

RESEARCH

Open Access



A real-world cost-effectiveness study of vancomycin versus linezolid for the treatment of late-onset neonatal sepsis in the NICU in China

Linjun Xie^{1†}, Leyun Ding^{1†}, Lian Tang^{1†}, Zuming Yang², Dan Wu¹, Wenjuan Wang³, Juehui Mao⁴, Lu Shi¹, Chun Liu¹, Lufen Duan¹, Jinhui Xu¹, Qin Zhou^{1*}, Jiantong Sun^{1*} and Xinyuan Ding^{1*}

Abstract

Background and objective Currently, the detection rates of methicillin-resistant *S. aureus* (MRSA) and methicillin-resistant coagulase-negative staphylococci (MRCoNS) in the blood cultures of neonates with sepsis exceed the national average drug resistance level, and vancomycin and linezolid are the primary antibacterial drugs used for these resistant bacteria according to the results of etiological examinations. However, a comprehensive evaluation of their costs and benefits in late-onset neonatal sepsis in a neonatal intensive care unit (NICU) has not been conducted. This study aimed to compare the cost and effectiveness of vancomycin and linezolid in treating neonatal sepsis in the NICU.

Methods A cost-effectiveness analysis of real-world data was carried out by retrospective study in our hospital, and the cost and effectiveness of vancomycin and linezolid were compared by establishing a decision tree model. The drug doses in the model were 0.6 g for linezolid and 0.5 g for vancomycin. The cost break down included cost of medical ward, NICU stay, intravenous infusion of vancomycin or linezolid, all monitoring tests, culture tests and drugs. The unit costs were sourced from hospital information systems. The effectiveness rates were obtained by cumulative probability analysis. One-way sensitivity analysis was used to analyze uncertain influencing factors.

Results The effectiveness rates of vancomycin and linezolid in treating neonatal sepsis in the NICU were 89.74% and 90.14%, respectively, with no significant difference. The average cost in the vancomycin group was ¥12261.43, and the average cost in the linezolid group was ¥17227.96. The incremental cost effectiveness was ¥12416.33 cost per additional neonate with treatment success in the linezolid group compared to vancomycin group at discharge. Factors that had the greatest influence on the sensitivity of the incremental cost-effectiveness ratio were the price of linezolid and the effectiveness rates.

[†]Linjun Xie, Leyun Ding and Lian Tang these authors have contributed equally to this work.

*Correspondence:

Qin Zhou
zhouyx1223@yeah.net
Jiantong Sun
18915591290@163.com
Xinyuan Ding
aladdine@163.com

Full list of author information is available at the end of the article



Conclusions The cost for treatment success of one neonate in linezolid group was ¥5449.17 more than that in vancomycin group, indicating that vancomycin was more cost-effective. Therefore, these results can provide a reference for a cost effectiveness treatment scheme for neonatal sepsis in the NICU.

Keywords Neonatal sepsis, Vancomycin, Linezolid, Real-world, Cost-effectiveness analysis

Background

Neonatal sepsis is a systemic condition of bacterial, viral, or fungal origin and leads to serious morbidity and mortality [1]. Between 1996 and 2015, the cause-specific mortality of neonatal sepsis in China decreased from 0.4 to 0.1 per 1000 neonates, which was substantially lower than the global estimate of 2.8 per 1000 neonates [2]. However, there is a serious lack of data on the costs/health care resources associated with neonatal sepsis. Gram-positive bacteria are important pathogenic bacteria in neonatal sepsis [3]. Coagulase-negative staphylococci rank first and account for more than 70% of methicillin-resistant bacteria [4]. In contrast to the drug resistance data reported by the China Antimicrobial Resistance Surveillance System (CARSS) in 2017, the detection rates of methicillin-resistant *S. aureus* (MRSA) and methicillin-resistant coagulase-negative staphylococci (MRCoNS) in the blood cultures of neonates with sepsis exceeded the national average drug resistance level.

Vancomycin is a type of glycopeptide antibiotic that inhibits bacterial cell wall synthesis and is used for MRSA infection. Linezolid is a type of oxazolidinone antibiotic that prevents the formation of the 70S initiation complex, which is essential for the bacterial translation process, and is an alternative antibiotic for MRSA. Both drugs have bacteriostatic and bactericidal activity against many kinds of gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* and methicillin-resistant coagulase-negative staphylococci [5]. Vancomycin and linezolid are important antimicrobials for severe late-onset neonatal sepsis, although efforts should be made to control the overuse of antimicrobials [6]. Treatment of neonatal sepsis with vancomycin and linezolid in the NICU has been poorly reported and requires real-world research in China. We reported that the effectiveness rates of vancomycin and linezolid in the treatment of neonatal sepsis in NICUs in China was equivalent [7]. However, the drug costs and treatment costs of vancomycin and linezolid, especially the costs involved in monitoring the blood concentration of vancomycin [8], have not yet been compared in China. Thus, the more cost effectiveness scheme needs to be further studied.

