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Linezolid more efficacious than vancomycin to eradicate infecting organism in critically ill patients with Gram-positive infections

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ABSTRACT

Objetive: A prospective and observational study has been conducted to analyze the efficacious of linezolid compared to vancomycin to eradicate the infecting organism in critically ill patients with Gram-positive infections.

Patients and Methods: Prospective, observational and non-controlled study in a medical-surgical intensive care unit (ICU) in a university hospital. A total number of 53 critically ill patients with therapy to proven Gram-positive bacterial infection were studied. Infected patients were diagnosed and treated according to international guidelines, following standard protocol for the critically ill infected patients. Microbiologic eradication of the infecting organism at the seventh day of treatment and patients' clinical outcome were analysed.

Results: Twenty-seventh patients received linezolid and twenty-six received vancomycin. Infection-site diagnoses were: hospital-acquired pneumonia (21 cases: 39.6%), complicated surgical-site infection (19 cases: 35.8%) and catheter-related bacteraemia (13 cases: 24.5%). The most important isolated microorganism was methicillin-resistant *Staphylococcus aureus* (MRSA) (28 cases: 52.8%). Clinical success was 20/27 (74.1%) in the linezolid group and 16/26 (61.5 %) in the vancomycin group, with p = 0.3. The adjusted logistic regression model demonstrated that the treatment with linezolid is associated to microbiologic eradication of the infecting organism at the seventh day of treatment [OR = 7.88 (95% CI 1.86-33.52)] and p = 0.005. In this model, the length of hospital stay was lower in the group with microbiologic eradication at the seventh day (p = 0.015). Drug-related adverse events were comparable in both groups of treatment.

Conclusion: Treatment with linezolid in critically ill patients with Gram-positive infections was equivalent to vancomycin in terms of efficacy and safety, but linezolid was associated to a higher rate of microbiologic eradication of the infecting organism at the seventh day of treatment.

Keywords: Linezolid. Vancomycin. Gram-positive infections. Critically ill patients. Microbiologic eradication.

Linezolid es más eficaz que vancomicina en la erradicación de los organismos infectantes en los pacientes críticos con infecciones por grampositivos

RESUMEN

Objetivo: Se realizó un estudio prospectivo y observacional con el objetivo de analizar la eficacia de linezolid comparado con vancomicina para erradicar los organismos infectantes en los pacientes críticos con infecciones por grampositivos.

Pacientes y Métodos: Estudio prospectivo, observacional y no controlado en una unidad de cuidados intensivos (UCI) de un hospital universitario. Se estudiaron un total de 53 pacientes críticos con tratamiento para una infección bacteriana probada y producida por grampositivos. Los pacientes infectados fueron diagnosticados y tratados siguiendo las guías internacionales y los protocolos estándares locales establecidos para las infecciones de los pacientes críticos. Se analizó la erradicación microbiológica del organismo infectante al séptimo día de tratamiento y la evolución clínica.

Resultados: Veintisiete pacientes recibieron tratamiento con linezolid y veintiséis recibieron vancomicina. Los focos infecciosos fueron: neumonía adquirida en el hospital (21 casos: 39.6 %), infección quirúrgica complicada (19 casos: 35.8 %) y bacteriemia relacionada con el catéter (13 casos: 24.5 %). El microorganismo más frecuentemente aislado fue *Staphylococcus aureus* (SARM) (28 casos: 52.8 %). El éxito clínico se obtuvo en 20/27 pacientes (74.1 %) en el grupo de linezolid y

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en 16/26 pacientes (61.5 %) en el grupo de vancomicina, con una p = 0.3. El modelo de regresión logística mostró que el tratamiento con linezolid se asoció de forma significativa a una erradicación microbiológica del organismo infectante al séptimo día de tratamiento [OR = 7.88 (95 % CI 1.86-33.52)], p = 0.005. En este modelo, la estancia en el hospital fue más baja en el grupo de pacientes con erradicación microbiológica al séptimo día, (p = 0.015). Los efectos adversos observados fueron similares en ambos grupos de tratamiento.

