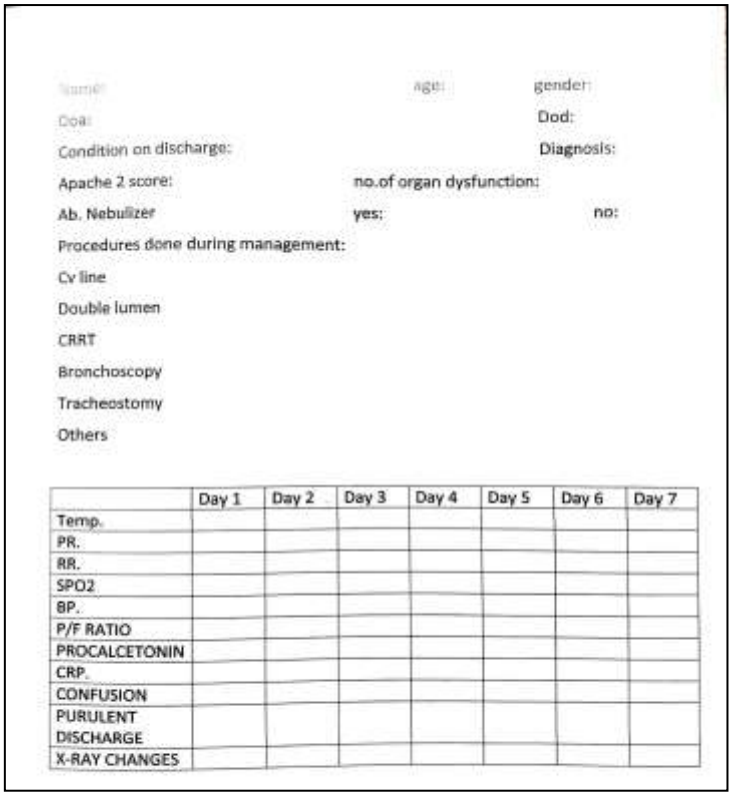

Name: age: gender:
Doa: Dod:
Condition on discharge: Diagnosis:
Apache 2 score: no.of organ dysfunction:
Ab. Nebulizer yes: no:
Procedures done during management:
Cv line
Double lumen
CRRT
Bronchoscopy
Tracheostomy
Others

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Temp.							
PR.							
RR.							
SPO2							
BP.							
P/F RATIO							
PROCALCETONIN							
CRP.							
CONFUSION							
PURULENT DISCHARGE							
X-RAY CHANGES							

Fig.1: Data Collection Sheet

The data analyzed using Statistical Package for Social Sciences (SPSS) version 25. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Independent t-test (two tailed) was used to compare the continuous variables accordingly. Z-test was used to compare the categorical variables accordingly. Chi square test was used to assess the association between study groups and certain information. A level of P – value less than 0.05 was considered significant.

RESULTS

The total number of patients in this study was 40. They were divided into two groups: Group A: Included 20 patients received nebulized amikacin and group B: Included the other 20 patients didn't receive nebulized amikacin.

The distribution of study patients by general characteristics is shown in figures (2 and 3). Study patient's age was ranging from 24 to 85 years with a mean of 52.95 years and standard deviation (SD) of ± 15.1 years. The highest proportion of study patients in groups A and B was aged ≥ 60 years (40% and 50% respectively).

Regarding gender, proportion of males was higher than females in groups A and B (55% and 50% respectively).