Our study conducted CEA and one-way sensitivity analysis of vancomycin versus linezolid in the treatment of neonatal sepsis in the NICU based on a real-world

study. We found that the effectiveness rates of vancomycin and linezolid in the treatment of neonatal sepsis in the NICU was equivalent. The objective of this study was to evaluate the cost-effectiveness of 0.5 g vancomycin versus 0.6 g linezolid for the treatment of late-onset neonatal sepsis.

Methods

Model structure

A decision tree model was established based on a real-world study. The use of vancomycin for neonatal sepsis was compared with the use of linezolid. This analysis was conducted from the perspective of the China's health care system. The time horizon covered the length of hospital stay [9].

Interventions and comparators

The drug doses in the model were linezolid 10 mg/kg every 12 h intravenously and vancomycin 10 mg/kg every 12 h intravenously.

Data collection and patient selection

This study was conducted at the Affiliated Suzhou Hospital of Nanjing Medical University. The neonates we recruited were aged 0 to 28 days. Patient data were collected prospectively from June 2014 through June 2020. Neonatal sepsis was defined as the growth of gram-positive bacteria in one or more blood cultures from a patient with fever (body temperature ≥ 38 °C). If the patient had multiple episodes of gram-positive bacteremia during the study period, only the first episode was included. Patients who had gram-positive bacteremia and were prescribed parenteral vancomycin or linezolid were included. Only late-onset neonatal sepsis cases were included in this study. A total of 220 patients were diagnosed with late-onset neonatal sepsis in the NICU, whose blood cultures showed gram-positive cocci. They had clinical symptoms such as abdominal distension, gastric retention, high fever, apnea, respiratory distress, and tachycardia. Patients who received medication for less than 7 days were completely excluded. Each patient's individual clinical data were collected, such as sex, postnatal age of medication initiation, weight on medication, gestational age, Apgar score, duration of therapy, disease type, and pathogenic bacteria. The test indices before medication initiated were also collected, such as white

blood cell, neutrophil, C-reactive protein, procalcitonin, hemoglobin, platelet, total bilirubin, albumin, alanine aminotransferase, and creatinine levels. All protocols were approved by the ethics committee of the Affiliated Suzhou Hospital of Nanjing Medical University in 2012, and ethical approval No. (L20129901).

Model inputs

The Guiding Principles for Clinical Research of Antibiotics established by China Health Bureau was used to define treatment outcome, which was the highest level of agreement in China. Two researchers independently judged the treatment outcome, and the third researcher discussed or resolve the differences. The experts in the field of neonatal sepsis made the final judgment on the treatment results to ensure their accuracy [7, 10]. The curative effects of antibacterial drugs were classified into four grades: cure, improved, ineffective and progressive. “Cure” was defined as the resolution of clinical symp-

calculated according to the price of the unit drug. Hence, we here collected the price of unit drug to calculate the drug cost.

Cost-effectiveness analysis

After establishing the decision tree model, the patients were split into two groups: success and failure. For each treatment arm, two clinical outcomes were modeled, success and failure, and probabilities for the different parameters were determined from our retrospective hospital data [12]. The average cost was calculated by the accumulated probability and total cost [13]. The cost year was 2020, and the cost currency was ¥. The time horizon of average clinical benefit and average cost was 14 to 90 days. We performed a cost-effectiveness analysis by calculating the ICER. In general, a higher value of the ICER indicates a less cost-effective treatment. The ICER was measured in terms of cost spent on linezolid group and vancomycin group relative to the effectiveness rate for the treatment of late-onset neonatal sepsis:

$$ICER = \frac{\text{Costs of linezolid group per patient} - \text{Costs of vancomycin group per patient}}{\text{Effectiveness rate of linezolid group} - \text{Effectiveness rate of vancomycin group}}$$

toms and two negative blood cultures. Clinical symptoms included abdominal distension, gastric retention, high fever, apnea, respiratory distress, and tachycardia. “Improved” was defined as clinical symptom improvement and patient discharge from the hospital. “Ineffective” was defined as no remission of symptoms and a prolonged treatment time. “Progressive” was defined as an increased number of clinical symptoms and even death. Cured and improved patients were defined as a “success”, and ineffective and progressive patients were defined as a “failure”. The effective rate was calculated as follows: effectiveness rates = successful cases/total cases × 100%. Our study adopted the perspective of the medical and health system, and the cost break down included cost of medical ward, NICU stay, intravenous infusion of vancomycin or linezolid, all monitoring tests, culture tests and drugs [11]. We identified these frequencies and unit costs from hospital information system (HIS), which is adopted by most hospitals in China. The Clinical Information System contained in HIS was used to collect and process clinical medical information of patients. We then searched the keywords for diagnosis test and drug, and obtained the frequencies and resource categories identified in the data. The actual dose for neonate was lower than the minimum drug unit regardless of vancomycin and linezolid, and the drug cost was

Sensitivity analysis

One-way sensitivity analysis was conducted to assess the robustness of the model results and find the key cost drivers. We conducted a series of one-way sensitivity analyses to evaluate the sensitivity of the model results to changes in the value of individual model parameters that were expected to have some impact on the overall results. The factors included the unit cost of vancomycin, unit cost of linezolid, effectiveness rates of vancomycin, and effectiveness rates of linezolid [13].