Conclusión: El tratamiento con linezolid en pacientes críticos con infecciones por grampositivos fue equivalente a vancomicina en términos de eficacia y seguridad. No obstante, linezolid se asoció a una mayor erradicación microbiológica del organismo infectante al séptimo día de tratamiento.

Palabras clave: Linezolid. Vancomicina. Infecciones por grampositivos. Pacientes críticos. Erradicación microbiológica.

INTRODUCTION

Infections caused by Gram-positive organisms have increased within the last decade, constituting nowadays the main cause of sepsis in in-hospital patients. Their resistance to beta-lactam antibiotics has also increased, being the reason why —when an infection by Gram-positive bacteria in critically ill patients admitted in intensive care units (ICU) is suspected— empirical treatment with vancomycin must be put into practice[1-2].

Antibiotic treatment with vancomycin in critically ill patients can have adverse effects such as renal-function worsening in patients in unstable hemodynamic condition, greater volume of distribution and probably, early acute kidney injury. As an alternative to vancomycin, linezolid is an oxazolidinone, the first new class of antibiotic developed in the last three decades. Although it is predominantly bacteriostatic, linezolid develops appropriate in-vitro and in-vivo activity against a wide variety of Gram-positive organisms including methicillin-susceptible *S. aureus* and methicillin-resistant *S.aureus* (MRSA), coagulase-negative *Staphylococcus* (CNS) and *Enterococcus* species[3]. Previous clinical trials have demonstrated that linezolid clinical efficacy and safety were comparable to vancomycin for treatment of Gram-positive bacterial infections including MRSA ventilator-associated pneumonia, surgical-site infections and complicated skin and soft-tissue infections[4-6].

We hypothesized that linezolid would be equivalent to vancomycin for the treatment of critically ill patients with Gram-positive infections, but more efficacious than vancomycin in microbiologic eradication of infecting organism. The main objective of this study is evaluating microbiologic eradication at the seventh day of treatment and, as secondary objectives, analysing clinical success, safety and 28-day mortality through a prospective and observational study involving critically ill patients with therapy to proven Gram-positive bacterial infection.

METHODS

Study design

A prospective and observational study involving critically ill patients admitted in ICU with therapy to proven Gram-positive bacterial infection was conducted from January 2005 to January 2008. Ours is a surgical, medical and trauma ICU with 16 beds in a 435-bed university hospital. Study protocol was approved by the hospital's institutional review board and ethics committee for clinical research. Inclusion criteria were patients with proven Gram-positive infection treated with vancomycin (VAN) or linezolid (LNZ) according to the attending ICU physician. Demographic data (age, sex), severity of illness score (Simplified Acute Physiology Score, SAPS II)[7], diagnosis for admission (surgical, medical or trauma), comorbidities and risk factors for infection were reported and registered.

Patient selection

Inclusion criteria included patients with proven infections by Gram-positive bacteria (Methicillin-resistant *S. aureus*, coagulase-negative *Staphylococcus* or *Enterococcus* species with beta-lactam resistance) and the origin of infections considered for the study was: hospital-acquired pneumonia (HAP), complicated surgical-site infection (CSSI) and catheter-related bacteraemia (CRB) diagnosed according to international definitions[8]. Each patient required at least two of the following: fever (body temperature ≥ 38.5°C) or hypothermia (body temperature ≤ 35.5°C); respiratory rate > 30 breaths/min; systolic hypotension (< 90 mmHg); heart rate > 120 beats/min; elevated peripheral white cell count (WBC) > 10.000/mm^3 or leukopenia with total WBC < 4.500 cells/mm^3. For clinical infections, the following enrolment criteria were required:

Hospital-acquired pneumonia: Symptoms starting after more than 48 h after hospitalization, with at least two of the following: purulent sputum or change in character; auscultatory findings consistent with pneumonia; chest X-ray at baseline consistent with pneumonia; positive culture of sputum or tracheal aspirate with isolation of a Gram-positive organism.

Complicated surgical-site infection: Severe skin infection involving deeper levels with extensive skin areas in a surgical wound. Signs and symptoms include drainage/discharge, erythema, fluctuance or swelling with cellulites; positive culture of drainage with isolation of, at least, one Gram-positive organism.

