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Linezolid versus Vancomycin for the Treatment of Methicillin-Resistant *Staphylococcus aureus* in Hospital-Acquired, Ventilator-Associated, and Healthcare-Associated Pneumonia at Tertiary Care Hospital

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Abstract

Aim: To evaluate morbidity and mortality rate, clinical cure rate and cost of linezolid versus vancomycin in patients who have hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP) or Healthcare-associated pneumonia (HCAP) caused by methicillin-resistant *Staphylococcus aureus* (MRSA). **Methods:** Retrospective analysis data. Data were collected for adult patients admitted to King Faisal Specialist Hospital and Research Centre-Jeddah (KFSH & RC-J) from January 2010 to May 2015. **Method:** A total of 88 patients with HAP, VAP and HCAP caused by MRSA treated with vancomycin (IV) or linezolid (IV or PO) either as empirically or directed therapy ≥ 7 days. They are retrospectively evaluated and analyzed. The primary end points are morbidity and mortality rate as well as clinical cure rate. The secondary end point is the cost analysis for each medication. **Results:** A total of 40 patients (ICU, n = 13 (32.5% and non ICU, n = 27 (67.5%)) were included in the study. Among vancomycin, n = 21 (52.5%); age (54.95 ± 18.255) and linezolid, n = 19 (74.5%); age (48.684 ± 25.593), there was no statistical differences in mortality and morbidity rate (P = 0.375). Clinical cure rate (fever improvement, 12 (57.1%) vs 12 (63.2%); P = 0.698, leukocytosis improvement, 15 (71.4%) vs 14 (73.7%); P = 0.873, purulent sputum improvement, 6 (28.6%) vs 4 (21.1%); P = 0.429, dyspnea improvement, 8 (38.1%) vs 3 (15.8%); P = 0.115,cough improvement 4 (19.0%) vs 4 (21.1%); P = 0.592, microbiological eradication of MRSA from sputum culture, 2 (9.5%) vs 6 (31.6%); P = 0.089 and improvement of radiographic finding (pulmonary infiltration), 17 (81.0%) vs 16 (84.2%); P = 0.559) of vancomycin vs linezolid, respectively. The cost

analysis in the treatment of MRSA pneumonia with linezolid is statistical significantly higher than vancomycin. The mean cost of vancomycin = 185.9143 SR and of linezolid = 4547.3684 SR ($P < 0.0001$) of one patient during the treatment period. **Conclusion:** There are no statistical differences in mortality and morbidity rate and clinical cure rate between linezolid and vancomycin in the treatment of MRSA in HAP, VAP, and HCAP. However, the cost of linezlid is significantly higher than vancomycin during the treatment period of one patient.

Keywords

Linezolid, Vancomycin, Pneumonia, Methicillin-Resistant *Staphylococcus aureus*

1. Introduction

Hospital-acquired pneumonia is the second most common hospital-associated infections in the United States after urinary tract infection [1]. The Hospital-Acquired Pneumonia (HAP), can be defined as pneumonia that occurs with patients who are admitted to the hospital for at least 48 hours. The Ventilator-Associated Pneumonia (VAP) is one type of hospital-acquired pneumonia and it arises 48 - 72 hours after endotracheal intubation. The Health Care-Associated Pneumonia (HCAP) occurs in patients with previous risk factors for infection caused by potentially drug-resistant pathogens. These risk factors of HCAP may include: hospitalization for 2 or more days within 90 days of infection, residence in long-term care facility, receipt of recent IV antibiotic therapy, chemotherapy, or wound care within the past 30 days, living in close contact with a person with a multidrug-resistant pathogen or attending a hospital or hemodialysis clinic [3] [4]. Unfortunately, it is associated with significant morbidity and mortality, increase length of hospital stay and increase cost of treatment. The mortality rate for HAP, VAP and HCAP is 18.8%, 29.3% and 19.8%, respectively [4].

The methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia is considered a leading cause of death among nosocomial infections. From 1999 through 2005, the MRSA pneumonia prevalence increased by 19.3% in the United States [2]. However, the MRSA pneumonia accounts for 10% - 40% of the HAP, HCAP and VAP cases [5] [6]. The Infectious Diseases Society of America (IDSA) recommends either vancomycin or linezolid for 7 - 21 days for treatment of MRSA pneumonia as first line therapy [3]. It is very crucial to administer the appropriate antibiotic to the patients because the delay in administering the antibiotic has been associated with high mortality [7]. It remains uncertain whether vancomycin or linezolid should be considered superior for treatment of MRSA pneumonia and additional studies are needed.

