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ORIGINAL RESEARCH

Initial Meropenem Plasma Concentration and Its Correlation with Sepsis Mortality: A Real-World Retrospective Study

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Purpose: Meropenem is a first-line antibiotic for sepsis in settings with high prevalence of multidrug-resistant organisms due to its broad-spectrum activity. However, the relationship between meropenem plasma concentration and prognosis of sepsis is unclear. This study aims to investigate whether optimizing meropenem plasma levels improves 28-day outcomes in sepsis patients, while also exploring the potential impact of continuous versus intermittent infusion methods.

Patients and Methods: This real-world retrospective study included 202 sepsis patients treated with meropenem at Hunan University of Medicine General Hospital from January 2022 to December 2023. Patients received either prolonged intravenous infusion or intermittent intravenous infusion of meropenem, as determined by the attending physician. Prolonged infusion involved a 3-hour duration with an infusion pump, while intermittent infusion lasted 30 minutes to 1 hour. Patients were grouped by the quartiles of meropenem plasma concentration (Q1, Q2, Q3, and Q4) to facilitate analysis of dose-response relationships and control for variability in plasma concentration distributions. Mortality rates at 7, 14, and 28 days, as well as the detection rates of resistant bacteria and ICU length of stay, were compared among groups.

Results: Prolonged intravenous infusion yielded higher meropenem plasma concentrations compared to intermittent infusion (P=0.024), aligning with expected therapeutic targets for optimal antimicrobial efficacy. However, no significant differences were observed in mortality rates at 7, 14, and 28 days between infusion methods or across plasma concentration quartiles. Multivariable logistic regression confirmed these findings after adjusting for confounding factors. Additionally, no significant differences were found in resistant bacteria detection rates or ICU length of stay across quartiles.

Conclusion: While prolonged infusion increases plasma meropenem concentration, it does not impact 28-day mortality risk, ICU stay, or resistant bacteria detection in sepsis patients. These findings suggest that prolonged infusion may not offer significant clinical advantages over intermittent infusion and highlight the importance of balancing antibiotic use with stewardship principles (Graphical abstract).

Keywords: meropenem, concentration, sepsis, mortality

Introduction

Sepsis is a life-threatening acute organ dysfunction syndrome caused by bacterial, fungal, parasitic, or viral infections, representing a significant global health burden.[1] Globally, it is estimated that 49 million cases of sepsis and 11 million related deaths occur annually, with over one-third of in-hospital deaths attributed to sepsis.[2] Statistics from 2017 indicate that treatment costs exceeded 38 million in USD, making sepsis the most common cause of in-hospital mortality and the leading driver of hospitalization costs.[3]

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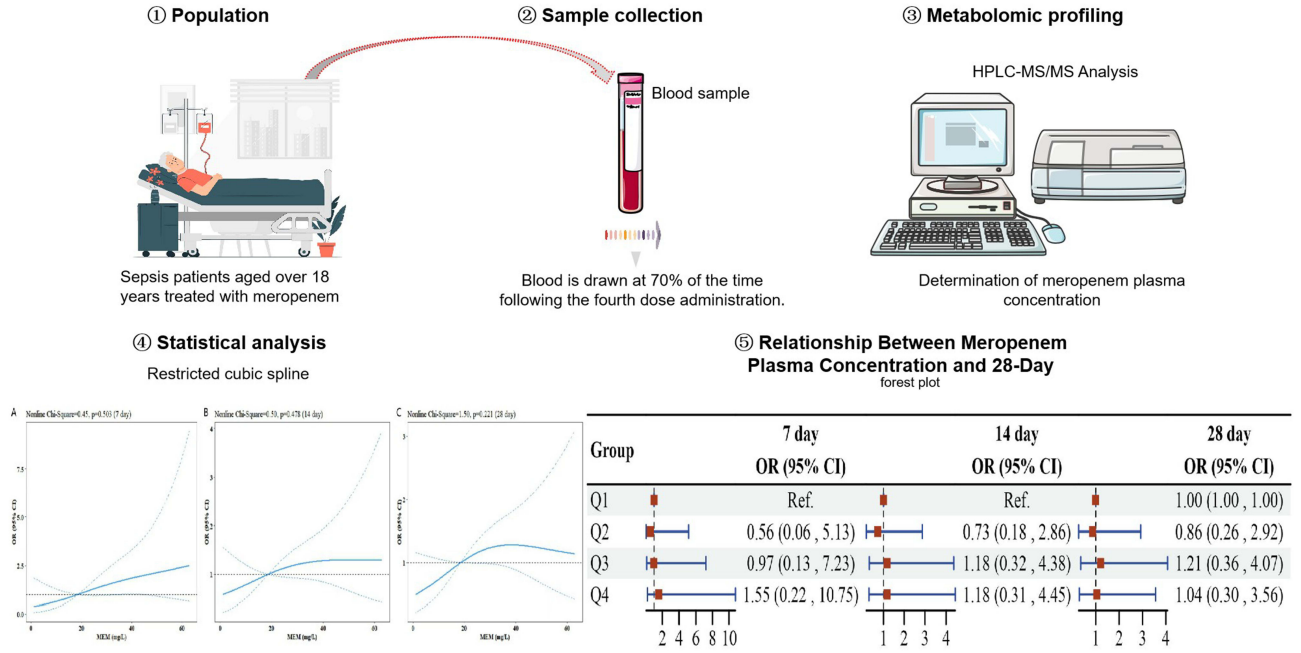
Graphical Abstract