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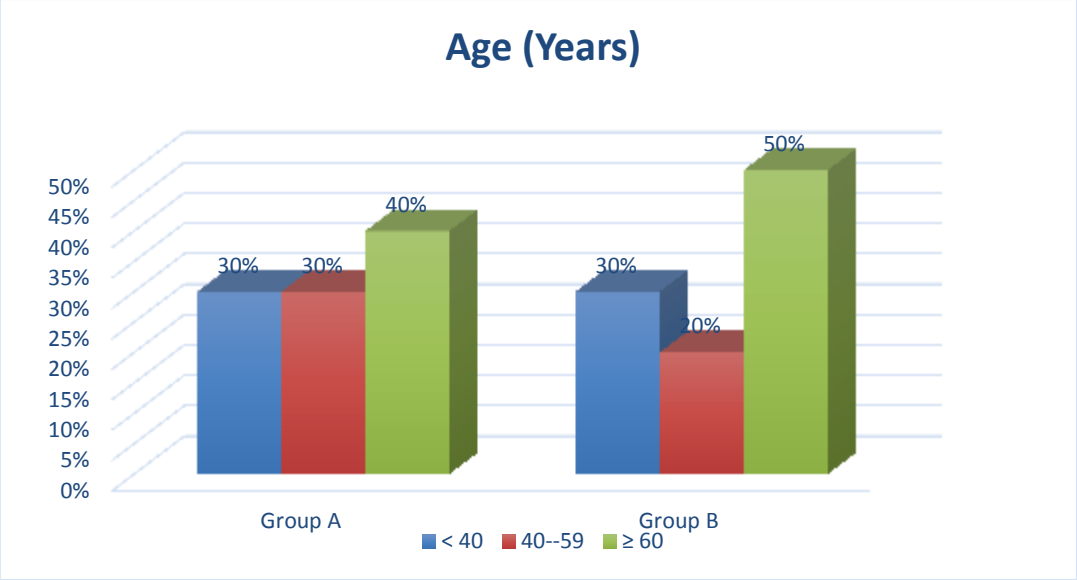

Fig2: Distribution of patients group by age

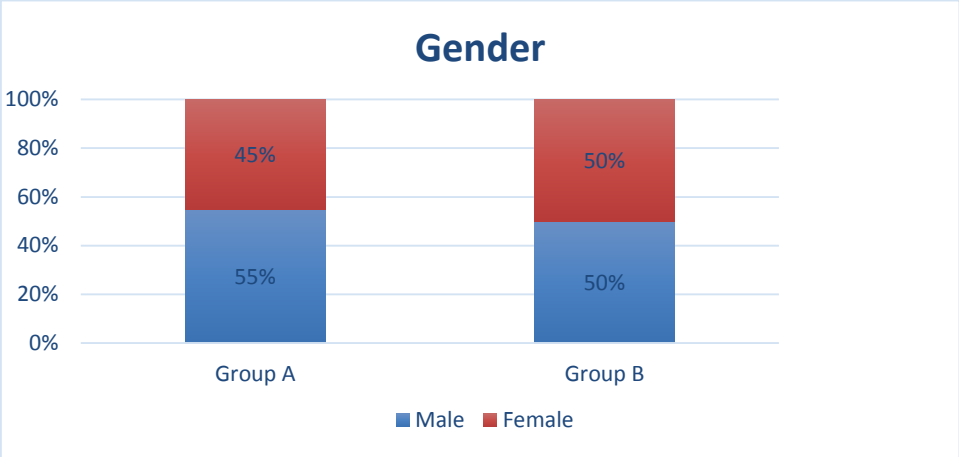

Fig.3: Distribution of study groups by gender

In comparison between study group by age and gender, we noticed that there were no statistical significant differences (P ≥ 0.05) in age and gender between study groups as shown in tables (1 and 2).

Table 1: Comparison between study groups in age

Age (Years)	Study Group		P - Value
	A Mean ± SD	B Mean ± SD	
	50.7 ± 12.22	55.2 ± 17.54	**0.353**

Table 2: Comparison between study groups in gender

Gender	Study Group		Total (%) n= 40	P- Value
	A n= 20	B n= 20		
Male	11 (55.0)	10 (50.0)	21 (52.5)	**0.748**
Female	9 (45.0)	10 (50.0)	19 (47.5)	

Table 3 shows the comparison in APACHE II score between study groups. No statistical significant difference (P= 0.089) in APACHE II score between study groups.