To compare between these two antibiotics for treatment of MRSA pneumonia, several clinical trials have been conducted. One multinational retrospective study compare linezolid versus vancomycin in treatment of patients with MRSA pneumonia, they found that the initial treatment with linezolid was associated

with better survival and clinical cure rate than was with vancomycin [8]. The ZEPHyR study also compares linezolid versus vancomycin for MRSA pneumonia and they conclude that linezolid is more effective and better-tolerated alternative than vancomycin for documented or suspected MRSA pneumonia [9]. On the other hand, Stevens *et al.* compare vancomycin and linezolid for the treatment of MRSA pneumonia and they conclude that linezolid was clinically and microbiologically effective as vancomycin [10]. A meta-analysis of nine randomized trials found that linezolid and vancomycin have similar efficacy and safety profiles [11]. Due to these controversial in clinical trials, this study will be performed to evaluate morbidity and mortality rate, clinical cure and total direct cost of vancomycin versus linezolid which used as empirical or direct therapy in treatment of MRSA pneumonia.

2. Method

2.1. Study Design

Data collection was conducted to enroll all adult patients admitted at King Faisal Specialist Hospital and Research Centre (KFSH & RC)-Jeddah and diagnosed with HAP, VAP or HCAP caused by MRSA. The data were be collected and evaluated from January 2010 to May 2015. All patients received vancomycin or linezolid either as empirically or directed therapy in treatment of MRSA pneumonia for more than 7 days were analyzed. The primary end points are morbidity and mortality rate as well as clinical cure rate. The secondary end point is the cost analysis for each medication.

2.2. Inclusion and Exclusion Criteria

This study was included all adult patients >18 years of age, critically and non-critically ill patients diagnosed with HAP, VAP and HCAP. The patients who were excluded are HIV-infected patients, patients have cancer or any types of malignancy, patients received linezolid or vancomycin for indications other than hospital-associated pneumonia caused by MRSA, patients who didn't complete the duration of treatment (<7 days) and patients who received both vancomycin and linezolid concurrently. Patients who received empiric vancomycin for ≤3 days then switched to linezolid after culture confirmation will be grouped with linezolid group and vice versa.

2.3. Data Gathering Method

Baseline demographics, laboratory data and radiographic finding were obtained from hospital electronic medical record (ICIS). Other patients' progress notes which needed in the study were obtained using the patients' medical files. Sputum culture will be used for confirmation diagnosis of MRSA pneumonia if available. Final pathogen identification and susceptibility testing were determined at laboratory of KFSH&RC. The Kerby Bauer and Microdilution methods are the two micobiological methods which are utilized to confirm MRSA growth.

2.4. Assessment

The morbidity and mortality rate were assessed by survival rate during treatment period, time to discharge from hospital or transfer to other ward (for ICU patients). Clinical cure defined as resolution or improvement three of the following: microbiological eradication of MRSA from sputum culture if available, improvement or lack of progression of radiographic finding (pulmonary infiltration), fever > 38˚C, leukocytosis > 10×10^9/L, purulent sputum, dyspnea and/or cough. The direct cost was calculated for every single vial/tablet of linezolid and every single vial of vancomycin consumed by every patient suffered from MRSA pneumonia and comparing the total cost between these two medications.

2.5. Statistical Analyses

The measure of central tendency, distribution of numerical data and percentage of categorical data were calculated to get the differences between treatment groups in the rates of morbidity and mortality, clinical cure and direct cost analysis. $P < 0.05$ are considered as statistically significant. Direct cost analysis was calculated for total cost of such medications

2.6. Statistical Software

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 19 software (SPSS Inc., Chicago, IL, USA).