Catheter-related bacteraemia: Sings and symptoms of infection with positives cultures of blood and the tip of the central venous catheter (semi-quantitative culture of Maki, ≥ 15 UFC), with isolation of the same Gram-positive organism in both sites.

At the seventh day of antibiotic treatment, cultures of sputum or tracheal aspirate (in HAP), wound drainage (in CSSI) or blood (in CRB) were performed.

Samples were immediately transported to a Microbiology laboratory into specific cultures for pathogen isolation. Pathogen identification and susceptibility testing were determined

at a local laboratory by microdilution techniques according to the guidelines established by the National Committee for Clinical Laboratory Standards.

Antibiotic treatment

Eligible patients were assigned to receive linezolid (600 mg every 12 h) or vancomycin (1 g every 12 h) according to the attending ICU physician, administered intravenously. Biochemistry and haematological data and adverse events were monitored and registered in accordance with clinical practice. There were no planned vancomycin dosage adjustments, but dosages were adjusted according to renal function impairment and based on monitoring vancomycin plasma-level. If drug monitoring was performed, a trough target of 10-15 mg/l and a peak target of 25-40 mg/l were recommended. Duration of antibiotic treatment was 7 to 14 days, but no longer than 21 days.

In CSSI (mixed infection), additional treatment against Gram-negative and anaerobes was permitted.

Patients who were receiving another investigational medication concurrently or suffered hypersensitivity to linezolid or vancomycin were excluded.

Microbiology and clinical outcome

Patients were assessed at baseline, during therapy, at both the seventh day of antibiotic treatment and the test-of-cure (TOC) visit, 7 days after completing therapy. Clinical success was defined as clinical cure (resolution of infection) or improvement. Failure was defined as persistence or progression of clinical infection or infection-attributable death. Microbiologic eradication at the seventh day was assessed as 'yes' with absence of the original pathogen (Gram-positive) from culture in the original site of infection at the seventh day of treatment. Clinical cure or failure was assessed at the TOC visit and repeated at hospital discharge.

Adverse events —considered to be related to study medication— were registered. Blood cell counts and serum creatinine level at baseline (pre-treatment) and end of antibiotic treatment (post-treatment), days of antibiotic treatment, length of ICU and hospital stay, and 28-day mortality were studied.

Statistical analysis

Descriptive statistics, including frequencies and percentages for categorical variables and means with standard deviations for continuous variables, was carried out. For unadjusted comparisons among groups, Student's t-test was used for continuous variables and chi-squared or Fisher's exact test was used for categorical data. Kaplan-Meier curves representing 28-day mortality stratified according to group assignment were compared by using a log-rank test.

A multiple logistic regression model was used to assess relationships between microbiologic eradication at the seventh day (dependent variable) and the treatment group, adjusted by severity of illness score (SAPS II) and other variables selected in univariate analysis. The list of other candidate variables was narrowed to include only those with univariate significance at $p < 0.2$ level. Firstly, a backward selection model —using $p < 0.05$ as an entry criterion— was performed to limit colinearity problems; the final model was constrained to a total number of 3 degrees of freedom. Odds ratio (OR) and 95 % CI was used to quantify association between risk factors and microbiologic eradication at the seventh day of treatment. The area under the receiver operating characteristics (ROC) curve (AUC) is reported to assess overall model discrimination. Calibration and possible over-fitting were evaluated with Hosmer and Lemeshow goodness-of-fit test[9]. Statistical tests were two-tailed and statistical significance was established at $p < 0.05$. All analyses were conducted by using SPSS 12.0 software (SPSS®, Chicago, Illinois, USA).

