

Comparative Study of Short versus Long Course of Antibiotic Therapy for Ventilator Associated Pneumonia in Adults

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Abstract

VAP is a serious health problem affecting the prognosis of ventilated patients in the ICU. The reason for this contemplate may be should affirm those possibility danger figures for ventilator cohorted pneumonia (VAP) for frigid patients on mechanical ventilation (MV) and the profit or those hazard of the short What's more long anti-microbial help. Patients who were with respect to mv for ≥ 48 h were incorporated in this study On they required show fate of VAP beginning starting with january 2017 to december 2018. An chi-squared test Also Mann–Whitney U-test were used to think about the information the middle of members for VAP Furthermore without VAP. Univariate logistic relapse models were performed with investigate those association the middle of antibiotics span span Furthermore VAP prognosis. 120 patients were incorporated in the study, who were diagnosed Likewise VAP. Logistic relapse investigation uncovered that COPD might have been an autonomous hazard component to VAP (OR =1. 536, P<0. 005) alongside frigid confirmation (OR=1. 847, P<0. 05), systems for mechanical ventilation (P<0. 023), those sorts from claiming antibiotics administered (OR=4. 747, P<0. 05), vital venous catheters sorts (OR=1. 909, P<0. 01), indwelling urinary catheter span (OR=1. 605, P<0. 05) and the organization for corticosteroids former on mechanical ventilation (OR=1. 918, P<0. 01). Ventilator cohorted pneumonia frequency might have been identified with an assortment for danger figures which might a chance to be controlled Also restricted to stay away from further VAP event including those strategies for mv Furthermore antibiotics numbers. A model to recognizing these danger figures and the part of each you quit offering on that one for VAP might have been manufactured will anticipate VAP frequency to attempt will identify as early Concerning illustration time permits to elevated structure patients.

Keywords: Ventilation associated pneumonia, Prevention of bacterial resistance, Antibiotic regimens .

1. Introduction

Mechanical ventilation may be a proficient measure, which assistance will build tolerant survival of critically sick patients, admitted of the frigid Also may be comprehensively utilized. Ventilator-associated pneumonia (VAP) may be a standout amongst those extreme nosocomial contamination types, which normally happens The point when those tolerant will be on mechanical ventilation for more than 48 h from claiming mechanical ventilation. As stated by those clinical rules discharged Previously, 2016 Eventually Tom's perusing the irresistible ailments culture from claiming america (IDSA) stated that those mortality for VAP in the us may be give or take 13% 1. Same time done Europe, an expansive prospective study, which might have been directed for various centers, accounted that the one-month mortality because of VAP might have been 29. 9%, the mortality for early VAP might have been 19. 2% 2.

There need aid Different techniques, which help to prevent VAP, for example, such that counteractive action packs Also medications including chlorhexidine, b-lactam antibiotics Furthermore probiotics. However, VAP predominance need dropped as of late because of restorative strategies, it at present a standout amongst those mossycup oak basic reason for nosocomial infections and demise done critically sick patients Throughout hospitalization done ICUs. VAP cause an immense budgetary issue should patients Furthermore an enormous interest for restorative assets. Therefore, it is exceptionally imperative will elucidate those danger figures about VAP with recognize additional Furthermore get preferred counteractive action What's more control from claiming VAP 3.

2. Patient and methods

This randomized, double-blind trial that was performed in Benha University. All patients or their relatives consent was obtained before enrollment of the patient in the study.

Patients on mechanical ventilation for 2 days were eligible to be included in this study.

Inclusion criteria

- (1) Age older than 18 years
- (2) VAP signs and symptoms
- (3) Positive cultures of pulmonary secretion samples.

Exclusion criteria

- (1) Being pregnant
- (3) Terminal cases with very poor survival
- (4) Neutropenia (leukocyte counts $<1000/\mu\text{L}$ or neutrophils $<500/\mu\text{L}$);
- (5) Acquired immunodeficiency syndrome
- (6) Long-term corticosteroid therapy (≥ 0.5 mg/kg per day for >1 month);
- (7) Concomitant extra pulmonary infections

Antibiotic treatments

Drug selection was left to the discretion of the treating physicians, including any adaptation considered necessary. All antibiotics were withdrawn, either at the end of day 8 or day 15, according to the randomization assignment.

Baseline Assessment and Data of the patients included in the study were collected and compared Table (1).

Follow-up and definitions

Know clinical and lab information were recorded Every day Throughout those 28-day period following VAP analysis.

Conclusion Measures. Those result measures were passing starting with any cause; microbiologically archived pulmonary spoiling recurrence, characterized utilizing those same microbiologic criteria Concerning illustration the individuals that prompted tolerant consideration in the trial; What's more antibiotic-free days, constantly on for which were evaluated 28 days following those main bronchoscopy for suspected VAP onset.