CHEERS checklist

We analyzed the cost effectiveness of two treatments by the conventional CHEERS checklist (Table S1).

Statistical analysis

The measurement data with a normal distribution are presented as means ± SEMs, and abnormal distributed measurement data are presented as medians (Q1, Q3). The statistical significance of continuous variables was evaluated using the Mann–Whitney U test, ANOVA and χ^2 test with GraphPad Prism (version 6.0) and Statistical Package for the Social Sciences software (version 22.0). TreeAge Pro software was used to analyze the decision tree model. $P < 0.05$ was considered statistically significant.

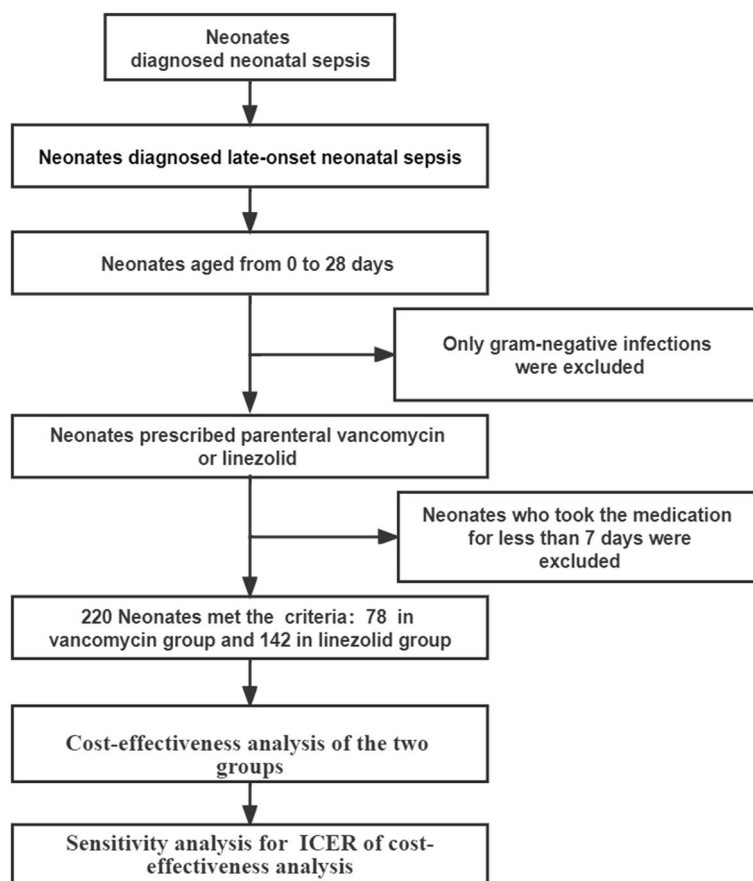


Fig. 1 The flow diagram designed in this paper for including/excluding patients and statistical analysis of pharmaceutical economics

Table 1 Basic data comparison of the vancomycin group versus the linezolid group of patients with neonatal sepsis in our hospital

Group	Vancomycin (0.5 g)	Linezolid (0.6 g)	P
n	78	142	-
Sex (male/female, n)	49/29	78/64	0.234
postnatal age of medication initiation (d)	19.03 ± 1.48	15.70 ± 0.97	0.089
Weight on medication (g)	2588.19 ± 140.85	2197.97 ± 88.23	0.022
Gestational age (w)	33.70 ± 0.50	32.60 ± 0.42	0.015
1-min Apgar score [M (Q ₁ , Q ₃)]	9.0 (8.0, 10.0)	9.0 (7.0, 10.0)	0.469
5-min Apgar score [M (Q ₁ , Q ₃)]	9.2 (9.0, 10.0)	9.2 (8.8, 10.0)	0.520
Duration of therapy [d, M (Q ₁ , Q ₃)]	14.5 (11.0, 21.0)	12.0 (10.0, 14.0)	< 0.001
Pneumonia (n)	66	127	0.370
Purulent meningitis (n)	53	6	< 0.001
Septic shock (n)	0	10	0.016
Respiratory failure (n)	40	76	0.791
Mechanical ventilation (n)	31	47	0.307

