

# Target serum concentration of vancomycin may be reached earlier with a loading dose

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## Abstract

**Background:** Vancomycin treatment failure against vancomycin-susceptible gram-positive cocci is not rare in the intensive care unit (ICU). One of the reasons for this is the substandard drug trough concentration. We aimed to examine the hypothesis that the target serum concentration could be reached earlier with a loading dose of vancomycin.

**Methods:** This retrospective cohort study was conducted at our ICU between June 2018 and June 2020 and involved patients who were suspected of having, or confirmed to have, gram-positive cocci infection and treated with vancomycin. One group of the patients was administered a loading dose of vancomycin (loading group) and compared with the group that did not receive a loading dose (control group). The baseline characteristics, vancomycin serum concentrations, and clinical outcomes were collected and analyzed.

**Results:** Fifty-five patients were finally included, of which 29 received a loading dose of vancomycin. The serum concentration of vancomycin before the second dose was significantly higher for the loading group than for the control group ( $10.3 \pm 6.1$  mg/L vs.  $5.7 \pm 4.4$  mg/L,  $P = 0.002$ ). The results for both groups were similar before the fifth dose ( $12.4 \pm 7.3$  mg/L vs.  $10.3 \pm 6.3$  mg/L in the loading and the control groups, respectively;  $P = 0.251$ ). The 28-day mortality was lower for the loading group than for the control group (6.7% vs. 34.6% in the loading and control groups, respectively;  $P = 0.026$ ). No significant differences were observed in serum creatinine (Cr) concentrations of the two groups.

**Conclusion:** With the loading dose of vancomycin, the target serum concentration of vancomycin may be reached earlier without increasing the risk of acute kidney injury.

**Trial registration:** <https://www.chictr.org.cn>; ChiCTR2000035369

**Keywords:** Infection; Loading dose; Serum creatinine; Trough concentration; Vancomycin

## Introduction

Vancomycin is still the first-line parenteral antibacterial agent for the treatment of invasive methicillin-resistant *Staphylococcus aureus* (MRSA) infections, especially MRSA bacteremia. Nevertheless, several observational studies have reported a frequent correlation between vancomycin treatment failures and *in-vitro* antimicrobial “susceptibility,” which is below the upper official minimum inhibitory concentration (MIC) range.<sup>[1-3]</sup> Sixty-three percent of physicians were reported to be anxious and tended to change the anti-infection agent from vancomycin to other antibiotics when fever was still present the day after vancomycin initiation.<sup>[4]</sup> Frequent changes in antibiotics are associated with the lack of pharmacokinetic knowledge on antibiotic dosing on the part of doctors.<sup>[5]</sup>

It is well-known that the serum concentration of vancomycin should be measured before the fifth dose, which would be mostly implemented on the third day after administration. However, the target therapeutic concentration may not be reached when vancomycin is withdrawn by excessively anxious clinicians. If the target trough serum concentration of vancomycin can be reached earlier, patient outcomes may be improved.

The loading dose of vancomycin has been investigated and recommended by several studies.<sup>[6-8]</sup> The results of these studies show that the loading dose facilitates an earlier increase in the serum vancomycin concentration without an increased incidence of renal injury. Mostly, the vancomycin loading dose is administered as a standardized dose (2 g) or 25–30 mg/kg, regardless of kidney function

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(renal injury or augmented renal clearance). Vancomycin dose should be individually adjusted according to renal function for reasons involving pharmacokinetics.

The vancomycin dosage was adjusted according to the patient's creatinine clearance (CCr) in the intensive care unit (ICU).<sup>[9]</sup> The loading dose was approximately 1.5 times the maintenance dose. This study aimed to compare the serum concentrations of vancomycin before the second dose in the loading dose and control groups to verify the hypothesis that the targeted trough concentrations of vancomycin can be reached earlier with the loading dose, and to ascertain the safety of the loading dose of vancomycin.

## Methods

### Ethics

The trial was conducted in accordance with the guiding principles of the *Declaration of Helsinki* and was approved by the Ethics Committee of Ruijin Hospital North (No. 2020-002-1).

This retrospective single-center study was conducted at the Department of Critical Care Medicine, Ruijin Hospital North Affiliated to Shanghai Jiao Tong University School of Medicine. It has a well-equipped ICU, and we admitted patients from both medical and surgical departments and accepted patients from the emergency department; there were 22 beds. The requirement for informed consent by each patient was waived by the Ethics Committee of Ruijin Hospital North because the patient and hospital data were anonymized.