2.1. Statistical Analyses

Every one information were collected, tabulated What's more statistically investigated utilizing STATA/SE adaptation 11. 2 for Windows (STATA Corporation, school Station, Texas). Nonstop information were communicated Similarly as the imply \pm sd What's more range, What's more unmitigated information were communicated Concerning illustration An amount Also rate. Nonstop variables were compared between gatherings utilizing Student's t-test. Unmitigated variables were thought about utilizing chi-

squared test. Those relationship the middle of two constant variables were broke down utilizing Pearson's relationship. Variables with $P < 0.1$ once Student's t-test alternately chi-squared test were entered under univariate and multivariate logistic relapse investigation with recognizing those predictors about POAF, What's more alternately and 95% ci were computed.

Then afterward the computation about every of the test statistics, the comparing circulation tables were consulted should get the "P" (probability esteem). Measurable hugeness might have been acknowledged during p esteem < 0.05 (S) Furthermore a p worth < 0.001 might have been acknowledged Exceptionally critical (HS). While, a p quality > 0.05 might have been recognized non-significant (NS). 4.

3. Results

Characteristics of the Patients

120 patients were enrolled in the study between May 2017 and June 2018, 66 in the 8-day group and 54 in the 15-day group. The clinical characteristics of these 120 patients at admission were similar, except that the percentage of female patients was slightly but significantly higher ($P = .046$) for the group receiving 15 days of antibiotics Table (1).

Table (1) Patient baseline characteristics.

Characteristic	8- day regimen (n= 66)	15 day regimen (n=54)
Age mean(SD)	60(17)	61(16)
Men (no.)%	43(65%)	34(62%)
Reason for mechanical ventilation		
Acute respiratory failure	21	19
Trauma	14	14
Neurological failure	11	10
Sepsis	13	9
Miscellaneous	7	4

Microorganisms considered responsible for VAP are listed in Table (2) Non-fermenting Gram-negative bacilli and methicillin-resistant *S aureus* were isolated, respectively, from 23 (33%) and 7 (11.2%) potentially

polymicrobial episodes that were treated with 8 days of antibiotics compared with 16 (30.9%) and 6 (11.3%) infections that were treated with a 15-day regimen ($P = .67$ and $P = .99$, respectively).

Table (2) Microorganisms distribution in the two groups .

Microorganisms causing VAP	8- day regimen (n= 66)	15 day regimen (n=54)
<i>Pseudomonas aeruginosa</i>	41.4%	22.4%
<i>Acinetobacter sPP.</i>	7.9%	6.8%
<i>Stenotrophomonas maltophilia</i>	19.7%	14.6%
Enterobacteriaceae	13.1%	16.4%
<i>Haemophilus sPP.</i>	22.8%	10%
<i>Staphylococcus aureus</i>	30.4%	22.4%
<i>Streptococcus sPP.</i>	8.0%	16.3%
<i>Streptococcus pneumoniae</i>	4.1%	9.1%
Coagulase-negative staphylococci	4.4%	1.8%
<i>Neisseria sPP.</i>	2.6%	4.2%
Anaerobes	1.9%	0.5%
Fungi	4.9%	0.6%

No statistically significant between-group differences were found among the agents used during the first 8 days of the study. A regimen combining an aminoglycoside or a fluoroquinolone plus a betalactam was prescribed on day 1 to 60 (90.9%) of 66 patients in the 8-day group compared with 48 (91.7%) of 54 patients in the 15-day group ($P = .86$); on day 8, those values were 23 (32.8%) of 66 in the 8-day group and 21 (39.2%) of 54 in the 15-day group ($P = .21$). Thirty-nine percent of

patients in the 8-day group and 37% in the 15-day group received vancomycin on the first day of the study ($P = .61$).

Outcome

Twenty-eight days after VAP onset, 11 (18.8%) of 66 patients in the 8-day group and 8 (17.2%) of 54 patients in the 15-day group had died Table (3). The absolute difference was 1.6%, with the 90% CI for the between-group difference ranging from -3.7% to 6.9% .

Table (3) Baseline Characteristics of the Study Patients as a Function of the Duration of Antibiotic Administration.