3. Results

From a total of 88 patients, forty eight patients are excluded from the study because they didn't adhere to the inclusion criteria (Figure 1). Forty patients with MRSA pneumonia (HAP, n = 27, VAP, n = 6 and HCAP, n = 7) (Figure 2 and Figure 3) were included in the study including critically ill and non-critically ill patients (Table 1). The patients were retrospectively analyzed and divided to Group (A) who received vancomycin, n = 21 (52.5%); age (54.95 ± 18.255) and Group (B) who received linezolid, n = 19 (74.5%); age (48.684 ± 25.593) (Table 2). Mean duration of treatment of vancomycin = 8.9 days, while in linezolid = 10.8 days. There was no statistical differences in mortality and morbidity rate ($P = 0.375$). Clinical cure rate (fever improvement, 12 (57.1%) vs 12 (63.2%); $P = 0.698$, leukocytosis improvement, 15 (71.4%) vs 14 (73.7%); $P = 0.873$,purulent sputum improvement, 6 (28.6%) vs 4 (21.1%); $P = 0.429$,dyspnea improvement, 8 (38.1%) vs 3 (15.8%); $P = 0.115$, cough improvement 4 (19.0%) vs 4 (21.1%); $P = 0.592$, microbiological eradication of MRSA from sputum culture, 2 (9.5%) vs 6 (31.6%); $P = 0.089$ and improvement of radiographic finding (pulmonary infiltration), 17 (81.0%) vs 16 (84.2%); $P = 0.559$) of vancomycin vs linezolid, respectively (Table 3). The cost analysis in the treatment of MRSA pneumonia with linezolid is statistical significantly higher than vancomycin. The mean cost of vancomycin = 185.9143 SR and of linezolid = 4547.3684 SR ($P < 0.0001$) of one patient during the treatment period.

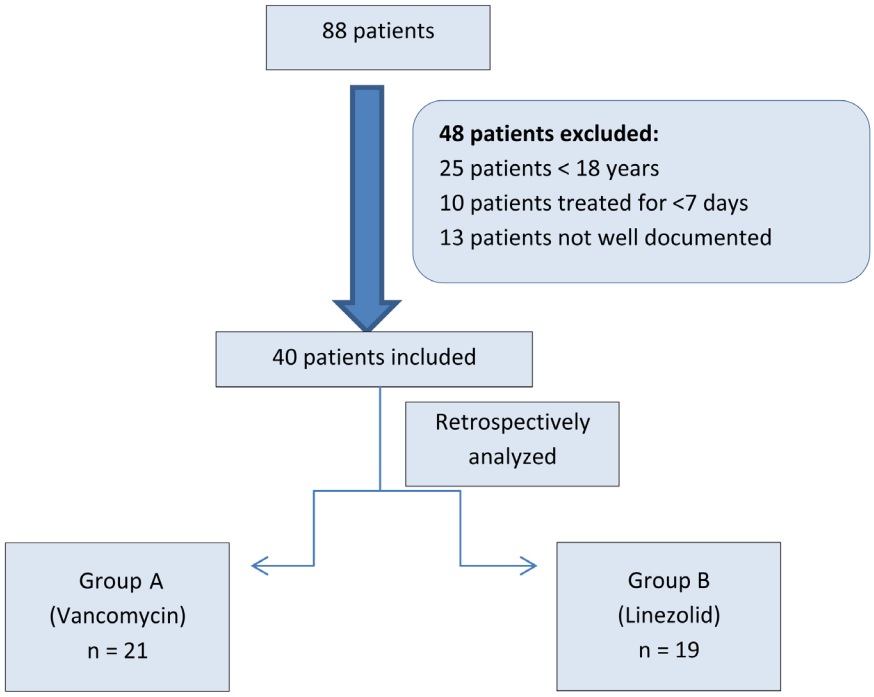

Figure 1. Flowchart for the study.

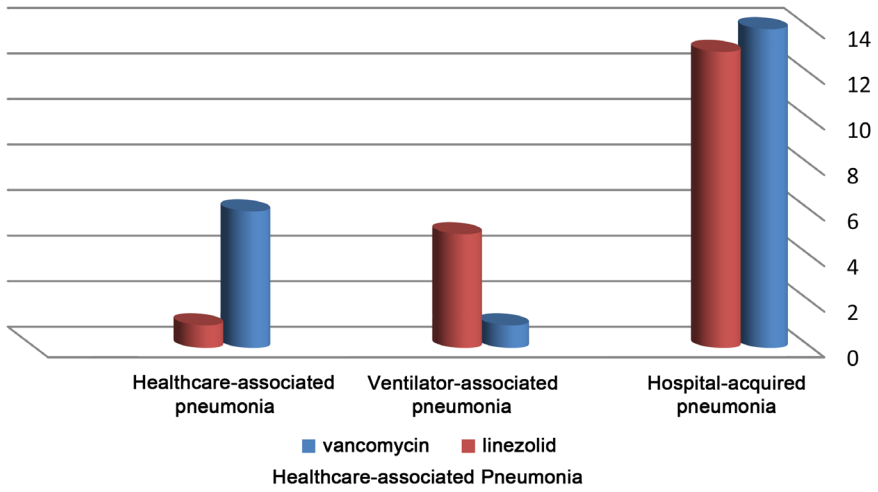

Figure 2. Types of MRSA pneumonia. Forty patients with MRSA pneumonia (HAP, n = 27, VAP, n = 6 and HCAP, n = 7).