RESULTS

A total number of 53 patients were included in this study: 27 patients were treated with linezolid and 26 with vancomycin. Demographic data, severity of illness score (SAPS II), diagnosis on admission, comorbidities and risk factors of infection, origin of infection, microorganism and outcome —as baseline characteristics of study patients in both groups— are shown in table 1. The greater frequency of surgical patients (31/53: 58.5%) shall be emphasized; most patients needed mechanical ventilation (48/53: 90.6%); the most common origin of infection was hospital-acquired pneumonia (21/53: 39.6%); and the most frequent isolated Gram-positive was MRSA (28/53: 52.8%). No significant statistical differences were observed in demographic data, SAPS II, comorbidities and risk factors of infection among different treatment groups, except a higher proportion of medical patients in the LNZ group ($p = 0.02$) and a trend of higher ratio of surgical patients in the VAN group ($p = 0.07$). Cardiovascular and COPD comorbidities were more frequent in the LNZ than in the VAN group ($p = 0.09$ and $p = 0.06$, respectively). In general, the baseline characteristics of both treatment groups were comparable. Clinical success rates were equivalent between both groups: 20/27 (74.1%) in the LNZ and 16/26 (61.5%) in the VAN group, $p = 0.3$. Nevertheless, significant statistical differences were observed between microbiologic eradication of infecting Gram-positive organism at the seventh day of treatment in the LNZ (18/24: 66.7%) and VAN (6/24: 23.1%) groups, $p = 0.002$; these data were finally evaluated in 48 patients. The characteristics of the patients and microbiologic eradication at the seventh day were analysed in a univariate way and results are shown in table 2. In patients with microbiologic eradication, the number of days with antibiotic treatment and the length of hospital stay were fewer than in patients without microbiologic eradication: 9.4 ± 4.8 vs. 12.2 ± 4.6 ($p = 0.05$) and 33.1 ± 26.2 vs. 62.8 ± 35.7 ($p = 0.002$), respectively.

Final multiple logistic regression adjusted model included the linezolid treatment, SAPS II score for adjustment and length of hospital stay. After controlling for confounding variables, treatment with linezolid was associated to microbiologic eradication at the seventh day of treatment of the initial focus of infection with OR = 7.88; 95% CI = 1.86-33.52, p =

Table 1 **Patients' characteristics in both treatment groups.**

Variables	Linezolid (n = 27)	Vancomycin (n = 26)	p-value
- Age, years (SD)	64.3 (11.3)	61.2 (14.1)	0.4
- Sex, male, n (%)	18 (66.7)	21 (80.8)	0.2
- SAPS II score (SD)	40.8 (10.1)	42.7 (15.4)	0.6
Diagnosis on admission			
- Surgical	13 (48.1)	18 (69.2)	0.07
- Medical	12 (44.4)	4 (15.4)	0.02
- Trauma	2 (7.4)	4 (15.4)	0.2
Comorbidities and risk factors			
- Alcohol	11 (40.7)	10 (38.5)	0.9
- Smoke	16 (59.3)	13 (50.0)	0.5
- Diabetes	6 (22.2)	6 (23.1)	0.9
- Cardiovascular	11 (40.7)	5 (19.2)	0.09
- COPD	9 (33.3)	3 (11.5)	0.06
- Corticoids	12 (44.4)	8 (32.0)	0.4
- Chronic renal failure	3 (11.1)	0 (0.0)	0.2
- Acute renal failure	9 (36.0)	6 (23.1)	0.3
- Parenteral nutrition	16 (59.3)	16 (61.5)	0.9
- Mechanical ventilation	24 (88.9)	24 (92.3)	0.7
Origin of infection			
- Hospital-acquired pneumonia	11 (40.7)	10 (38.5)	0.9
- Complicated surgical-site infection	10 (37.0)	9 (34.6)	0.9
- Catheter-related bacteraemia	6 (22.2)	7 (26.9)	0.7
Microorganism			
- MRSA	15 (55.6)	13 (50.0)	0.4
- Coagulase-negative *Staphylococcus*	8 (29.6)	8 (30.8)	0.2
- *Enterococcus* species	4 (14.8)	5 (19.2)	0.3
Outcome			
- Creatinine pre-treatment, mg/dl (SD)	1.5 (1.3)	1.1 (0.7)	0.2
- Creatinine post-treatment, mg/dl (SD)	1.1 (0.7)	0.9 (0.6)	0.6
- Days of MV, days (SD)	24.8 (20.5)	25.0 (19.3)	0.9
- ICU stay, days (SD)	29.7 (24.8)	28.0 (19.8)	0.8
- Hospital stay, days (SD)	40.9 (31.1)	55.2 (34.9)	0.1
- Days of antibiotic treatment, days (SD)	10.0 (4.5)	11.8 (4.7)	0.2
- Clinical success, n (%)	20 (74.1)	16 (61.5)	0.3
- Eradication at 7th day of treatment, n (%)	18 (66.7)	6 (23.1)	0.002
- Mortality 28-day, n (%)	4 (14.8)	5 (19.2)	0.7

Abbreviations: SAPS II, Simplified Acute Physiology Score; COPD, Chronic obstructive pulmonary disease; MRSA, Methicillin-resistant *Staphylococcus aureus*; MV, Mechanical ventilation; ICU, Intensive Care Unit.