The following patients were included in this study: (1) patients who were treated at the Department of Critical Care Medicine, Ruijin Hospital North, Shanghai Jiao Tong University School of Medicine, between June 2018 and June 2020; (2) patients who were suspected of or confirmed to have gram-positive cocci infection and had been treated with vancomycin; (3) patients whose serum concentrations of vancomycin before the second and fifth doses were measured; and (4) patients aged >18 years.

The exclusion criteria were as follows: (1) receiving renal replacement therapy during the treatment; (2) duration of vancomycin treatment of <3 days; (3) missing data such as vancomycin concentrations; (4) having been administered vancomycin within 3 days before admission to the ICU; (5) change in the administration route of vancomycin from bolus injection to continuous infusion before the fifth dose; and (6) pregnancy.

The included patients were divided into two groups according to their first dosage: Group 1 (Loading group): the patients received intermittent bolus doses, and the first dose was greater than the maintenance dose; Group 2 (Control group): the patients received intermittent bolus doses, and the first dose was the same as the maintenance dose.

A standard case report form was used to collect data, including demographic characteristics (e.g., age, sex, body

weight, and height), diagnosis, acute physiology, and chronic health evaluation (APACHE) II score, sequential organ failure assessment (SOFA) score before using vancomycin, site of infection, type of pathogens, MIC of vancomycin for cocci, creatinine (Cr), CCr (CCr was calculated using the following formula:  $CCr = (140 - \text{age}) \times \text{weight} \times 88.4 / (72 \times \text{Scr})$ ), dosage and frequency of vancomycin, treatment duration, total dose of vancomycin, and outcome. Sepsis was represented as Sepsis-3.<sup>[10]</sup>

### Statistical analysis

All statistical analyses were performed using the Statistical Package for Social Sciences 23.0 (SPSS, Inc., Chicago, IL, USA). The continuous data are expressed as mean  $\pm$  standard deviation or median (interquartile range), and the categorical data are expressed as the number of cases (*n*) and percentage (%). The unpaired Student's *t* test and unpaired Wilcoxon rank-sum test were used to analyze the continuous variables. The paired Student's *t* test was used to compare the in-group data. The chi-squared ( $\chi^2$ ) test was used to compare the categorical data. Statistical significance was set at  $P < 0.05$ .

### Results

Fifty-five patients were included in the study [Figure 1], of which 29 received a loading dose of vancomycin, whereas the other 26 received the traditional dose of vancomycin. The general patient characteristics are presented in Table 1. There were no significant differences in age, sex, height, weight, SOFA score, and APACHE II score. For the 55 patients, the sources of infection were the lung, blood, skin and soft tissue, brain, abdomen, and urinary tract. There were no significant differences between the sources of infection in the two groups. The incidence of sepsis was the same in the groups. Pathogens were detected in 81% (21/26) and 34% (10/29) of the patients in the control and loading groups, respectively. The gram-positive pathogens detected included *S. aureus*, *Staphylococcus epidermidis*, *Staphylococcus cephalis*, *Staphylococcus hemolyticus*, *Streptococcus*, *Corynebacterium striatum*, *Enterococcus faecalis*, and *Enterococcus faecium*. Among the aforementioned gram-positive cocci, only *S. haemolyticus* had different prevalence in the two groups, with five cases in the control group, but none in the loading group. The MICs for 24%, 36%, and 40% of the cultured pathogens were 0.5 mg/L, 1 mg/L, and 2 mg/L, respectively.

The baseline body temperature and biochemical parameters are shown in Table 2. Body temperature was higher in the loading group than that in the control group. There were no differences in the white blood cell count (WBC), neutrophil ratio, C-reactive protein (CRP), procalcitonin (PCT), sodium (Na), potassium (K), albumin, prealbumin, transaminase, bilirubin, urea nitrogen, and lactate concentrations. In this study, there was no difference in serum Cr level, bodyweight, or CCr.