Infection control is a crucial component of sepsis management.[1] Meropenem, a carbapenem antibiotic, is known for its potent antibacterial activity and broad-spectrum efficacy, frequently employed in anti-infective regimens for sepsis patients. Like other β-lactam antibiotics, meropenem exhibits time-dependent antibacterial activity.[4] The pharmacokinetic/pharmacodynamic (PK/PD) parameter most predictive of clinical efficacy is maintaining plasma drug concentrations above the minimum inhibitory concentration (MIC) of the pathogen throughout the dosing interval.[5]

Reports suggest that the minimum inhibitory concentration (*f*T>MIC) for carbapenem antibiotics should be at least 40% of the dosing interval, while critically ill patients may require a higher target of *f*T>MIC >70% to ensure bactericidal efficacy.[6] Some studies even indicate that achieving T>100% of the dosing interval could result in significantly improved clinical outcomes and better microbial clearance.[6] However, factors such as hypoalbuminemia, increased capillary permeability, large fluid resuscitation volumes, and increased renal clearance in sepsis may lead to reduced concentrations of hydrophilic antibiotics.[7]

In previous studies, the relationship between meropenem plasma concentration and sepsis prognosis has remained unclear. Therefore, we analyzed the correlation between initial plasma concentration of meropenem upon admission and sepsis prognosis. The results are reported below.

Materials and Methods

Study Population

Patients diagnosed with sepsis and treated with meropenem at the General Hospital of Hunan Medical University from January 2022 to December 2023 were included. Inclusion criteria:[8,9] (1) Diagnosed with sepsis per Sepsis-3 criteria (infection combined with a SOFA score ≥2); (2) Treated with meropenem for at least 3 days; (3) Plasma meropenem concentration monitored. Exclusion criteria: (1) Pregnant women; (2) Patients with underlying diseases causing immunosuppression (eg, cancer, hematologic disorders); (3) Patients who died within 48 hours of admission. The study was approved by the Ethics Committee of the General Hospital of Hunan Medical University (KY-2022071908), and written informed consent was waived for this retrospective study. As this was a retrospective analysis of anonymized medical

records posing minimal risk to participants, and obtaining individual written informed consent was deemed impractical due to the large cohort size and time frame, the Ethics Committee granted a waiver of informed consent. All patient data were handled with strict confidentiality, accessed only by authorized research personnel for study purposes, and stored securely in compliance with institutional data protection policies. This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

Meropenem Administration and Plasma Monitoring

The treatment regimen for meropenem was determined by the attending physician and included prolonged intravenous infusion or intermittent intravenous infusion.[10] Prolonged infusion was defined as a 3-hour infusion using a 50 mL solvent with an infusion pump, while intermittent infusion involved a duration of 30 minutes to 1 hour. Plasma concentrations were quantitatively monitored after 70% of the fourth dose using high-performance liquid chromatography combined with mass spectrometry. The threshold was defined as 70%*f*T>MIC (free meropenem concentration exceeding the MIC value during 70% of the dosing interval). Blood sampling time points were calculated accordingly (eg, 5.6 hours for an 8-hour dosing interval) following guidelines from literature references.[6]