Table 1. Number of critically ill and non-critically ill patients who included in the study.

			Antibiotic		Total
			Vancomycin	linezolid	
ICU	yes	Count	7	6	13
		%	33.3%	31.6%	32.5%
	no	Count	14	13	27
		%	66.7%	68.4%	67.5%
Total		Count	21	19	40

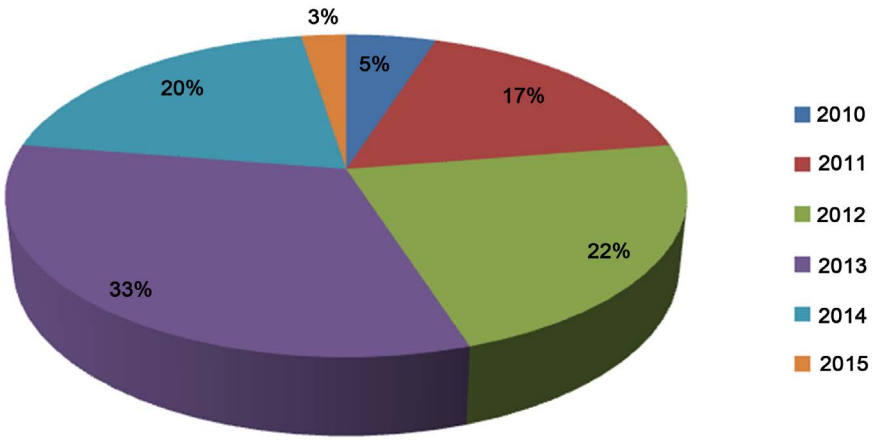

Figure 3. Percentage of patients who have MRSA pneumonia from January 2010 to May 2015 in tertiary care hospital-Jeddah. Forty patients with MRSA pneumonia (HAP, n = 27, VAP, n = 6 and HCAP, n = 7).

Table 2. Baseline characteristics of study patients.

	Group A (vancomycin)	Group B (linezolid)
Total (%)	n = 21 (52.5%)	19 (74.5%)
Male (%)	9 (42.9%)	13 (68.4%)
Female (%)	12 (57.1%)	6 (31.6%)
Age	54.95 ± 18.255	48.684 ± 25.593
weight	69.143 ± 19.35	63.053 ± 21.279

Table 3. Morbidity and mortality rate and clinical cure rate in both groups of the study; *P* value < 0.05 considered as statistical significant.

Morbidity and mortality	Vancomycin	Linezolid	*P* value
Expired Transferred to ward Discharged	4 (19.0%) 6 (28.6%) 11 (52.4%)	1 (5.3%) 5 (26.3%) 13 (68.4%)	0.375
Resolution/improvement of fever	12 (57.1%)	12 (63.2%)	0.698
Resolution/improvement of leukocytosis	15 (71.4%)	14 (73.7%)	0.873
Resolution/improvement of purulent sputum	6 (28.6%)	4 (21.1%)	0.429
Resolution/improvement of dyspnea	8 (38.1%)	3 (15.8%)	0.115
Resolution/improvement of cough	4 (19.0%)	4 (21.1%)	0.592
Microbiological eradication of MRSA from sputum culture	2 (9.5%)	6 (31.6%)	0.089
Improvement or lack of progression of radiographic finding (pulmonary infiltration)	17 (81.0%)	16 (84.2%)	0.559

4. Discussion

This study performed to evaluate morbidity and mortality rate, clinical cure rate and total direct cost of vancomycin versus linezolid in treatment of patients with MRSA pneumonia. The data collection was being conducted to enroll all adult

hospitalized patients with MRSA pneumonia from January 2010 to May 2015 who received either linezolid or vancomycin for >7 days at King Faisal Specialist Hospital and Research Centre (KFSH & RC) in Jeddah. Although, a lot of clinical trials were published to compare between vancomycin versus linezolid in treatment of MRSA pneumonia, it still uncertain which one should be superior. One multinational retrospective study compare linezolid versus vancomycin in treatment of patients with MRSA pneumonia, they found that the initial treatment with linezolid was associated with better survival and clinical cure rate than was with vancomycin [8]. The ZEPHyR study also compares linezolid versus vancomycin for MRSA pneumonia and they conclude that linezolid is more effective and better-tolerated alternative than vancomycin for documented or suspected MRSA pneumonia [9]. This study shows that there isno superiority of linezolid over vancomycin in treatment of MRSA in HAP, VAP, and HCAP. The study of Dennis, L. S., Daniel *et al.* stated that there was no statistical difference between the 2 treatment groups with respect to clinical cure rates or microbiological success rates and that both regimens were well -tolerated, with similar rates of adverse events [12]. However, the cost of linezolid is significantly higher than vancomycin ($P < 0.0001$) of one patient during the treatment period. Further studies with multicenter prospective randomized design may be needed to evaluate efficacy, safety and cost between these two medications.