The doses and serum vancomycin concentrations are shown in Table 3. The first dose of vancomycin in the loading group was significantly higher than that in the control group (22.2 [19.4–26.7] vs. 14.2 [11.9–16.8],

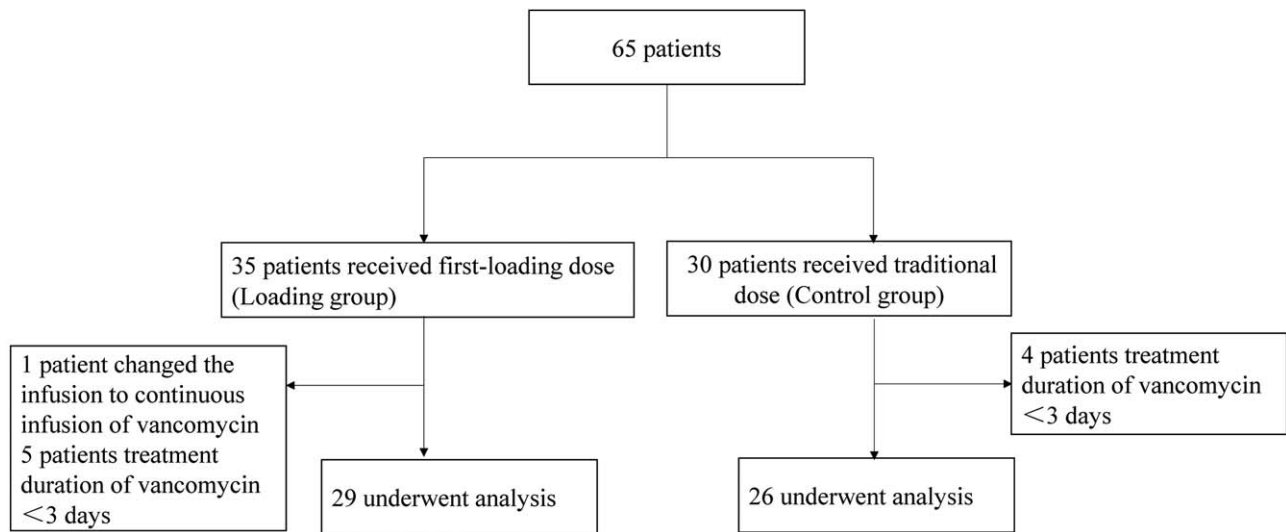


Figure 1: Flowchart of the screen of the study.

Variables	Loading group (n = 29)	Control group (n = 26)	t/ $\chi^2$	P value
Age (years)	59 ± 14	57 ± 15	0.624	0.535
Female	8 (27.6)	7 (26.9)	0.003*	0.956
Height (cm)	166.1 ± 7.4	168.5 ± 5.1	-1.360	0.180
Weight (kg)	65.7 ± 11.0	67.3 ± 17.6	-0.403	0.689
Body mass index (kg/m <sup>2</sup> )	23.8 ± 3.6	23.5 ± 5.3	0.167	0.868
SOFA score	5 ± 3	6 ± 3	-1.192	0.238
APACHEII score	12 ± 6	15 ± 7	-1.768	0.083
Source of infection			4.143*	0.529
Lung	16 (55.2)	16 (61.5)		
Blood	7 (24.1)	6 (23.1)		
Skin and soft tissue	4 (13.8)	3 (11.5)		
Intracranial	5 (17.2)	2 (7.7)		
Abdominal	5 (17.2)	2 (7.7)		
Urinary tract	3 (10.3)	0		
Sepsis	8 (27.6)	11 (40.7)	1.314*	0.252
Bacteria cultured			11.441*	0.120
<i>Staphylococcus aureus</i>	1 (3.4)	6 (23.1)		
<i>Staphylococcus epidermidis</i>	2 (6.9)	4 (15.4)		
<i>Staphylococcus cephalis</i>	2 (6.9)	0		
<i>Staphylococcus hemolyticus</i>	0	5 (19.2)		
<i>Streptococcus</i>	2 (6.9)	1 (3.8)		
<i>Corynebacterium striatum</i>	2 (6.9)	1 (3.8)		
<i>Enterococcus faecalis</i>	1 (3.4)	3 (11.5)		
<i>Enterococcus faecium</i>	0	1 (3.8)		

The data are shown as mean ± standard deviation, or number and percentage. \*  $\chi^2$  values, otherwise *t*-values. APACHE: Acute physiology and chronic health evaluation; SOFA: Sequential organ failure assessment.