Data Collection

Patient information was collected using a case report form designed per the study protocol, including: (1) General clinical information such as age, sex, and comorbidities; (2) Clinical and laboratory data within 24 hours of admission, including white blood cell count (WBC), hemoglobin, platelet count (PLT), C-reactive protein (CRP), prothrombin time (PT), activated partial thromboplastin time (APTT), serum pH, lactate, serum procalcitonin (PCT), alanine transaminase (ALT), total bilirubin (TB), blood urea nitrogen, serum creatinine (SCr), blood glucose, SOFA score, fluid intake/output, and diuretic use.

Study Outcomes

Primary outcomes were mortality within 7, 14, and 28 days of admission. Secondary outcomes included the detection rates of resistant bacteria and ICU length of stay.

Statistical Analysis

Normally distributed prolonged data were expressed as mean±standard deviation, while skewed data were expressed as median (IQR). Differences in prolonged variables between groups were analyzed using *t*-tests or Mann–Whitney *U*-tests. Categorical variables were expressed as frequencies and proportions, with differences analyzed using chi-square ($\chi 2$) tests. Patients were grouped into quartiles of meropenem plasma concentration: Q1 (1.48–5.42 μmol/mL), Q2 (11.97–16.02 μmol/mL), Q3 (22.10–29.95 μmol/mL), and Q4 (41.60–57.70 μmol/mL). Logistic regression was used to analyze the relationship between plasma concentration and mortality risk at 7, 14, and 28 days, with Q1 as the reference group. Adjustments were made for potential confounders (age, SOFA score, creatinine clearance, and furosemide treatment). Results were expressed as odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was defined as a two-sided P-value <0.05. All analyses were performed using R 3.4.1 software.

Results

Patient Baseline Characteristics

The study included 202 sepsis patients with a median age of 66 years (IQR 53, 75 years), of whom 117 (56.52%) were male. The median plasma concentration of meropenem was 18.6 μmol/L (IQR 8.2, 35.1 μmol/L). Figure 1 shows the distribution of 7-day, 14-day, and 28-day mortality rates, which were 7.42% (15/202), 16.33% (33/202), and 23.26% (47/202), respectively.

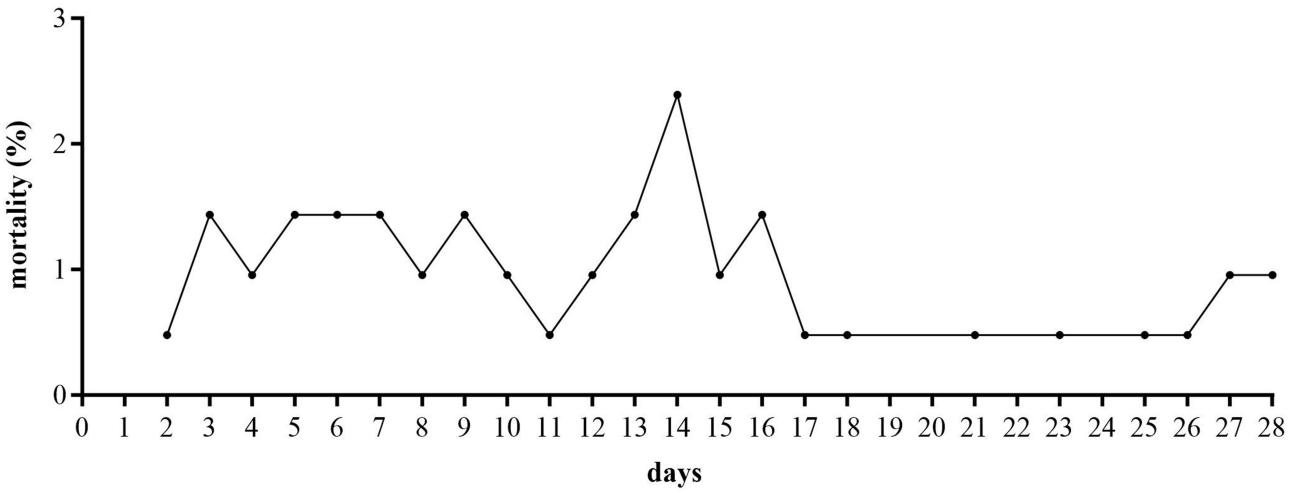


Figure 1 Distribution map of mortality within 28 days.