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Table 3: Comparison between study groups by APACHE II Score

APACHE II score	Study Group		P - Value
	A Mean ± SD	B Mean ± SD	
	20.2 ± 5.2	22.9 ± 4.8	0.**089**

The distribution of study groups by clinical information is shown in tables (4). We noticed that 57.5% of patients complained from two organs dysfunction, 45% needed double lumen, 40% needed CCRT, 45% needed bronchoscopy, and 65% needed tracheostomy. No statistical significant differences (P ≥ 0.05) between study groups regarding all clinical information.

Table 4: Distribution of study patients by clinical information

Variable	Study Group		Total (%) n= 40	P - Value
	A (%) n= 20	B (%) n= 20		
No. of organ dysfunction				
1	9 (45.0)	8 (40.0)	17 (42.5)	**0.749**
2	11 (55.0)	12 (60.0)	23 (57.5)	
Need for double lumen				
Yes	8 (40.0)	10 (50.0)	18 (45.0)	**0.525**
No	12 (60.0)	10 (50.0)	22 (55.0)	
Need for continuous renal replacement therapies (CCRT)				
Yes	6 (30.0)	10 (50.0)	16 (40.0)	**0.196**
No	14 (70.0)	10 (50.0)	24 (60.0)	
Need for bronchoscopy				
Yes	6 (30.0)	12 (60.0)	18 (45.0)	**0.056**
No	14 (70.0)	8 (40.0)	22 (55.0)	
Need for tracheostomy				
Yes	12 (60.0)	14 (70.0)	26 (65.0)	**0.507**
No	8 (40.0)	6 (30.0)	14 (35.0)	

In this study, core temperature was significantly higher in group B than that in group A in days 3, 4, and 5 (37.27 versus 36.76 °C, P= 0.001; 37.41 versus 36.69 °C, P= 0.002; and 37.52 versus 36.71 °C, P= 0.001 respectively).

No statistical significant differences (P ≥ 0.05) in core temperature between study groups at all other days.

Table 5: Comparison between study groups by core temperature

Time	Core temperature (°C) in study group		P - Value
	Group A Mean ± SD	Group B Mean ± SD	
Day 1	36.99 ± 0.28	37.31 ± 0.88	**0.244**
Day 2	36.96 ± 0.53	36.32 ± 3.42	**0.434**
Day 3	36.76 ± 0.41	37.27 ± 0.42	**0.001**
Day 4	36.69 ± 0.3	37.41 ± 0.88	**0.002**
Day 5	36.71 ± 0.32	37.52 ± 0.96	**0.001**
Day 6	36.68 ± 0.31	37.01 ± 0.86	**0.119**
Day 7	36.67 ± 0.6	37.08 ± 0.4	**0.206**

The comparison between study groups by procalcitonin levels and WBC count is shown in table (3.6). In this study, means of procalcitonin levels were significantly lower in group A than that in group B at middle, and last readings (2.52 versus 4.91 ng/mL, P= 0.002; and 0.8 versus 3.61 ng/mL, P= 0.001).

Means of WBC count were significantly lower in group A than that in group B at middle, and last

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readings (13.21 versus 15.7 (* 109/L), P= 0.045; and 10.14 versus 16.6 (* 109/L), P= 0.001 respectively).

No significant difference (P ≥ 0.05) in WBC count and procalcitonin level at starting reading.