$P < 0.001$ ). The first dose was approximately 1.5 times that of the control group. The concentrations of vancomycin before the second dose were  $10.3 \pm 6.1$  mg/L and  $5.7 \pm 4.4$  mg/L for the loading and control groups, respectively. The concentration of vancomycin before the second dose in the loading group was significantly higher than that in the control group ( $P = 0.002$ ) [Figure 2]. The concentrations of vancomycin before the fifth dose were

$12.4 \pm 7.3$  mg/L and  $10.3 \pm 6.3$  mg/L for the loading and control groups, respectively; there was no inter-group difference ( $P = 0.251$ ). In the loading group, there was no difference between the vancomycin concentrations before the second and fifth doses. In the control group, the concentration of vancomycin before the fifth dose was significantly higher than that before the second dose ( $10.3 \pm 6.3$  vs.  $5.7 \pm 4.4$ ,  $P = 0.004$ ). Mortality in the

**Table 2: Baseline body temperature and biochemical parameters.**

Variables	Loading group (n = 29)	Control group (n = 26)	t	P value
Temperature (°C)	38.5 ± 0.9	37.9 ± 1.0	2.231	0.030
WBC (×10 <sup>9</sup> /L)	12.2 ± 4.7	10.2 ± 6.4	1.347	0.184
N (%)	84.0 ± 7.4	83.6 ± 7.8	0.144	0.886
CRP (mg/L)	69.5 (39.0–131.8)	56.0 (35.0–88.3)	1.358	0.181
PCT (ng/mL)	4.8 ± 15.6	7.0 ± 20.6	-0.436	0.665
Na (mmol/L)	143.0 ± 8.6	140.2 ± 7.3	1.296	0.201
K (mmol/L)	3.9 ± 0.5	4.1 ± 0.4	-1.043	0.302
Albumin (g/L)	32.0 (30.0–35.0)	29.0 (27.0–36.0)	1.204	0.235
Pre-albumin (mg/L)	149.0 ± 70.3	131.3 ± 61.9	0.971	0.336
ALT (IU/L)	36.4 ± 29.5	39.2 ± 38.7	-0.308	0.759
AST (IU/L)	44.6 ± 39.2	53.6 ± 97.0	-0.452	0.653
TB (μmol/L)	19.7 ± 16.3	33.3 ± 73.3	-0.940	0.351
DB (μmol/L)	7.5 ± 10.7	16.9 ± 51.7	-0.928	0.358
ALP (IU/L)	97.0 ± 54.8	76.6 ± 39.8	1.557	0.126
Cr (μmol/L)	85.0 ± 52.7	68.5 ± 22.0	1.478	0.146
BUN (mmol/L)	13.5 ± 22.1	16.9 ± 44.1	-0.364	0.718
Cystatin C (mg/L)	1.4 ± 0.7	1.1 ± 0.5	1.357	0.183
Lactate (mmol/L)	2.1 ± 0.9	2.1 ± 1.4	0.004	0.997
CCr (mL/min)	90.7 ± 36.2	105.4 ± 34.5	-1.522	0.134

The data are expressed as mean ± standard deviation or median (interquartile range). ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; AST: Aspartate aminotransferase; BUN: Blood urea nitrogen; CRP: C-reactive protein; Cr: Creatinine; CCr: Creatinine clearance; DB: Direct bilirubin; K: Potassium; N: Neutrophils; Na: Sodium; PCT: Procalcitonin; TB: Total bilirubin; WBC: White blood cell.

**Table 3: Results of serum concentrations of vancomycin and dosages of vancomycin.**

Variables	Loading group (n = 29)	Control group (n = 26)	t/χ <sup>2</sup>	P value
The first dose (mg/kg)	22.2 (19.4–26.7)	14.2 (11.9–16.8)	8.408	<0.001
Serum concentration of vancomycin before the second dose (mg/L)	10.3 ± 6.1	5.7 ± 4.4	3.214	0.002
Serum concentration of vancomycin before the fifth dose (mg/L)	12.4 ± 7.3	10.3 ± 6.3*	1.162	0.251
Ratio of serum concentration of vancomycin between that before the second and before the fifth dose	1.0 ± 0.7	0.9 ± 1.4	0.379	0.706
Total dosage of vancomycin (g)	14.3 ± 8.9	15.1 ± 11.4	-0.266	0.791
Days of using vancomycin (days)	7.0 ± 8.0	8.0 ± 6.0	-0.292	0.771
28-day mortality No. /total No. (%)	2/29 (6.7)	9/26 (34.6)	4.965†	0.026