* P < 0.05 value was set for highly significant differences

Results

Base case analysis

This study included 78 active patients in the vancomycin group and 142 in the linezolid group, all of whom were diagnosed with late-onset gram-positive bacterial sepsis (Fig. 1). There were 13 and 18 neonates in each group infected with a mixture of gram-positive bacteria. The distribution of pathogenic bacteria was dominated by coagulase-negative staphylococci, which was 50.00% in the vancomycin group and 59.86% in the linezolid group. The proportions of methicillin-resistant strains in blood cultures were 30.77% and 59.15%, respectively. There were no significant differences except for purulent meningitis (Table 1; Table S2), considering multiple interfering factors, the difference in purulent meningitis did not have an impact on the ultimate treatment effectiveness, so the treatment plans of the two groups were comparable (Table S3).

Costs and effectiveness

A total of 70 of 78 patients with neonatal sepsis administered 0.5 g vancomycin were successfully treated (55 cured and 15 improved), with an effective rate of 89.74%. A total of 128 of 142 patients with neonatal

sepsis administered 0.6 g linezolid were successfully treated (114 cured and 14 improved), with an effective rate of 90.14%. There was no statistically significant difference between the effectiveness in the vancomycin and linezolid groups (Table S4). The per-day cost of vancomycin was ¥180.14, the per-day cost of linezolid was ¥408.47, the per-day cost of the medical ward in vancomycin group was ¥468.71, the per-day cost of the medical ward in linezolid group was ¥639.74, the intravenous infusion per-day cost of vancomycin and linezolid was ¥20.00, the cost of all monitoring tests in vancomycin group was ¥1815.70, the cost of all monitoring tests in linezolid group was ¥1293.48, and cost for culture test was ¥800.00 (Table S5). Treatment with vancomycin was estimated to be less costly than treatment with linezolid (¥12261.43 versus ¥17227.96). The date range of our study was 2014 to 2020.

Cost-effectiveness analysis

The average cost of the vancomycin group versus the linezolid group was shown in Fig. 2. The average cost for patients (including those who were successfully treated and those who were not) treated with 0.5 g vancomycin

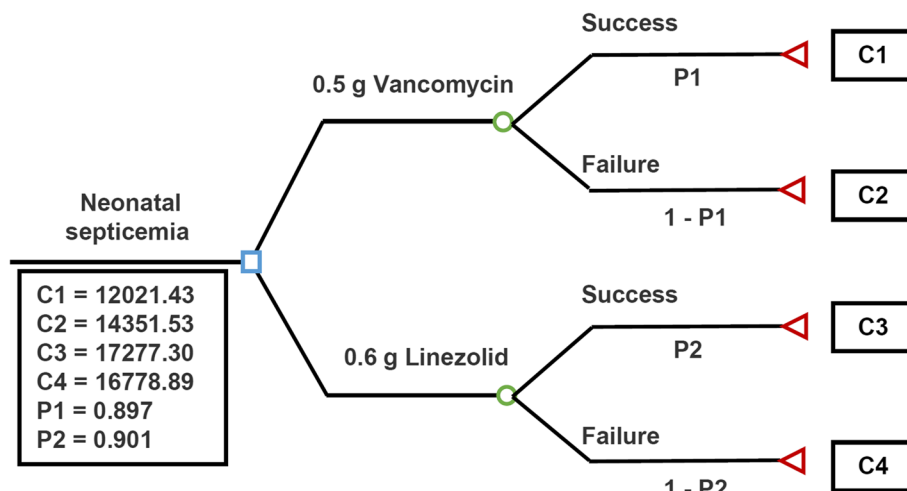


Fig. 2 Decision tree model analysis of vancomycin group versus linezolid group of patients with neonatal sepsis in our hospital. C1: Success cost of vancomycin, C2: Failure cost of vancomycin, C3: Success cost of linezolid, C4: Failure cost of linezolid, P1: Probability of success of vancomycin, P2: Probability of success of linezolid

Table 2 Cost-effectiveness of the vancomycin group versus the linezolid group of patients with neonatal sepsis in our hospital

Group	Average cost (¥)	Effective rate (%)	C/E (¥/%)	Incremental cost effectiveness ratio (ICER)
Vancomycin (0.5 g)	12261.43	89.74%	13663.28	12416.33
Linezolid (0.6 g)	17227.96	90.14%	19112.45	-

was lower than patients treated with 0.6 g linezolid (¥12261.43/person versus ¥17227.96/person) according to the total cost and cumulative probability analysis (Table S6; Table 2).

The difference in average cost between the 0.5 g vancomycin and 0.6 g linezolid treatment was mostly reflected in the drug cost. The CEA showed that the effective rate in the vancomycin group was 89.74%, and the average cost was ¥12261.43. The effective rate in the linezolid group was 90.14%, and the average cost was ¥17227.96. It was ¥12416.33 cost per additional neonate with treatment success in the linezolid group compared to vancomycin group at discharge. (Table 2).