Plasma Concentration Differences by Administration Method

Prolonged intravenous infusion resulted in significantly higher plasma concentrations of meropenem [20.40 (10.30, 36.40) μmol/L] compared to intermittent infusion [11.40 (1.80, 28.50) μmol/L] (P=0.024). However, no statistically significant differences in dosing or 28-day mortality rates were observed between the two groups (see Table 1). Baseline characteristics of patients grouped by prolonged vs intermittent administration of meropenem (see Supplementary Table S1).

Table 1 Comparison of Continuous vs Intermittent Administration of Meropenem

Variable	Continuous Administration (n=177)	Intermittent Administration (n=25)	p-value
Blood concentration M (IQR)	20.40 (10.30, 36.40)	11.40 (1.80, 28.50)	0.024
Duration of administration (days)	9.00 (6.00, 13.00)	7.00 (5.00, 9.00)	0.037
Administration interval, n (%)			0.036
qd	0 (0)	1 (4)	
q12h	14 (7.91)	0 (0)	
q8h	113 (63.84)	19 (76)	
q6h	48 (27.12)	4 (16)	
Other	2 (1.13)	1 (4)	
Adjusted interval, n (%)			0.646
qd	2 (1.13)	0 (0)	
q12h	14 (7.91)	1 (4)	
q8h	102 (57.63)	18 (72)	
q6h	54 (30.51)	5 (20)	
Other	5 (2.82)	1 (4)	
7-day survival outcome n (%)			>0.999
Survived	164 (92.66)	23 (92)	
Deceased	13 (7.34)	2 (8)	
14-day survival outcome n (%)			0.773
Survived	147 (83.05)	22 (88)	
Deceased	30 (16.95)	3 (12)	
28-day survival outcome n (%)			0.154
Survived	133 (75.14)	22 (88)	
Deceased	44 (24.86)	3 (12)	

Abbreviations: qd, once daily; q12h, every 12 hours; q8h, every 8 hours; q6h, every 6 hours; M (IQR), Median (Interquartile Range).

Correlation Between Plasma Concentration and Sepsis Prognosis

Grouping patients by meropenem plasma concentration quartiles revealed significant differences in age, hypertension, furosemide treatment, serum creatinine, and SOFA score among groups (P<0.05). Higher plasma concentration groups had higher age, hypertension prevalence, furosemide treatment rates, and SOFA scores but lower serum creatinine levels than lower concentration groups (see Table 2).

Table 3 shows the relationship between meropenem plasma concentration and 28-day prognosis. Univariate logistic regression analysis indicated no significant differences in mortality risk at 7, 14, or 28 days among groups. Multivariate logistic regression adjusting for potential confounders (age, hypertension, SOFA score, creatinine clearance, furosemide treatment) confirmed no significant differences in mortality risk. Restricted cubic spline analysis further showed that the 95% confidence interval of OR values across the entire plasma concentration range included 1 (see Figure 2), indicating no correlation between plasma concentration and sepsis mortality risk.

Relationship Between Plasma Concentration, Resistant Bacteria, and ICU Length of Stay

No statistically significant differences in overall Gram-negative bacterial including Klebsiella pneumoniae, Escherichia coli pseudomonas, aeruginosa Acinetobacter and baumannii detection rates were observed across quartiles (P=0.260). Additionally, no significant differences in meropenem plasma concentrations were observed between patients with resistant and sensitive bacteria (see Supplementary Figure S1). The analysis of ICU length of stay showed that patients in the higher plasma concentration groups had longer ICU stays than those in the lower concentration groups, but the differences were not statistically significant (see Table 4).