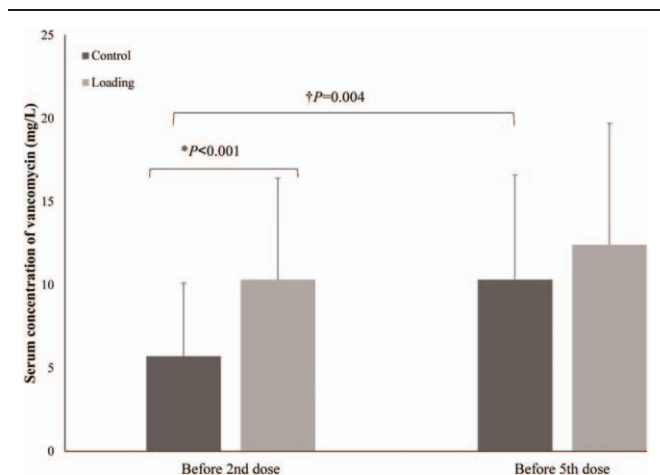
The data are expressed as median (interquartile range) or mean ± standard deviation or n (%). \* Compared with the serum concentration of vancomycin before the second dose in the same group, P < 0.05. † χ<sup>2</sup> values, otherwise t-values.

loading group was significantly lower in the loading group than that in the control group (P = 0.026).

Renal function information for 1 week after vancomycin administration was collected. Two patients in the loading group and one patient in the control group had abnormal renal function before vancomycin administration. The results showed that there was no significant change in the serum Cr concentrations in either group, and there was no statistical difference between the serum Cr concentrations of the two groups [Table 4, Figure 3].

**Discussion**

Vancomycin, a glycopeptide antibiotic, is often used to treat infections caused by gram-positive cocci. After 3–5 doses or at least 24 hours of continuous infusion (to reach a steady state), the serum vancomycin concentration is routinely determined (therapeutic drug monitoring). The target trough concentration was 10–15 mg/L or 15–20 mg/L.<sup>[11,12]</sup> Some studies have reported that the trough concentration of vancomycin should be maintained at 20 mg/L or higher to reach the target area under the



**Figure 2:** Serum concentrations of vancomycin. The concentrations of vancomycin before the second dose were  $10.3 \pm 6.1$  mg/L and  $5.7 \pm 4.4$  mg/L for the loading and control groups, respectively. The concentration of vancomycin before the second dose in the loading group was significantly higher than that in the control group ( $P=0.002$ ). The concentrations of vancomycin before the fifth dose were  $12.4 \pm 7.3$  mg/L and  $10.3 \pm 6.3$  mg/L for the loading and control groups, respectively; there was no intergroup difference ( $P=0.251$ ). \* Compared with control group at the same time,  $P < 0.05$ . † Compared with the serum concentration before the second dose within the same group,  $P < 0.05$ .

concentration-time curve (AUC)/MIC ratio of 400 or higher.<sup>[13]</sup> The problem is that a higher dose of vancomycin cannot be used because of its toxicity. The most recent guidelines of the Infectious Diseases Society of America

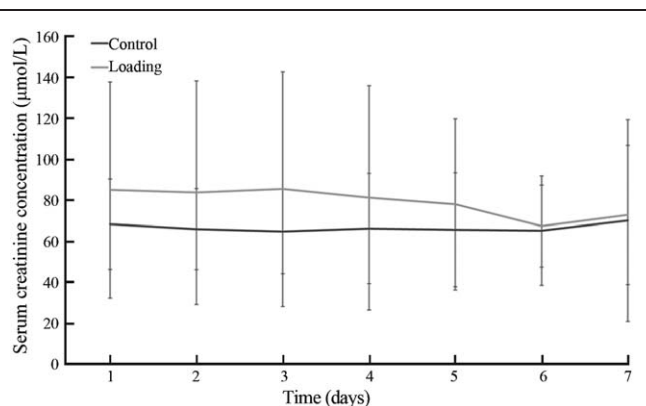
suggest a higher trough concentration of 15–20 mg/L, which is related to the expected reduced susceptibility of the microorganisms to vancomycin (MIC > 1 mg/L).<sup>[14]</sup> Elevated vancomycin concentrations are correlated with the risk of nephrotoxicity, especially after prolonged therapy (>7–14 days). A meta-analysis showed an odds ratio of 2.7 for nephrotoxicity in patients treated with vancomycin doses leading to trough concentrations of >15 mg/L relative to those treated with doses leading to trough concentrations of  $\leq 15$  mg/L.<sup>[15]</sup> Therefore, new guidelines aimed at higher vancomycin serum concentrations should be carefully considered. In pediatric patients, a trough concentration of vancomycin of 8–15 mg/dL is considered therapeutic.<sup>[16]</sup> In the present study, the trough concentration was 10–20 mg/L. New Chinese guidelines have suggested that steady-state concentrations should be maintained at 10–20 mg/L in adult patients with serious MRSA infections.<sup>[17]</sup> The serum Cr concentration was measured daily, and we found that the first loading dose did not cause kidney injury.