Table 6: Comparison between study groups by procalcitonin levels and WBC count

Time	Study group		P - Value
	A Mean ± SD	B Mean ± SD	
Procalcitonin level (ng/mL)			
Starting reading	4.5 ± 1.96	5.24 ± 4.87	**0.535**
Middle reading	2.52 ± 1.1	4.91 ± 2.8	**0.002**
Last reading	0.8 ± 0.67	3.61 ± 2.16	**0.001**
WBC count (* 10^9/L)			
Starting reading	15.25 ± 5.1	13.22 ± 8.0	**0.345**
Middle reading	13.21 ± 3.2	15.7 ± 4.2	**0.045**
Last reading	10.14 ± 2.9	16.6 ± 4.8	**0.001**

Table 7 and figure 4 show the association between using amikacin with purulent discharge x-ray finding, and culture results. At the second two days, purulent discharge was noticed in 80% and x-ray was positive in 85% of group B which were significantly higher (P < 0.05) than that in group A.

At the last three days, purulent discharge was noticed in 80% and x-ray was positive in 90% of group B which were significantly higher (P < 0.05) than that in group A.

Culture results were positive in 45% of patients in group B, while there were positive in 10% of patients in group A, and this difference was statistically significant (P= 0.001).

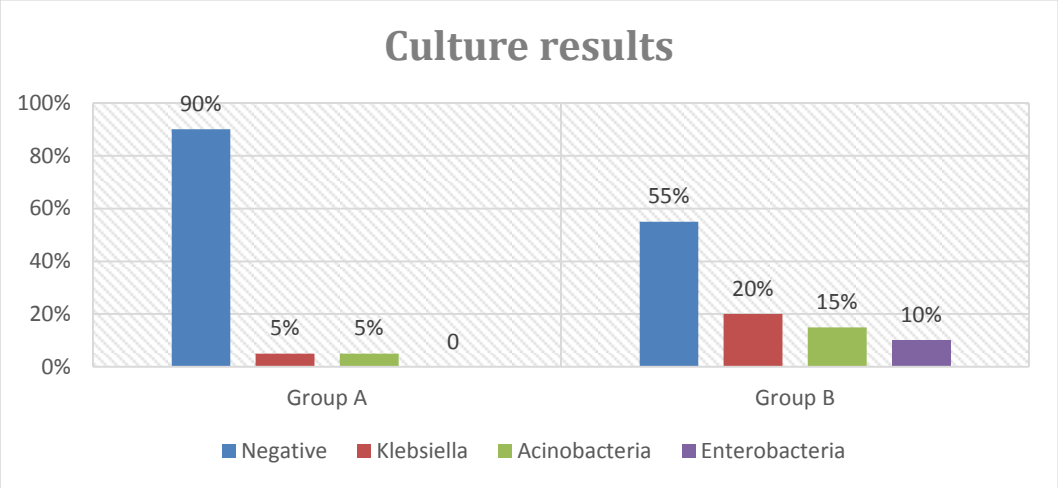

Figure 4: Culture results in study groups

Table 7: Association between using amikacin with purulent discharge and x-ray finding

Time	Study group		Total (%) n= 40	P- Value
	A n= 20	B n= 20		
Purulent discharge				
First three days	8 (40.0)	8 (40.0)	16 (40.0)	**1.0**
Second two days	6 (30.0)	16 (80.0)	22 (55.0)	**0.004**
Last three days	0 (0)	16 (80.0)	16 (40.0)	**0.001**
Positive X-ray finding				
First three days	10 (50.0)	12 (60.0)	22 (55.0)	**0.522**
Second two days	7 (35.0)	17 (85.0)	24 (60.0)	**0.001**

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Last three days	6 (30.0)	18 (90.0)	24 (60.0)	**0.001**
Culture results				
Positive	2 (10.0)	9 (45.0)	11 (27.5)	**0.001**
Negative	18 (90.0)	11 (55.0)	29 (72.5)	

The comparison between study groups by means of certain parameters is shown in table (8). In this study, mean of HR at days 5, 6, and 7 was significantly higher in group B than that in group A.

No significant difference ($P \geq 0.05$) in mean of HR at the other days between study groups.

Mean of RR at day 7 was significantly higher in group B than that in group A. No significant difference ($P \geq 0.05$) in mean of RR at all the other days between study groups.