Table 2 **Patient's characteristics and microbiologic eradication at the seventh day.**

Variables	Microbiologic eradication at the seventh day*		
	Yes (n = 24)	No (n = 24)	*p*-value
- Age, years (SD)	62.9 (11.9)	61.7 (14.3)	0.7
- Sex, male, n (%)	20 (83.3)	16 (66.7)	0.2
- SAPS II score (SD)	42.0 (12.1)	42.4 (14.4)	0.9
Diagnosis on admission			
- Surgical	10 (41.7)	18 (75.0)	0.02
- Medical	11 (45.8)	5 (20.8)	0.06
- Trauma	3 (12.5)	1 (4.2)	0.3
Comorbidities and risk factors			
- Alcohol	6 (25.0)	12 (50.0)	0.07
- Smoke	14 (58.3)	12 (50.0)	0.6
- Diabetes	6 (25.0)	6 (25.0)	1.0
- Cardiovascular	8 (33.3)	6 (25.0)	0.5
- COPD	6 (25.0)	5 (20.8)	0.7
- Corticoids	9 (37.5)	10 (43.5)	0.7
- Chronic renal failure	2 (8.3)	1 (4.2)	0.6
- Acute renal failure	9 (37.5)	6 (25.0)	0.4
- Parenteral nutrition	11 (45.8)	17 (70.8)	0.08
- Mechanical ventilation	21 (87.5)	23 (95.8)	0.6
Origin of infection			
- Hospital-acquired pneumonia	9 (37.5)	10 (41.7)	0.8
- Complicated surgical-site infection	7 (29.2)	10 (41.7)	0.4
- Catheter-related bacteraemia	8 (33.3)	4 (16.7)	0.2
Microorganism			
- MRSA	11 (45.8)	15 (62.5)	0.1
- Coagulase-negative *Staphylococcus*	10 (41.7)	5 (20.8)	0.07
- *Enterococcus* species	3 (12.5)	4 (16.7)	0.3
Outcome			
- Creatinine pre-treatment, mg/dl (SD)	1.5 (1.2)	1.2 (1.0)	0.4
- Creatinine post-treatment, mg/dl (SD)	1.1 (0.7)	0.9 (0.6)	0.3
- Days of MV, days (SD)	22.8 (21.0)	27.1 (20.1)	0.5
- ICU stay, days (SD)	25.7 (24.1)	32.4 (21.8)	0.3
- Hospital stay, days (SD)	33.1 (26.2)	62.8 (35.7)	0.002
- Days of antibiotic treatment, days (SD)	9.4 (4.8)	12.2 (4.6)	0.05
- Clinical success, n (%)	18 (75.0)	14 (58.3)	0.2
- Mortality 28-day, n (%)	5 (20.8)	4 (16.7)	1.0

(*) Microbiologic eradication at the 7th day of treatment was evaluated in 48 patients

Abbreviations: SAPS II, Simplified Acute Physiology Score; COPD, Chronic obstructive pulmonary disease; MRSA, Methicillin-resistant *Staphylococcus aureus*; MV, Mechanical ventilation; ICU, Intensive Care Unit.

Table 3 Multiple logistic regression adjusted analysis of factors associated to microbiologic eradication at the seventh day.