Sensitivity analysis

The tornado diagram depicts the effect of each input across the range of fluctuations analyzed by one-way sensitivity analysis (Fig. 3). As shown in the diagram, three uncertain factors that had the greatest influence on the sensitivity of the ICER were the price of linezolid (¥71.00~¥351.21), the price of vancomycin (¥57.69~¥103.99), and the effectiveness rates of patients treated with 0.6 g linezolid (83.67%~94.65%).

Then, we performed a sensitivity analysis for these three factors. The drug cost of linezolid was analyzed in subgroups according to its two specifications. The sensitivity analysis showed that even if 0.6 g linezolid had the lowest price, its cost-effectiveness ratio was still higher

Table 3 Sensitivity analysis of vancomycin versus linezolid for patients with neonatal sepsis

Group	Vancomycin (0.5 g)		Linezolid (0.6 g)	
	Lowest	Highest	Lowest	Highest
Cost of drug daily (¥)	57.69	103.99	197.10	351.21
Average cost (¥/person)	10925.42	12261.43	16013.10	19559.67
Effective rate (%)	89.74	89.74	90.14	90.14
Cost-effectiveness ratio (¥/%)	12179.96	13663.28	17772.58	21708.85

than that of 0.5 g vancomycin, which had the highest price, indicating that 0.5 g vancomycin had more cost effectiveness advantages than 0.6 g linezolid (Table 3).

Considering that the price of drugs has little effect on the effectiveness of treatment, the sensitivity analysis of effectiveness rates was conducted on patients treated with 0.5 g vancomycin versus 0.6 g linezolid. As the effectiveness rates of linezolid changed, the cost-effectiveness ratio of linezolid was always higher than that of vancomycin when the cost-effectiveness ratio of vancomycin was fixed (Fig. 4).

Discussion

Vancomycin and linezolid are both important drugs for neonatal sepsis in the NICU. At present, there is no economic evaluation of the use of both drugs for neonatal

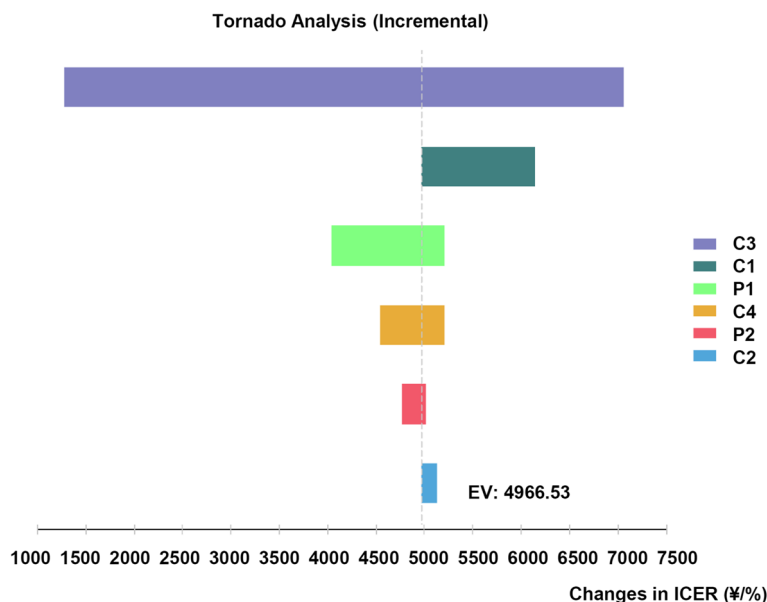


Fig. 3 Tornado diagram of different influencing factors on the results of sensitivity of incremental cost-effectiveness ratio (ICER). Tornado diagram represented the ICER gained in the one-way sensitivity analysis for linezolid versus vancomycin. The width of the bars represented the range of the results when the variables were changed. The drug prices were derived from publicly drug procurement platform, and the effectiveness rates were cited from references. ICER = incremental cost-effectiveness ratio. C1: Success cost of vancomycin, C2: Failure cost of vancomycin, C3: Success cost of linezolid, C4: Failure cost of linezolid, P1: Success of vancomycin, probability, P2: Success of linezolid, probability