Discussion

In this real-world study, prolonged intravenous infusion of meropenem significantly increased plasma concentrations compared to intermittent infusion, yet this pharmacokinetic advantage did not translate into reduced mortality at 7, 14, or 28 days, shorter ICU stays, or lower rates of resistant bacteria detection. These findings align with recent large-scale randomized trials and meta-analyses, which collectively challenge the assumption that optimizing β-lactam antibiotic exposure through prolonged infusion universally improves clinical outcomes in sepsis. For instance, the MERCY trial,[11] a double-blind RCT involving 607 critically ill patients with sepsis, found no difference in 28-day mortality (30% vs 33%, P=0.50) or resistance emergence between continuous and intermittent meropenem administration. Similarly, the BLING III trial[12]—the largest RCT to date, enrolling 7200 patients across 104 ICUs—reported no statistically significant reduction in 90-day mortality with continuous β-lactam infusion (24.9% vs 26.8%, P=0.08), despite improved clinical cure rates. These results are consistent with our observations and underscore the complex interplay between pharmacokinetic targets and clinical efficacy in heterogeneous sepsis populations.

A 2023 JAMA editorial[13] contextualizes these findings, emphasizing that while prolonged β-lactam infusion has a compelling pharmacological rationale (eg, maintaining concentrations above MIC for time-dependent killing), its clinical benefits remain uncertain. The editorial highlights that prior meta-analyses suggested mortality reductions (RR 0.70–0.92)[14,15] but notes that recent high-quality trials like MERCY and BLING III have tempered enthusiasm by demonstrating no significant survival benefit. Some small RCTs and observational studies have noted benefits, other studies have found no differences, potentially due to variations in infection severity, patient comorbidities, and antibiotic resistance profiles.[16,17] This discrepancy may reflect differences in study populations, such as the inclusion of patients with advanced organ failure or delayed antibiotic initiation. Few studies have explored the relationship between meropenem plasma concentrations and sepsis prognosis.[16] In our cohort, higher plasma concentrations failed to mitigate mortality in resistant infections (eg, pan-drug-resistant Klebsiella or Acinetobacter), aligning with the perspective that host-pathogen interactions and timely source control may outweigh pharmacokinetic factors. Notably, even when meropenem concentrations exceeded MIC values by 2–3 times in resistant infections, mortality remained high due to intrinsic pathogen virulence and treatment complexities.

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Table 2 Baseline Characteristics of Patients Grouped by Meropenem Blood

Variable	Quartile 1 (n=50)	Quartile 2 (n=50)	Quartile 3 (n=51)	Quartile 4 (n=51)	p-value
Meropenem blood concentration, M (IQR)	3.07 (1.50, 5.38)	13.75 (11.53, 15.17)	25.10 (21.85, 29.65)	48.50 (42.30, 58.00)	<0.001
Demographics					
Age (years), M (IQR)	56.00 (38.25, 70.75)	65.50 (56.25, 74.75)	69.00 (62.00, 75.50)	69.00 (54.50, 76.50)	0.002
Gender					0.362
Male, n (%)	27 (54)	32 (64)	30 (58.82)	24 (47.06)	
Female, n (%)	23 (46)	18 (36)	21 (41.18)	27 (52.94)	
Weight (kg), M (IQR)	60 (53, 60)	60 (55, 60)	60 (55, 60)	60 (55, 60)	0.219
History of alcohol use, n (%)	4 (8)	5 (10)	1 (1.96)	4 (7.84)	0.379
Smoking history, n (%)	3 (6)	7 (14)	3 (5.88)	3 (5.88)	0.389
Drug use history, n (%)	1 (2)	0 (0)	0 (0)	0 (0)	0.496
Comorbidities, n (%)					
History of severe infections	47 (94)	46 (92)	50 (98.04)	48 (94.12)	0.58
History of malignancy	48 (96)	47 (94)	50 (98.04)	50 (98.04)	0.585
Hypertension	39 (78)	31 (62)	33 (64.71)	26 (50.98)	0.044
Diabetes mellitus	37 (74)	39 (78)	38 (74.51)	39 (76.47)	0.964
Coronary artery disease	46 (92)	41 (82)	42 (82.35)	44 (86.27)	0.449
Chronic kidney disease	45 (90)	46 (92)	41 (80.39)	42 (82.35)	0.252
Liver cirrhosis	48 (96)	49 (98)	50 (98.04)	50 (98.04)	0.887
History of COPD	48 (96)	49 (98)	51 (100)	49 (96.08)	0.581
Site of infection, n (%)					0.563
Abdominal cavity	2 (4)	3 (6)	4 (7.84)	4 (8)	
Lungs, n (%)	31 (62)	27 (54)	30 (58.82)	27 (54)	
CNS	0 (0)	1 (2)	1 (1.96)	2 (4)	
Urinary tract	10 (20)	10 (20)	11 (21.57)	14 (28)	
Skin/soft tissue	3 (6)	0 (0)	3 (5.88)	0 (0)	
Biliary tract	2 (4)	3 (6)	0 (0)	1 (2)	
Bloodstream	2 (4)	6 (12)	2 (3.92)	2 (4)	
Clinical Treatment					
Duration of meropenem treatment (days), M (IQR)	7.50 (5.00, 12.00)	8.00 (6.00, 10.75)	9.00 (6.00, 15.00)	9.00 (5.00, 14.00)	0.266
Initial fluid resuscitation (mL), M (IQR)	1963.50 (948.25, 2761.66)	2512.68 (1627.25, 3020.76)	2600.58 (1676.00, 3059.66)	2438.75 (1710.20, 3582.40)	0.094
Output (mL), M (IQR)	2258.40 (1679.12, 2798.12)	2505.84 (1796.57, 3048.55)	2470.00 (1779.57, 3642.08)	2269.17 (1708.12, 3743.72)	0.635
Furosemide treatment, n (%)	22 (44)	37 (74)	37 (72.55)	35 (68.63)	0.005
Microbiological culture					0.260
Gram-negative bacteria, n (%)	4 (8)	5 (10)	4 (7.84)	12 (23.53)	
Klebsiella pneumoniae	2	0	1	2	
Escherichia coli	1	3	1	3	
Pseudomonas aeruginosa	0	0	1	1	
Acinetobacter baumannii	1	2	1	4	
Laboratory indicators, M (IQR)					
WBC (x10^9/L)	10.70 (6.38, 16.08)	10.55 (7.23, 16.45)	12.10 (6.90, 18.30)	13.00 (8.40, 18.60)	0.72
PCT (μg/L)	19.43 (1.66, 82.22)	21.92 (4.29, 60.76)	29.36 (2.84, 78.58)	19.01 (7.14, 79.18)	0.884