Variable	β-coefficient	Standard error	Odds ratio (95 % CI)	*p*-value
Linezolid treatment	2.065	0.74	7.88 (1.86-33.52)	0.005
SAPS II score	-0.017	0.03	0.98 (0.92-1.05)	0.584
Length of hospital stay (days)	-0.032	0.01	0.97 (0.94-0.99)	0.015
Model calibration and discrimination				
Nagelkerke R-square	0.46			
Hosmer and Lemeshow $\chi 2$	8.34	(p = 0.46)		
Area under the curve	0.85	95% CI (0.74-0.96)		

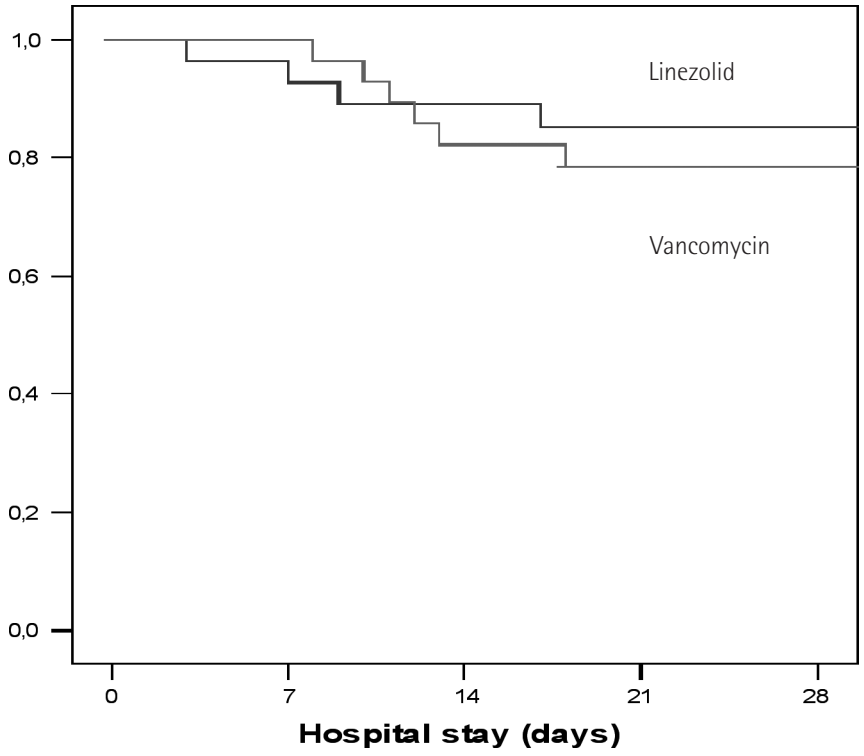

Figura 1 Probability of survival in the LNZ and VAN groups according to the length of hospital stay (Log Rank test; p = 0.73).

0.005. In addition, in this adjusted model, length of hospital stay was inversely associated to microbiologic eradication, OR = 0.97; 95 % CI = 0.94-0.99, p = 0.015. This model obtained acceptable discrimination and calibration performance. Additional details on the model are shown in table 3.

Frequencies of mild-intensity drug-related adverse events were comparable between both treatment groups: Two cases of vomiting and one case of thrombocytopenia were registered in the LNZ group, while one case of dermatitis skin rash was reported in the VAN group.

Mortality at the 28th day of hospital stay was similar in both treatment groups. Four deaths were reported in the LNZ group, while five deaths were registered in the VAN group. The Kaplan-Meyer curve with comparative mortality rate between both groups was estimated by a log-rank test and no significant statistical differences were observed, p = 0.73; see Figure 1.

DISCUSSION

In this study, linezolid is equivalent in efficacy and safety to vancomycin in critically ill patients infected by Gram-positive bacteria. However, linezolid-treated patients were significantly associated to microbiologic eradication at the seventh day of treatment of the initial focus of infection. This topic is more relevant for medical patients and patients with infection by coagulase-negative *Staphylococcus*. The clinical impact of this early microbiologic eradication involves a favourable benefit ratio in terms of days of antibiotic treatment and length of hospital stay.

Equivalent efficacy and safety of linezolid regarding vancomycin has been proved in several previous, large studies on ventilator-associated pneumonia[4], complicated skin and soft tissue infections[5-6] and febrile neutropenic patients with cancer[10]. In addition, in comparative studies of linezolid versus oxacillin in complicated skin and soft tissue infections, linezolid turns out to be equivalent in both clinical success and microbiologic terms[11]. On the other hand, initial linezolid therapy in critically ill patients was associated to significant better clinical cure and higher survival rates than those obtained with initial vancomycin therapy in patients with MRSA ventilator-associated pneumonia. A potential explanation for these results is that vancomycin was insufficient for achieving adequate lung levels in patients with MRSA pneumonia[3-4]. Nowadays, sufficient available data ascertain that linezolid can act as an alternative antibiotic for critically ill patients with Gram-positive infections such as pneumonia, soft tissue or surgical-site, and catheter-related bacteraemia with formation of a biofilm in devices[3-6,12,13].