There are some limitations in this study including a retrospective study design, the number of patients who were included in the study was small (n = 40), the study was not evaluate the safety profile between vancomycin versus linezolid and the medical records were not well-documented some of patients data.

5. Conclusion

There are no statistical differences in mortality and morbidity rate and clinical cure rate between linezolid and vancomycin in the treatment of MRSA in HAP, VAP, and HCAP. However, the cost of linezolid is significantly higher than vancomycin during the treatment period of one patient.

References

[1] Emori, T.G. and Gaynes, R.P. (1993) An Overview of Nosocomial Infections, Including the Role of the Microbiology Laboratory. *Clinical Microbiology Reviews*, **6**, 428-442. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC358296/ https://doi.org/10.1128/CMR.6.4.428

[2] Klein, E., Smith, D. and Laxminarayan, R. (2007) Hospitalizations and Deaths Caused by Methicillin-Resistant *Staphylococcus aureus*, United States, 1999-2005. *EID Journal*, **13**, 60-70. http://wwwnc.cdc.gov/eid/article/13/12/07-0629_article

[3] Liu, *et al.* (2011) Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Infections in Adults and Children. *CID*, **52**, 1-38. http://cid.oxfordjournals.org/

[4] Kimble, K. (2013) Applied Therapeutic: The Clinical Use of Drugs. Lippincott Williams & Wilkins, a Wolters Kluwer, Philadelphia, 1526-1533.

[5] Rubinstein, E., Kollef, M.H. and Nathwani, D. (2008) Pneumonia Caused by Methicillin-Resistant *Staphylococcus aureus*. *Clinical Infectious Diseases*, **46**, S378-S385.

https://doi.org/10.1086/533594

[6] Chastre, J. and Fagon, J.Y. (2002) Ventilator-Associated Pneumonia. *American Journal of Respiratory and Critical Care Medicine*, **165**, 867-903. https://doi.org/10.1164/ajrccm.165.7.2105078

[7] American Thoracic Society Documents (2005) Guidelines for the Management of Adults with Hospital-Acquired, Ventilator-Associated, and Healthcare-Associated Pneumonia. *American Journal of Respiratory and Critical Care Medicine*, **171**, 388-416. https://doi.org/10.1164/rccm.200405-644ST

[8] Wunderink, R.G., Rello, J., Cammarata, S.K., Croos-Dabrera, R.V. and Kollef, M.H. (2003) Linezolid vs Vancomycin: Analysis of Two Double-Blind Studies of Patients with Methicillin-Resistant *Staphylococcus aureus* Nosocomial Pneumonia. *Chest*, **124**, 1789-1797. http://www.ncbi.nlm.nih.gov/pubmed/14605050 https://doi.org/10.1016/S0012-3692(15)33412-7

[9] Chavanet, P. (2013) The ZEPHyR Study: A Randomized Comparison of Linezolid and Vancomycin for MRSA Pneumonia. *Médecine et Maladies Infectieuses*, **43**, 451-455. http://www.sciencedirect.com/science/journal/0399077X

[10] Stevens, *et al.* (2002) Linezolid versus Vancomycin for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Infections. *Clinical Infectious Diseases*, **34**, 1481-1490. http://www.ncbi.nlm.nih.gov/pubmed/12015695 https://doi.org/10.1086/340353

[11] Kalil, A., Klompas, M., Haynatzki, G. and Rupp, M. (2013) Treatment of Hospital-Acquired Pneumonia with Linezolid or Vancomycin: A Systematic Review and Meta-Analysis. *BMJ*, **3**, e003912. https://doi.org/10.1136/bmjopen-2013-003912 http://bmjopen.bmj.com/content/3/10/e003912.full.pdf+html

[12] Dennis, L.S., Daniel, H., Harry, L., John, L.H., Donald, H.B. and Barry, H., Linezolid MRSA Study Group (2002) Linezolid versus Vancomycin for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Infections. *Clinical Infectious Diseases*, **34**, 1481-1490. https://doi.org/10.1086/340353