Mean of SPO2 at days 3, 6, and 7 was significantly lower in group B than that in group A. No significant difference ($P \geq 0.05$) in mean of SPO2 at all the other days between study groups.

Mean of MAP at day 6 was significantly lower in group B than that in group A. No significant difference ($P \geq 0.05$) in mean of MAP at all the other days between study groups.

Mean of P/F ratio at days 2, 4, 5, and 7 was significantly lower in group B than that in group A. No significant difference ($P \geq 0.05$) in mean of P/F ratio at all the other days between study groups.

Table 8: Comparison between study groups by means of certain parameters

Variable	Study Group		P - Value
	A Mean ± SD	B Mean ± SD	
HR (Beats/mint)			
Day 1	101.3 ± 14.94	112.3 ± 22.42	**0.08**
Day 2	90.0 ± 12.14	96.6 ± 17.76	**0.178**
Day 3	93.1 ± 8.55	98.7 ± 13.63	**0.145**
Day 4	86.5 ± 9.23	94.5 ± 16.97	**0.072**
Day 5	83.5 ± 11.75	92.3 ± 9.32	**0.013**
Day 6	84.1 ± 13.69	93.1 ± 14.21	**0.047**
Day 7	83.2 ± 12.91	97.4 ± 16.2	**0.004**
RR (Breaths/mint)			
Day 1	25.3 ± 10.48	21.5 ± 6.58	**0.178**
Day 2	23.0 ± 7.07	19.9 ± 5.53	**0.131**
Day 3	20.6 ± 6.37	21.1 ± 4.57	**0.777**
Day 4	19.6 ± 6.77	17.8 ± 5.24	**0.354**
Day 5	17.7 ± 4.4	16.8 ± 3.39	**0.474**
Day 6	17.9 ± 3.93	19.1 ± 6.09	**0.464**
Day 7	16.3 ± 3.78	26.3 ± 15.77	**0.017**
SPO_2 (%)			
Day 1	96.1 ± 2.48	95.4 ± 4.21	**0.523**
Day 2	97.55 ± 3.07	96.9 ± 3.53	**0.548**
Day 3	98.8 ± 1.7	96.1 ± 3.79	**0.006**
Day 4	98.0 ± 2.97	96.9 ± 3.12	**0.261**
Day 5	98.3 ± 2.51	97.0 ± 3.27	**0.167**
Day 6	98.9 ± 1.55	96.8 ± 2.85	**0.006**
Day 7	98.5 ± 1.96	95.7 ± 3.07	**0.001**
MAP (mmHg)			
Day 1	94.29 ± 10.31	105.99 ± 27.64	**0.084**
Day 2	95.2 ± 11.83	96.83 ± 19.23	**0.749**
Day 3	90.33 ± 14.78	87.33 ± 15.5	**0.535**
Day 4	92.99 ± 10.64	88.0 ± 13.43	**0.2**
Day 5	88.99 ± 8.1	83.16 ± 14.72	**0.129**

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Day 6	89.03 ± 8.47	78.99 ± 13.25	**0.007**
Day 7	85.33 ± 7.82	84.26 ± 15.79	**0.788**
P/F ratio			
Day 1	243.75 ± 84.88	245.44 ± 128.02	**0.964**
Day 2	274.16 ± 87.14	192.22 ± 72.5	**0.009**
Day 3	245.75 ± 122.41	201.0 ± 70.18	**0.194**
Day 4	288.12 ± 107.57	220.12 ± 71.57	**0.044**
Day 5	275.87 ± 61.56	216.57 ± 85.66	**0.036**
Day 6	276.37 ± 97.26	216.11 ± 98.76	**0.083**
Day 7	286.44 ± 95.49	195.75 ± 45.63	**0.002**

Table 9 shows the comparison between study groups by CRP result and confusion. At last days, positive CRP results were noticed in 50% and confusion was presented in 60% of group B which were significantly higher ($P < 0.05$) than that in group A.