LAC (mmol/L)	2.30 (1.49, 3.96)	2.60 (1.74, 3.94)	2.44 (1.56, 3.42)	2.27 (1.53, 3.41)	0.874
IL-6 (pg/mL)	137.69 (19.85, 528.22)	252.24 (48.20, 1186.00)	87.59 (25.05, 447.15)	123.50 (47.98, 1880.50)	0.486
CRP (mg/L)	115.67 (50.21, 201.00)	137.10 (83.23, 196.40)	107.80 (52.95, 186.25)	151.40 (76.89, 195.00)	0.348
Albumin (g/L)	31.20 (27.88, 34.53)	30.55 (26.05, 34.75)	29.00 (26.10, 32.90)	29.80 (26.85, 32.10)	0.235
Creatinine (μmol/L)	75.10 (40.41, 105.59)	47.08 (23.63, 74.68)	29.72 (14.70, 54.42)	20.55 (11.93, 50.67)	<0.001
SOFA score	5.00 (3.25, 7.00)	6.00 (3.00, 8.00)	6.00 (4.00, 8.00)	8.00 (4.00, 10.00)	0.015

Abbreviations: M (MQR), Median (Interquartile Range); COPD, Chronic Obstructive Pulmonary Disease; CNS, Central Nervous System; WBC, White Blood Cell; PCT procalcitonin; LAC, Lactic Acid; IL-6, Interleukin-6; CRP, C-reactive protein; SOFA, Sequential Organ Failure Assessment.

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Table 3 Relationship Between Meropenem Plasma Concentration and 28-Day

Group	Case	7 Day					14 Day					28 Day				
		Death (%)	Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	p	Death (%)	Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	p	Death (%)	Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
Q1	50	2 (4.00)	Ref		Ref		6 (12.00)	Ref		Ref		8 (16.00)	Ref		Ref	
Q2	50	2 (4.00)	1.00 (0.14,7.39)	>0.999	0.56 (0.06,5.13)	0.609	6 (12.00)	1.00 (0.30,3.344)	>0.999	0.73 (0.18,2.86)	0.648	10 (20.00)	1.31 (0.47,3.66)	0.603	0.86 (0.26,2.92)	0.841
Q3	51	4 (7.84)	2.04 (0.36,11.69)	0.422	0.97 (0.13,7.23)	0.976	10 (19.61)	1.79 (0.60,5.36)	0.299	1.18 (0.32,4.38)	0.804	14 (27.45)	1.98 (0.75,5.26)	0.167	1.21 (0.36,4.07)	0.76
Q4	51	7 (13.73)	3.82 (0.75,19.37)	0.106	1.55 (0.22,10.75)	0.657	11 (21.57)	2.02 (0.68,5.96)	0.204	1.18 (0.31,4.45)	0.809	15 (29.41)	2.19 (0.83,5.75)	0.112	1.04 (0.30,3.56)	0.951