We had to test the serum concentration of vancomycin before the fifth dose for the traditional regimen of vancomycin infusion, meaning that we had to wait to obtain the serum vancomycin concentrations for >2 days. This is a long waiting period, and the patient may still have a fever. At this point, most doctors choose to switch antibiotics.<sup>[4]</sup> The target concentration of vancomycin was reached earlier with the loading dose. Some studies have focused on the application of continuous infusion of

**Table 4: Renal function after vancomycin used in the two groups.**

Time	Variables	Loading group	Control group	t	P value
Day 2	Cr ( $\mu\text{mol/L}$ )	$83.9 \pm 54.5$	$66.1 \pm 19.7$	1.510	0.138
	BUN (mmol/L)	$9.9 \pm 4.8$	$8.9 \pm 5.5$	0.735	0.466
	Cystatin C (mg/L)	1.1 (0.8–1.7)	1.0 (0.8–1.3)	1.437	0.163
	CCr (mL/min)	$92.0 \pm 39.4$	$109.3 \pm 41.2$	-1.523	0.134
Day 3	Cr ( $\mu\text{mol/L}$ )	$85.6 \pm 57.2$	$65.0 \pm 20.6$	1.660	0.103
	BUN (mmol/L)	8.6 (4.8–14.2)	7.0 (4.9–9.7)	1.674	0.105
	Cystatin C (mg/L)	1.1 (0.9–2.0)	1.0 (0.9–1.1)	2.366	0.026
	CCr (mL/min)	$88.8 \pm 37.1$	$109.5 \pm 32.8$	-2.082	0.043
Day 4	Cr ( $\mu\text{mol/L}$ )	$81.4 \pm 54.7$	$66.4 \pm 26.8$	1.158	0.253
	BUN (mmol/L)	$9.8 \pm 4.4$	$8.4 \pm 6.5$	0.829	0.412
	Cystatin C (mg/L)	$1.3 \pm 0.5$	$1.1 \pm 0.5$	1.332	0.192
	CCr (mL/min)	$88.7 \pm 35.7$	$114.5 \pm 38.7$	-2.298	0.027
Day 5	Cr ( $\mu\text{mol/L}$ )	$78.2 \pm 41.7$	$65.8 \pm 27.7$	1.122	0.268
	BUN (mmol/L)	$9.0 \pm 4.2$	$9.0 \pm 7.5$	-0.021	0.983
	Cystatin C (mg/L)	$1.3 \pm 0.5$	$1.1 \pm 0.5$	1.369	0.182
	CCr (mL/min)	$93.7 \pm 38.7$	$117.4 \pm 45.0$	-1.877	0.067
Day 6	Cr ( $\mu\text{mol/L}$ )	$67.6 \pm 19.9$	$65.4 \pm 26.6$	0.274	0.785
	BUN (mmol/L)	$9.4 \pm 3.6$	$8.6 \pm 7.4$	0.376	0.709
	Cystatin C (mg/L)	$1.2 \pm 0.3$	$1.1 \pm 0.4$	1.079	0.291
	CCr (mL/min)	$96.7 \pm 38.0$	$112.3 \pm 43.6$	-1.104	0.277
Day 7	Cr ( $\mu\text{mol/L}$ )	$73.0 \pm 33.9$	$70.3 \pm 49.2$	0.211	0.834
	BUN (mmol/L)	$24.1 \pm 70.4$	$14.8 \pm 28.5$	0.576	0.568
	Cystatin C (mg/L)	$1.3 \pm 0.5$	$1.2 \pm 0.8$	0.584	0.564
	CCr (mL/min)	$100.2 \pm 39.6$	$109.6 \pm 37.8$	-0.800	0.428

The data are expressed as mean  $\pm$  standard deviation or median (interquartile range). BUN: Blood urea nitrogen; Cr: Creatinine; CCr: Creatinine clearance.