At starting days, no statistical significant differences ($P \geq 0.05$) between study groups by CRP result and confusion.

Table 9: Comparison between study groups by CRP result and confusion

Time	Study group		Total (%) n= 40	P- Value
	A (%) n= 20	B (%) n= 20		
Positive CRP result				
Starting result	4 (20.0)	6 (30.0)	10 (25.0)	**0.465**
Last result	6 (30.0)	11 (50.0)	17 (42.5)	**0.046**
Confusion				
Starting days	12 (60.0)	10 (50.0)	22 (55.0)	**0.525**
Last days	1 (5.0)	12 (60.0)	13 (32.5)	**0.001**

The association between study groups and final diagnosis of pneumonia is shown in table (10). We noticed that 45% of patients in group B were diagnosed with pneumonia, while 10% of patients in group A were diagnosed with pneumonia with a significant association (P= 0.013) between using amikacin and final diagnosis.

Table 10: Association between study groups and final diagnosis of pneumonia

Final diagnosis	Study group		Total (%) n= 40	P - Value
	A (%) n= 20	B (%) n= 20		
Pneumonia	2 (10.0)	9 (45.0)	11 (27.5)	**0.013**
No	18 (90.0)	11 (55.0)	29 (72.5)	

DISCUSSION

The respiratory tract infection is a common complication among patients who receive medical care in the Intensive care unit (ICU). Colonization of the respiratory tract by Gram-negative and Gram-positive bacteria may precede infection of the lower respiratory tract, including pneumonia, that is associated with considerable morbidity and mortality (Falagas, M. E, *et al.*, 2006).

We studied 40 patients into two groups, group (A) received nebulized amikacin in addition to the systemic antibiotics and group (B) received only the systemic antibiotics. 2 patients from group (A) which represent 10% of the group who received amikacin nebulizer in addition to the systemic antibiotics were developed ventilator associated pneumonia while 18 patients from this group not developed signs, symptoms or radiological features suggesting a diagnosis of pneumonia.

Group (B) who received just the systemic antibiotics 9 patients which represent 45% of the group were developed ventilator associated pneumonia and the other 11 patients didn't develop VAP.

According to this study, inhaled antibiotic as adjuvant to the systemic antibiotics play a significant role in prevention of ventilator associated pneumonia in comparison with systemic antibiotic were the p-Value was 0.013

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Michael S. Niederman used inhaled amikacin with a dose of 400mg twice plus systemic antibiotic daily for a group of 87 patient versus a group of 47 patient who received only systemic antibiotic and found that there were a significant difference of cure from VAP with inhaled amikacin with p-Value was 0.002 with clinical cure on day 7 from the treatment.(Niederman, M. S, 2009)

Michael S. Niederman study goes with our study in the result of prevention and cure of VAP.

Chang Liu, *et al*., revealed that as an adjunctive therapy for prevention of VAP, nebulized amikacin effectively improved CPIS without inducing new drug resistance or change in serum creatinine. However, improvement of morality was not found, Were the p-value for CPIS not significant (0.526) at the start of study and were declines for the amikacin group at the end of study with significant difference (0.007) temperature (37.0°C ± 1.3°Cvs. 38.0°C ± 0.9°C, P = 0.002), and the WBC (8.4 ± 6.1 × 103 /mm3 vs. 12.1 ± 4.7 × 103 /mm3, P = 0.031), were significantly reduced in AA group.(Liu, C, *et al*., 2017)

Hence Chang Liu, *et al*., study goes with our study in prevention of VAP. Frederico Castro, *et al*., found that Prophylactic antibiotics administered through the respiratory tract by nebulization reduce the occurrence of VAP, without a significant effect on either the ICU mortality or occurrence of VAP due to MDR pathogens.