Notes: Adjusted variables: age, hypertension, SOFA, creatinine clearance, furosemide treatment.

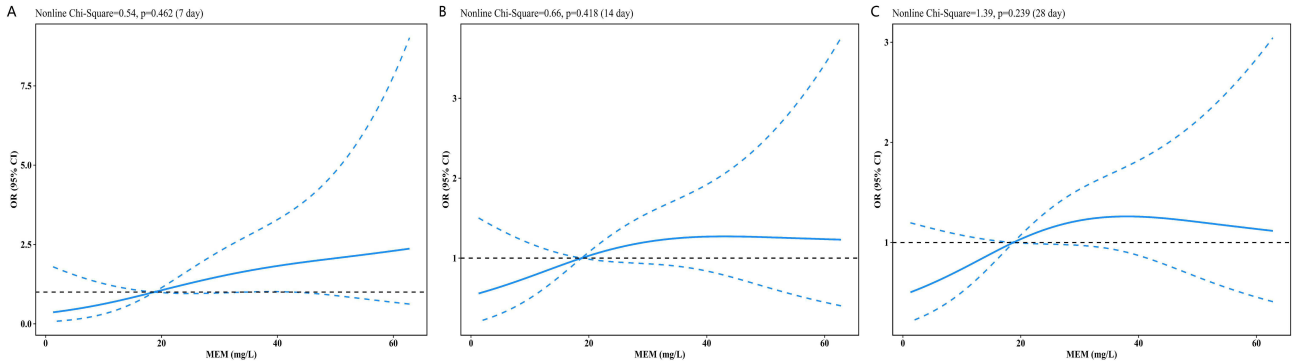

Figure 2 Restricted cubic spline diagram of meropenem plasma concentration and sepsis prognosis. (**A**) the risk of death within 7 days after admission; (**B**) the risk of death within 14 days after admission; (**C**) Risk of death within 28 days of admission (Restricted cubic spline analysis further showed that the 95% confidence interval of OR values across the entire plasma concentration range included 1, indicating no correlation between plasma concentration and sepsis mortality risk).

In this study, the initial blood samples were collected at 70% of the dosing interval after 4–5 doses of meropenem. Among 23 patients with bacterial cultures that included meropenem susceptibility results, 10 isolates were sensitive to meropenem. Among these, 8 isolates had a MIC cutoff of 0.25 μmol/L, and 2 isolates had a MIC cutoff ≤ 4 μmol/L. Regardless of the administration method, the initial plasma concentrations of meropenem exceeded the sensitivity cutoff values. Among the 13 isolates resistant to meropenem (MIC ≥ 16 μmol/L), 7 patients died. The causes of death included gastrointestinal bleeding in one patient and withdrawal of treatment in another. The remaining five deaths were due to uncontrolled infections, with two patients having pan-drug-resistant Klebsiella pneumoniae in blood cultures, two patients with pan-drug-resistant Acinetobacter baumannii in sputum cultures, and one patient with mixed infections involving bacteria, viruses, and fungi. In these fatal cases, the meropenem plasma concentrations for each bacterial isolate exceeded 2–3 times the MIC values, indicating that the high mortality rate was primarily attributed to the inherent high fatality risk associated with resistant Gram-negative bacteria. Furthermore, the use of meropenem-based combination therapies for carbapenem-resistant strains carries a high risk of failure, even when meropenem concentrations remain elevated. The results of our study indicate that achieving the therapeutic target of 70% $fT > MIC$ with meropenem does not impact prognosis, irrespective of the administration method. This finding explains why both prolonged and intermittent administration of meropenem showed no association with 28-day mortality in sepsis patients. There were 10 strains with meropenem MIC ≤4 μmol/L, and all cases survived. Therefore, achieving higher meropenem plasma concentrations facilitates microbial eradication targets.