**Figure 3:** Serum creatinine concentrations in 1 week. There were no significant changes in serum creatinine levels in 7 days in both groups. There were also no significant differences in serum creatinine concentrations between the two groups.

vancomycin to reach target trough serum concentrations.<sup>[18-21]</sup> Byl *et al*<sup>[19]</sup> found that the continuous infusion of vancomycin resulted in sustained drug concentrations in the blood. Akers *et al*<sup>[20]</sup> reported similar results. However, therapeutic vancomycin concentrations were achieved infrequently in this study, with the target drug concentration achieved in only 22.6%–30.7% of the no-continuous veno-venous hemofiltration patients. Wysocki *et al*<sup>[21]</sup> found that with continuous infusion of vancomycin, the target concentration could be reached earlier with low variability. However, they found no differences in the clinical outcomes and treatment failure rates of the two groups. At the same time, there was a moderate increase in the Cr concentrations of both groups. In 2013, Eldemiry *et al*<sup>[18]</sup> reported a contrasting result. They found a significant decline in the serum Cr concentrations after vancomycin treatment. It is important to achieve an effective drug concentration as quickly as possible. A loading dose can help address the problem without renal injury before continuous infusion.

Vancomycin is mainly excreted from the kidney; thus, its dose should be adjusted based on renal function. In our ICU, the dosage of vancomycin was adjusted according to the individualization of renal function. The first loading dose was approximately 1.5 times that of the adjusted single dose. In this study, we found that there was no difference between the Cr concentrations of the loading and control groups, suggesting that the first loading dose of vancomycin was safe for ICU patients.

In our study, we observed a lower mortality rate of the loading dose group. This may be related to the fact that vancomycin reached the target concentration earlier. The loading dose may be beneficial for improving the prognosis of critically ill patients. However, our study sample was small, and this finding needs to be confirmed by larger prospective studies.

Bacterial drug resistance is becoming worse. The MIC of vancomycin for MRSA has been increasing gradually.<sup>[22]</sup> Some experts are concerned that vancomycin may no longer be effective. The sample of the present study was

small, which indicates inadequacy in data for the analyses of the susceptibility and resistance of pathogenic bacteria to vancomycin. However, it was observed that the number of pathogenic bacteria with an MIC of 2 increased.

MIC creep was observed not only with vancomycin but also with linezolid and daptomycin.<sup>[23]</sup> New antibiotics are currently being developed. The combined effects of antibiotics have been studied, and certain combinations have been shown to enhance therapeutic effects.<sup>[24]</sup> Other important aspects, including hand hygiene, antibiotic management, and single isolation, should be considered to reduce the proliferation of resistant bacteria.

Due to the critical conditions of ICU patients, clinicians often have a small window to adjust antibiotics. Some patients may die before the doses of antibiotics are increased. Therefore, ICU physicians tend to administer strong antibiotics, such as carbapenems, vancomycin, and linezolid; both vancomycin and linezolid are first-line antibiotics for MRSA. It has been reported that systemic treatment with linezolid has more benefits than vancomycin in limiting the MRSA burden in the endotracheal tube cuff. However, the effects of these two antibiotics on patient outcomes remain unknown.<sup>[25]</sup>

The present study is a rare study that reports the effects of the loading dose of vancomycin on the time to reach the trough serum concentration in Chinese patients. The serum Cr concentrations were measured daily, and there were no acute kidney injuries. Our study showed that the first loading dose was safe, and the trough concentration of vancomycin was reached earlier after the loading dose.

There are some limitations to our study. First, it is a retrospective study with several confounding factors, such as the use of other antibiotics that may cause nephrotoxicity. Second, the small sample of our study may have led to selection bias. Third, the serum Cr concentrations were assessed for 1 week. Information on the long-term nephrotoxicity of vancomycin was not obtained. Fourth, our study did not include patients who had received renal replacement therapies; therefore, the effect of the loading dose on these patients was not established. Fifth, we focused on the concentration of vancomycin in this study, but not on the outcome of patients. Although we found the difference on mortality, several factors can affect mortality. Further studies on these patients are warranted.

In conclusion, the loading dose of vancomycin was effective for achieving the target trough concentration earlier and had no deleterious acute effects on renal function. The loading dose may improve patients' outcomes. The results should be corroborated in a future study involving a larger sample.

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