Frederico Castroa, *et al*., included 6 comparative trials involving 1158 patients (632 received prophylactic antibiotic).this meta-analysis revealed that prophylactic antibiotics administered through the respiratory tract reduced the occurrence of VAP when compared to placebo or no treatment. This effect was seen when the antibiotics were given by nebulization, but not when they were administered by intratracheal instillation .he did not find a significant difference between the compared groups in the intensive care unit (ICU) mortality.(Castroa, F, *et al*., 2018)

Frederico Castroa, *et al*., study goes with our study in the prevention of VAP.

Marin H. Kollef, *et al*., found that trial of adjunctive aerosol therapy compared with standard of care IV antibiotics in patients with gram-negative VAP, the amikacin fosfomycin inhalation system (AFIS) was ineffective in improving clinical outcomes despite reducing bacterial burden.

Were 143 patients randomized: 71 to the AFIS group, and 72 to the placebo group. Comparison of CPIS change from baseline between treatment groups was not different (P = .70). The secondary hierarchical end point of no mortality and clinical cure at day 14 or earlier was also not significant (P = .68) nor was the hierarchical end point of no mortality and ventilator-free days (P = .06). The number of deaths in the AFIS group was 17 (24%) and 12 (17%) in the placebo group (P = .32). The AFIS group had significantly fewer positive tracheal cultures on days 3 and 7 than placebo (Kollef, M. H, *et al*., 2017).

In spite that Marin H. Kollef, *et al*., doesn't goes with our study in the prevention of VAP but the significantly decrement in the positive tracheal culture give an impression that the infection will be less.

Nassar, *et al*., found that The addition of Inhaled Colistin showed a significantly better organism clearance after 5 days compared to inhaled Ceftazidime and Amikacin and compared to iv antibiotics without additional inhaled antibiotics, in treating gram negative VAP.

The clearance of organism was (75% vs. 80% vs. 50%), resistance was (5% vs. 5% vs. 20%), superinfection was (0% vs. 10% vs. 15%), while combined resistance and super infection was (20% vs. 5% vs. 15%) in the group with inhaled colistin vs. the group with inhaled ceftazidime and amikacin vs. the group with IV antibiotics only respectively. Comparing the group with amikacin and ceftazidime vs. the group with only systemic antibiotics: a significantly greater clearance (80% vs. 50%, p 0.047) while no significant difference regarding resistance (5% vs. 20%, p 0.151), superinfection (2% vs. 15%, p 0.633). Comparing the group inhaled colistin vs. the group with systemic AB only: no significant difference in clearance (75% vs.50%, p 0.102), resistance (5% vs. 20%, p 0.151), superinfection (0% vs. 15%, p 0.072), combined resistance and super infection (20% vs. 15%, p 0.667). Comparing the group with nebulized colistine vs. the group with inhaled amikacin and ceftazidime: no significant difference in clearance (75% vs.80%, p 0.705), resistance (5% vs. 5%, p 1.0), superinfection (0% vs. 10%, p 0.147), combined resistance and super infection (20% vs. 5%, p 0.151) .(Nassar, *et al*., 2015)

So there is no differences between inhaled colistin and nebulized amikacine with ceftazidime in the

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prevention of VAP but there is a significant differences with these two group comparing with only systemic Antibiotics.

Nassar, *et al*., study goes with our study in the effect of nebulized Amikacin treating and prevention of VAP.

According to those studies in compression with our study we found that most of the studies are support our study in the prevention of VAP in ICU and all studies confirm the use of amikacin nebulizer Decreased the prevalence of the development of VAP.

CONCLUSION

- Nebulized amikacin is an effective tool in the prevention of VAP.
- Nebulized amikacin is easy to be performed.
- Nebulized amikacin doesn't need specific and complicated technique.

RECOMMENDATIONS

- We recommend the use of nebulized amikacin in the prevention of VAP.
- Doing studies with larger samples size and other antibiotics.
- Amikacin should be diluted well with previously measured amount of distil water.

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