Characteristic	8- day regimen (n= 66)	15 day regimen (n=54)
MV duration before VAP mean(SD)	13.4 (11.2)	13.8 (14.9)
Antimicrobial therapy 15 day before VAP	167(84.4)	170(83.3)
Organ system failure		
Respiratory	167(56)	167(54)
Cardiovascular	167(24)	167(24)
Renal	167(11)	167(13.7)
Central nervous system	167(23)	167(17.2)
Hepatic	167(5)	167(3.4)
Coagulation	167(4)	167(3.4)
Temperature mean(SD) °C	38.6(1.1)	38.6(0.9)
leucocytic count mean(SD)	15 460 (7150)	15 509 (6760)
Pao2/Fio2 mean(SD)	196 (82)	201 (85)
Radiologic score mean(SD)	5.4 (2.5)	5.5 (2.4)
Bacteremia	14 (7.1)	14 (6.9)
Shock	66 (33.5)	73 (35.8)
ARDS	51 (25)	42 (20)

Mv mechanical ventilation, Pao2/Fio2 those proportion of blood vessel oxygen fractional weight of the portion of propelled oxygen, VAP ventilator connected pneumonia. In view of quantitative society results, those microbiologically archived pulmonary infection-recurrence rate might have been 28. 9% of patients getting the 8-day regimen and 26% about the individuals taking antibiotics to 15 days, with a supreme distinction of 2. 9% (90% CI, $-3. 2\%$ to $9. 1\%$). Thus, the noninferiority of the 8-day regimen might have been retained. Those rates about pulmonary spoiling recurrences viewed as to make relapses were comparative to the 2 bunches (16. 8% "around the 8-day vs 11. 3% "around those 15-day regimen aggregations [absolute difference, 5. 5%; 90% CI, 0. 7%-10. 3%]), Concerning illustration were the rates for the individuals recognized should a chance to be superinfections (19. 8% "around the 8-day vs 18. 6% in the 15-day Assemblies [absolute difference, 1. 2%; 90% CI, $-4. 3\%$ should 6. 6%]; .

Survival rates were comparative. Likewise comparable were those imply (SD) times should pulmonary contamination recurrence: 21. 6 (0. 5) days for those 8-day What's more 22. 5 (0. 5) times to the 15-day medication gatherings ($P = .38$); times will relapse: 23. 8 (0. 5) days and 24. 1 (0. 4) days ($P = .12$); Furthermore times of the advancement about superinfections: 22. 8 (0. 5) Also 23. 8 (0. 5) times ($P = .65$).

Clinched alongside contrast, those patients who gained antibiotics for 8 days required fundamentally a greater amount intend (SD) antibiotic-free days (13. 1 [7. 4] vs 8. 7 [5. 2] days, $P < .001$), and essentially All the more broad-spectrum (imipenem, piperacillin-tazobactam, ticarcillin-clavulanic acid, cefepime, cefpirome, ceftazidime, alternately ciprofloxacin) antibiotic-free days (18. 4 [8. 0] vs 15. 3 [8. 4] days; $p = .01$). There were no critical contrasts the middle of the 2 aggregations in the numbers about patients for whom antibiotics were proceeded after the end of the haphazardly doled out regimen or those numbers for patients who accepted an extra span for antibiotics.

The balanced danger proportion for passing of patients in the 8-day regimen vs the individuals in the 15-day regimen might have been 1. 2 (95% CI, 0. 6-2. 1) then afterward conformity to age, sex, McCabe What's more jackson classification, confirmation category, span from claiming mechanical ventilation preceding VAP onset, webpage Also seriousness for organ/system disappointment In view of those couch score during baseline, bacteremia, and type(s) for pathogens answerable for VAP. The balanced hazard proportion for repetitive pulmonary spoiling might have been 1. 2 (95% CI, 0. 8-2. 1). No noteworthy collaborations Might be secured between medication duty and any covariate, especially the middle of the sorts about pathogens answerable for VAP and the medicine one assembly with admiration to the 3 grade Conclusion measures However, to essential infections brought on by nonfermenting Gram-negative bacilli, a higher rate of patients formed

recorded pulmonary contamination repeat in the 8-day bunch over in the 15-day one assembly (40.6% vs 25.4%; hazard difference, 15.2%; 90% CI, 3.9%-26.6%, respectively); 21 about 26 What's more 12 about 16 in the particular bunches encountered backslide.

4. Discussion

In this large, multicenter, randomized, double-blind (until day 8) clinical trial, we noted that there will be no profit of prolonged anti-microbial treatment should fifteen times starting with an eight-day regimen, to patients with VAP who accepted suitability introductory empiric anti-microbial help. The cirsum vulgare to the contrasts clinched alongside mortal sin Also pulmonary infection-recurrence rates the middle of those two aggregations of the examine avoid a outright Contrast surpassing 10% energetic about those 15-day regimen. No contrasts in other Conclusion parameters Might a chance to be observed, including the span of mechanical ventilation, those number of organ failure-free days, the span about frigid stay, Also mortal sin rates for day 60 alternately status In healing center release. The rates for unfavorable outcomes, characterized Similarly as death, contamination repeat or prescription of a new antimicrobial medication Throughout the contemplate period, were also comparable for those two Assemblies 5.