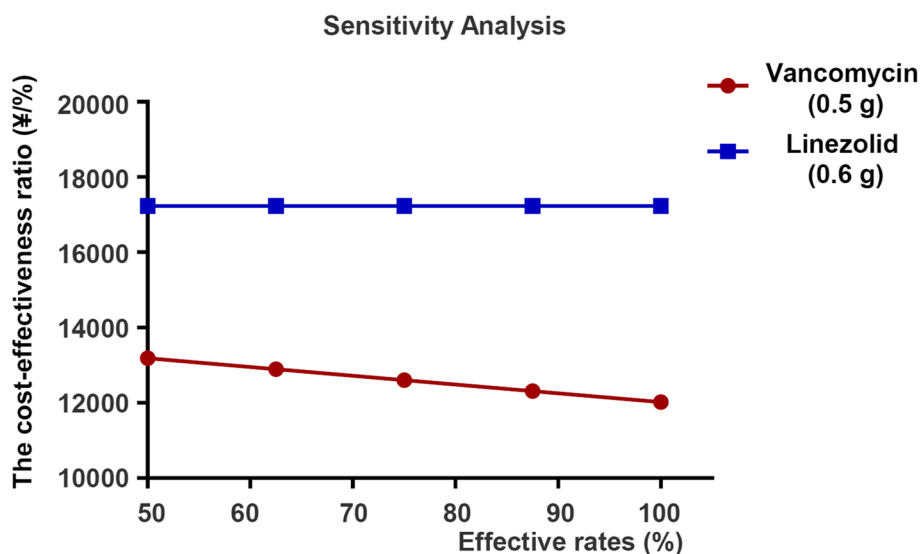


Fig. 4 Sensitivity analysis of the effectiveness rates of treatments for patients with neonatal sepsis treated with vancomycin. According to one-way sensitivity analysis, the cost-effectiveness ratio of 0.6 g linezolid was kept as invariable and the effectiveness rates of 0.5 g vancomycin was kept as variable

sepsis in neonatal intensive care units. Thus, further economic research is needed to find a superior economic treatment scheme for patients with neonatal sepsis in the NICU. Here, we found that vancomycin and linezolid indeed had the same effect in treating neonatal sepsis in the NICU. With changes in linezolid specifications, the superior treatment scheme of vancomycin and linezolid in treating neonatal sepsis in the NICU changed.

Real-world studies can exhibit the cost effectiveness differences between different treatment schemes in China more directly and truly [14]. Real-world studies of vancomycin and linezolid for neonatal sepsis in NICUs in China have not been reported recently. Our study was a retrospective analysis of 0.5 g vancomycin and 0.6 g linezolid for the treatment of 220 patients with neonatal sepsis in the NICU in our hospital. Although the inclusion criteria were established, there was a significant difference between the two groups at baseline due to sex. The reason for the baseline difference might be the sample sizes of the vancomycin and linezolid groups, which were 78 and 142, respectively. Because the sample sizes were small, there might have been a serious imbalance in the sex of newborns. However, sex is not a factor that is considered in the selection of clinical treatment for neonatal sepsis [15], and it is also not a high-risk factor for neonatal sepsis [16]. Therefore, the analysis results of this real-world study were not affected by the sex of the newborns. Moreover, there was no significant difference between other clinical features, indicating that the pharmacoeconomic comparison of these two strategies in our hospital was feasible.

It was reported that CEA was employed to research the use of linezolid versus vancomycin in the empiric treatment of nosocomial pneumonia [17] and to survey the use of fidaxomicin versus vancomycin in patients with clostridium difficile infection [18]. All these studies employed CEA to evaluate the economics of the treatment of real-world diseases, which proved the feasibility of CEA. However, the CEA of vancomycin versus linezolid in the treatment of neonatal sepsis based on real-world research has not been studied before.

The difference in average total medical costs in the vancomycin and linezolid groups was mostly reflected in the drug costs. The costs of treatment programs were fixed in our hospital. However, the drug costs for patients with neonatal sepsis were different. In China, if the drug dose used is less than the minimum unit packaging dose, the unit drug price determines the drug cost. The drug dose for neonates was much less than the minimum unit packaging dose. The dose of linezolid for neonatal sepsis was much less than 0.2 g, which would not impact effectiveness and only impact the cost. In the sensitivity analysis, we found final CEA conclusion of using various specifications was totally different. Hence, it was very reasonable that the sensitivity analysis of linezolid should be conducted for different specifications. In our study, 0.5 g vancomycin was more cost-effectiveness than 0.6 g linezolid in our hospital and was supplemented by a sensitivity analysis.

Our retrospective review was in accordance with international norms, and we also consulted many relevant references. However, there were some limitations. First, as the samples in this study were collected in our hospital and the sample size was limited, the results need to be

verified in multiple centers [19]. Second, it was reported that patients with neonatal sepsis often have anemia, premature birth, jaundice and other basic diseases [20, 21]. Among them, anemia was a possible adverse reaction to linezolid [22]. Since it was impossible to completely distinguish whether anemia was caused by diseases or drugs, the treatment costs for anemia were not included in the total medical costs, which interfered with the pharmacoeconomic results to a certain extent. Finally, as false-positive results may exist in the blood cultures of patients with MRCoNS infection, we tried to exclude false-positive results through clinical symptoms and bilateral double-bottle sampling to ensure the accuracy of antibiotic use.