The lack of correlation between plasma concentration and clinical outcomes may also reflect broader sepsis management principles. Early antibiotic initiation—emphasized in the Surviving Sepsis Campaign's 1-hour bundle—likely plays a more critical role in survival than pharmacokinetic optimization.[1] In our study, delayed hospital presentation and delayed broad-spectrum antibiotic adjustments contributed to adverse outcomes despite adequate meropenem levels. This underscores the importance of integrating rapid diagnostics, timely antimicrobial stewardship, and comprehensive supportive care into sepsis protocols.

Importantly, logistical barriers to prolonged infusion (eg, resource constraints) are minimal in ICUs, and the absence of harm in trials supports its continued use in select cases. However, future research should focus on identifying patient

Table 4 Relationship Between Meropenem Plasma Concentration, Resistant Bacteria Detection Rate, and ICU Length of Stay in Sepsis Patients

Variable	Quartile 1 (n=50)	Quartile 2 (n=50)	Quartile 3 (n=51)	Quartile 4 (n=51)	p-value
Resistant Bacteria, n (%)					
Absent	43 (86.00)	40 (80.00)	43 (84.31)	45 (88.24)	
Present	7 (14.00)	10 (20.00)	8 (15.69)	6 (11.76)	0.703
ICU Length of Stay (days)	4.5 (0, 12)	7 (3, 11)	6 (3, 11.5)	8 (3.5, 14)	0.125

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subgroups that might benefit from pharmacokinetic optimization, such as those with confirmed bloodstream infections or pathogens with high MICs. Additionally, integrating biomarkers or advanced PK/PD models could refine dosing strategies for individualized therapy.

In conclusion, while prolonged infusion achieves higher plasma meropenem levels, its clinical utility in sepsis remains unproven. Guidelines may continue to endorse prolonged infusion based on safety and theoretical benefits, but clinicians should prioritize early antibiotic initiation, pathogen identification, and stewardship to address sepsis mortality and resistance. As emphasized in recent literature, the path forward lies in personalized approaches that balance pharmacokinetic targets with the multifactorial nature of sepsis management.

Limitations

First, this study was retrospective in nature, and clinical physicians might have adjusted meropenem doses based on initial plasma concentration results or changes in renal function during the study period. Future prospective studies could address this limitation by standardizing dosing protocols and monitoring plasma concentrations longitudinally to better understand their impact on clinical outcomes. The impact of these adjustments on subsequent plasma concentration changes was not analyzed. Additionally, due to prior educational efforts by clinical pharmacists, the number of cases using intermittent intravenous infusion was much smaller than those using prolonged infusion, introducing potential evaluation bias. Second, the microbiological target used in this study was 70% fT > MIC, and we did not explore the relationship between plasma concentrations and prognosis at the 100% fT > MIC target. This might result in incomplete conclusions. Third, the simultaneous use of other antibiotics may have enhanced the anti-infective effects of low-dose meropenem. Fourth, we lacked detailed data on microbiological cures, which may not always reflect clinical recovery.

Conclusion

Prolonged intravenous infusion can increase the initial plasma concentration of meropenem in septic patients, but the plasma concentration is not significantly associated with 7-day, 14-day, or 28-day mortality rates, ICU length of stay, or the proportion of resistant bacteria detected subsequently. Future studies should focus on identifying patient subgroups that might benefit from specific dosing strategies, exploring advanced pharmacokinetic-pharmacodynamic models, and conducting prospective trials to better understand the clinical utility of plasma concentration monitoring in sepsis management.

Abbreviations

PK/PD, pharmacokinetic/pharmacodynamic; MIC, minimum inhibitory concentration; M (MQR), Median (Interquartile Range); COPD, Chronic Obstructive Pulmonary Disease; CNS, Central Nervous System; WBC, white blood cell count; PLT, platelet count; CRP, C-reactive protein; PCT procalcitonin; LAC, Lactic Acid; IL-6, Interleukin-6; PT, prothrombin time; ALT, alanine transaminase; TB, total bilirubin; SCr, serum creatinine; SOFA, Sequential Organ Failure Assessment.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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