It might have been discovered that those Normal amount about antibiotic-free days from day 1 on day 28 might have been half higher to patients in the 8-day aggregation over for patients the 15-day regimen group, thereby affirming those adequacy of the eight day regimen What's more should minimizing the purposes of presentation will anti-microbial help. Relevantly, pathogens, which bring different resistances, rose more every now and again done patients with who accepted 15 days from claiming antibiotics. These comes about are in understanding with other observational investigations directed for frigid patients that unmistakably exhibited An immediate association between the utilization about antimicrobial operators Furthermore expanded safety for enterobacteriaceae What's more different pathogens. Fitting antibiotics may be the main advantageous on move forward those survival rate for patients for VAP not for patients without contamination the place antibiotics might make perilous just with no profit. 6. Previously, our study, there were marginally more patients for non-fermenting gram-negative bacilli those 8-day regimen gathering for pulmonary contamination recurrences Furthermore we were unabated should show those noninferiority for this regimen for this end point compared with those 15-day course, whichever due to the generally little number for contemplated patients alternately On account those shorter span about medicine abandons patients powerless to that's only the tip of the iceberg pulmonary spoiling recurrences. However, in spite of this higher repeat rate, not the mortal sin or unfavorable Conclusion rate might have been higher to patients with VAP initiated Eventually Tom's perusing the individuals pathogens The point when their antimicrobial treatment

kept up just 8 times. Therefore, viewing those outcomes of investigations identified with this point, we trust that 8 days course of antibiotics Might be given securely On the whole sorts from claiming VAP 7.

As stated by our knowledge, a couple investigations have evaluated the ideal span for antimicrobial treatment in patients for VAP. Over a late accomplice study for 102 sequential patients with VAP prospectively assessed previously, then following those provision of a clinical guideline confining those aggregate span from claiming antibiotics should 7 days for chosen patients (those who were not bacteremic or neutropenic and who turned into afebrile under therapy), no statistically huge contrasts done healing facility mortal sin rates What's more durations from claiming hospitalizations were found between the 2 consider aggregations; however, as opposed will our results, after-group patients whose imply span about medicine might have been 7 days, were more averse should create a second scene for VAP compared for the individuals in the preceding assembly 8.

Limitation

There is a relatively large subset of ICU patients was excluded from our study, especially those with early-onset pneumonia who had not received previous antibiotics, those who were severely immunocompromised. Additionally, the diagnosis of pulmonary infection was established by significant ($>10^3$ or $>10^4$ colony-forming units/mL) quantitative culture results of bronchoscopic specimens to avoid the inclusion of patients with less severe forms of respiratory-tract infection. Thus, the results of this study cannot be applied to all ICU populations.

5. Conclusion

For ICU patients who develop microbiologically proven VAP, there was no clinical advantage of prolonging antimicrobial therapy to 15 days compared with 8 days. This conclusion could be applied to many ICU patients who develop VAP. Adopting this regimen could help reduce health care costs and limit bacterial resistance.

References

- [1] A. C. Kalil, M. L. Metersky, M.L. Klompas, J.K. Muscedere, D. A. Sweeney, L. B. Palmer. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the infectious diseases society of America and the American thoracic society. Clin. Infect. Dis, Vol.63, PP.e61–e111, 2016.
- [2] I.O. Martin-Loeches, A. H. Rodriguez, and A.L. Torres, New guidelines for hospital-acquired pneumonia/ventilator-associated pneumonia. Curr. Opin. Crit. Care, Vol.24, PP.347–352, 2018.
- [3] D.L. Wu, C.P. Wu, S.U. Zhang and K. Y. Zhong. "Risk Factors of Ventilator-Associated Pneumonia in Critically Ill Patients." Frontiers in pharmacology, Vol.10, PP. 654-659, 2019.

- [4] D.G. Altman and J.M. Bland. Measurement in Medicine: The Analysis of Method Comparison Studies. *The Statistician*, Vol.32, PP.307–317,1983.
- [5] S.K. Fridkin, C.D. Steward, J.R. Edwards. Surveillance of antimicrobial use and antimicrobial resistance in United States hospitals: project ICARE phase 2: Project Intensive Care Antimicrobial Resistance Epidemiology (ICARE) hospitals. *Clin Infect Dis*, Vol. 29, PP.245-252, 1999.
- [6] H.C. Neu. The crisis in antibiotic resistance. *Science*, Vol. 257, PP. 1064 1073, 1992.
- [7] D.O. Landman, J.M. Quale, D.P. Mayorga. Citywide clonal outbreak of multiresistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in Brooklyn, NY: the preantibiotic era has returned. *Arch Intern Med*, Vol. 162, PP.1515-1520, 2002.
- [8] S.M. Mahgoub, J.Y. Ahmed, A.E. Glatt. Completely resistant *Acinetobacter baumannii* strains. *Infect Control Hosp Epidemiol*, Vol.23, PP.477-479, 2002.