Conclusion

In summary, these results indicated that different drug specifications of linezolid and vancomycin had substantial economic differences in the treatment of neonatal sepsis. The effectiveness rates of vancomycin and linezolid for the treatment of neonatal sepsis in the NICU was equivalent, but treatment cost of vancomycin group was lower than linezolid group. Hence, vancomycin was more cost-effective than linezolid. Therefore, these findings will provide a clear reference for the selection of cost-effective drugs and provide clear economic options for a subset of NICU sepsis patients with unspecified bacterial infections.

Abbreviations

CARSS	China antimicrobial resistance surveillance system
CEA	Cost-effectiveness analysis
ICER	Incremental cost-effectiveness ratio
MRCoNS	Methicillin-resistant coagulase-negative staphylococci
MRSA	Methicillin-resistant <i>S. aureus</i>
NICU	Neonatal intensive care unit
QALYs	Quality-adjusted life years

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12913-023-09628-9>.

Additional file 1: Table S1. CHEERS checklist—items to include when reporting economic evaluations of health interventions.

Additional file 2: Table S2. Basic data comparison of the vancomycin group versus the linezolid group of patients with neonatal sepsis in our hospital.

Additional file 3: Table S3. Multivariate logistic regression analysis for the effect rates of vancomycin group versus linezolid group.

Additional file 4: Table S4. Clinical effectiveness in the vancomycin group versus linezolid group.

Additional file 5: Table S5. Base-case cost for the decision analytic model in 2020.

Additional file 6: Table S6. Total medical cost and cumulative probability analysis based on the decision tree model of the vancomycin group versus the linezolid group.

Acknowledgements

We thank all the involved doctors and technicians for supporting this study.

Authors' contributions

XYD and JTS conceived of and designed this study. LJX, LYD, LT, ZMY, WJW and JHM performed the experiments and analyzed the data. LJX and LYD wrote the manuscript. LS, CL, LFD, JHX, QZ and DW participated in the data collection of clinical parameters. All authors read and approved the manuscript for publication.

Funding

This work was supported by grants from the Jiangsu Pharmaceutical Association (Grant Nos. H202052, H202024 and H202011), Science and Technology Funds of Suzhou Municipality (Grant No. SYS2020188), and Wu Jie ping Medical Foundation (Grant Nos. 320.6750.2020–4-37 and 320.6750.2020–12-69). The funders were not involved in the study design, data collection, data analysis or the writing of the paper.

Availability of data and materials

The original contributions presented in this study are included in the article/ Additional Material, and further inquiries can be directed to the corresponding authors.

Declarations

Ethics approval and consent to participate

This study was submitted to the Ethics Committee of the Affiliated Suzhou Hospital of Nanjing Medical University and ethical approval No. (L20129901). All methods were carried out in accordance with relevant guidelines and regulations. All participants signed informed consent form about voluntary participation in the study. For all participants who under 16 years of age, we obtained informed consent from their parents or legal guardians.

Consent for publication

Not applicable.

Competing interests

The authors declared that they have no competing interests.

Author details

¹Department of Pharmacy, the Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou, China. ²Department of Neonatology, the Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou, China. ³Children's Hospital of Soochow University, Medical College of Soochow University, Soochow University, Suzhou, China. ⁴School of Basic Medicine and Clinical Pharmacy, China Pharmaceutical University, Nanjing, China.

Received: 9 November 2022 Accepted: 31 May 2023

Published online: 19 July 2023

References

- Esposito S, Principi N. Adjunctive therapy to treat neonatal sepsis. *Expert Rev Clin Pharmacol.* 2020;13(1):65–73.
- He C, Liu L, Chu Y, Perin J, Dai L, Li X, Miao L, Kang L, Li Q, Scherpbier R, et al. National and subnational all-cause and cause-specific child mortality in China, 1996–2015: a systematic analysis with implications for the Sustainable Development Goals. *Lancet Glob Health.* 2017;5(2):e186–97.
- Tang XJ, Sun B, Ding X, Li H, Feng X. Changing trends in the bacteriological profiles and antibiotic susceptibility in neonatal sepsis at a tertiary children's hospital of China. *Transl Pediatr.* 2020;9(6):734–42.
- Pokhrel B, Koirala T, Shah G, Joshi S, Baral P. Bacteriological profile and antibiotic susceptibility of neonatal sepsis in neonatal intensive care unit of a tertiary hospital in Nepal. *BMC Pediatr.* 2018;18(1):208.
- Hashemian SMR, Farhadi T, Ganjparvar M. Linezolid: a review of its properties, function, and use in critical care. *Drug Des Devel Ther.* 2018;12:1759–67.