The study of Cepeda et al.[14] —which compares the efficacy of linezolid vs. teicoplanin in the treatment of Gram-positive infections in critically ill patients— observed that linezolid was superior to vancomycin at initial clearance of methicillin-resistant *Staphylococcus aureus* colonization at the end of treatment. This point suggests a better skin and mucosal penetration of linezolid. In the same way, a recent study[15] showed that linezolid may be more effective than vancomycin in achieving microbiologic eradication of MRSA infections; similar results on bacterial eradication rates of MRSA ventilator-associated pneumonia was observed by Kollef, et al.[4] We also observed this potential effect of linezolid in a pilot study with critically ill patients infected by MRSA, and —for that reason— we started this prospective and observational study to test this hypothesis. In the study presented here, linezolid's efficacy to eradicate initial focus of infection evaluated at the seventh day of treatment remains clear. This objective has been demonstrated in a robust logistic regression analysis adjusted by severity of illness (SAPS II). Besides, we have observed in the present study that hospital stay is shorter in patients with microbiologic eradication than in patients without microbiologic eradication, a fact which may have a favourable impact on morbidity in critically ill infected patients. No differences were observed in clinical success, adverse events or 28-day mortality between both treatment groups, so it can be concluded that both linezolid and vancomycin are effective and safe drugs to treat Gram-positive infections in critically ill patients, as been proven by previous effectiveness and safety studies[10,11,14,15].

The main limitation of this study is that it is not randomized —the inclusion of patients in one or another group of treatment depends on the subjective opinion of the attendant physician, probably influenced by the patients' previous renal function and illness severity, giving rise to a clear selection bias in inclusion criteria in this observational study. Another limitation is the inclusion of Gram-positive infections with different origin; this point offers a heterogeneous group, a fact which decreases the study's statistical power in specific infections such as pneumonia, where linezolid can achieve greater effect.

Linezolid's efficacy in microbiologic eradication of the tissue-infecting or colonizing organism can be implications in the reduction of the necessary resources for the treatment of resistant infections by Gram-positive bacteria. These benefits are probably attributable to clinical outcomes: shorter duration of intravenous therapy, shorter duration of isolation procedures for MRSA infected patients and perhaps early hospital discharge. Likewise, linezolid compared to vancomycin can be a cost-effective treatment[16].

Currently, the scientific community agrees about the importance of an early control of hospitalized patients colonized by MRSA and the benefits of a complete eradication of colonized patients or patients with pneumonia by MRSA[17-18]. Nevertheless, we shall still be very cautious and have in mind the recent meta-analysis developed by Falagas et al.[19], which concludes that the use of linezolid may be restricted to specific patient populations or infections that are difficult to treat with other antibiotics. Within our working field, we certainly believe that the application of the guidelines for treatment of Gram-positive infections in critically ill patients —recently agreed upon by expert's Spanish societies[20]— constitute an appropriate strategy for habitual clinical practice.

Due to the foregoing, we believe that —when the infection's aetiology is known— patients shall be treated with an antibiotic which favours fast microbiological eradication in critically ill patients with Gram-positive infections, thus increasing the efficiency of the global therapeutic approach.

In summary, in spite of its limitations, this study indicates that treatment with linezolid in critically ill patients with Gram-positive infections is equivalent to that with vancomycin in terms of efficacy and safety; in addition, linezolid is associated with a higher rate of microbiologic eradication of the infecting organism at the seventh day of treatment, proven here by means of an adjusted logistic regression model. However, further prospective and randomized clinical trials are required to support or refute these findings.

Acknowledgements

We would like to thank our colleges and nurses in ICU for their collaboration in the study. We would also like to give thanks to Nuri Vila and Francisco Trujillo García for language assistance.

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