6. Sicard M, Moussa A, Barrington K, Martin B, Luu TM, Ting JY, Roberts A, Paquette V, Shah PS, Kelly E, et al. Neonatal and neurodevelopmental outcomes following linezolid for coagulase-negative staphylococcal infection: real world evidence. *Pediatr Infect Dis J*. 2020;39(7):598–603.
7. Tang L, Fang J, Wang SN, Weng XH, Li JJ, Shang EN. Clinical efficacy and safety of vancomycin compared with linezolid for the treatment of neonatal gram-positive bacterial sepsis. *Zhonghua Er Ke Za Zhi*. 2016;54(9):686–91.
8. Sosnin N, Curtis N, Cranswick N, Chiletto R, Gwee A. Vancomycin is commonly under-dosed in critically ill children and neonates. *Br J Clin Pharmacol*. 2019;85(11):2591–8.
9. Voermans AM, Mewes JC, Broyles MR, Steuten LMG. Cost-effectiveness analysis of a procalcitonin-guided decision algorithm for antibiotic stewardship using real-world u.s. hospital data. *Omics*. 2019;23(10):508–15.
10. Ueda T, Takesue Y, Nakajima K, Ichiki K, Ishikawa K, Takai Y, Yamada K, Tsuchida T, Otani N, Takahashi Y, et al. Clinical efficacy and safety in patients treated with teicoplanin with a target trough concentration of 20 µg/mL using a regimen of 12 mg/kg for five doses within the initial 3 days. *BMC Pharmacol Toxicol*. 2020;21(1):50.
11. Zhu J, He W, Ye M, Fu J, Chu YB, Zhao YY, Zhang YJ, Kuo D, Wu B. Cost-effectiveness of afatinib and erlotinib as second-line treatments for advanced squamous cell carcinoma of the lung. *Future Oncol*. 2018;14(27):2833–40.
12. Bounthavong M, Hsu DI, Okamoto MP. Cost-effectiveness analysis of linezolid vs. vancomycin in treating methicillin-resistant *Staphylococcus aureus* complicated skin and soft tissue infections using a decision analytic model. *Int J Clin Pract*. 2009;63(3):376–86.
13. Borba HHL, Steimbach LM, Riveros BS, Tonin FS, Ferreira VL, Bagatim BAQ, Balan G, Pontarolo R, Wiens A. Cost-effectiveness of amphotericin B formulations in the treatment of systemic fungal infections. *Mycoses*. 2018;61(10):754–63.
14. Huang M, Tian Y, He M, Liu J, Ren L, Gong Y, Peng F, Wang Y, Ding Z, Wang J, et al. Crizotinib versus chemotherapy: a real-world cost-effectiveness study in China. *J Comp Eff Res*. 2020;9(2):93–102.
15. El-Madbouly AA, El Sehemawy AA, Eldesoky NA, Abd Elgalil HM, Ahmed AM. Utility of presepsin, soluble triggering receptor expressed on myeloid cells-1, and neutrophil CD64 for early detection of neonatal sepsis. *Infect Drug Resist*. 2019;12:311–9.
16. Murthy S, Godinho MA, Guddattu V, Lewis LES, Nair NS. Risk factors of neonatal sepsis in India: a systematic review and meta-analysis. *PLoS ONE*. 2019;14(4):e0215683.
17. Collins CD, Schwemm AK. Linezolid Versus Vancomycin in the Empiric Treatment of Nosocomial Pneumonia: A Cost-Utility Analysis Incorporating Results from the ZEPHYR Trial. *Value Health*. 2015;18(5):614–21.
18. Rubio-Terrés C, Aguado JM, Almirante B, Cobo J, Grau S, Salavert M, González Antona Sánchez E, López Gutiérrez C, Rubio-Rodríguez D. Extended-pulsed fidaxomicin versus vancomycin in patients 60 years and older with clostridium difficile infection: cost-effectiveness analysis in Spain. *Eur J Clin Microbiol Infect Dis*. 2019;38(6):1105–11.
19. Powell J, Williams V, Atherton H, Bennett K, Yang Y, Davoudianfar M, Hellsing A, Martin A, Mollison J, Shanyinde M, et al. Effectiveness and cost-effectiveness of a self-guided internet intervention for social anxiety symptoms in a general population sample: randomized controlled trial. *J Med Internet Res*. 2020;22(1):e16804.
20. Mitra S, Rennie J. Neonatal jaundice: aetiology, diagnosis and treatment. *Br J Hosp Med (Lond)*. 2017;78(12):699–704.
21. Aher S, Malwatkar K, Kadam S. Neonatal anemia. *Semin Fetal Neonatal Med*. 2008;13(4):239–47.
22. Hanai Y, Matsuo K, Ogawa M, Higashi A, Kimura I, Hirayama S, Kosugi T, Nishizawa K, Yoshio T. A retrospective study of the risk factors for linezolid-induced thrombocytopenia and anemia. *J Infect Chemother*. 2016;22(8):536–42.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

