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Infection timeline guided by pharmacodynamics based on pharmacokinetics and inflammatory biomarkers during antibiotic therapy in burn patient – case report

Abstract

Introduction: Infection is the most common complication and cause of death in patients suffering burn injuries, once these patients are susceptible to infection and burn sepsis. It is well known that pharmacokinetics is altered by changes related to renal function in ICU extensive burn patients. In general antibiotic (ATB) de-escalation in Gram-negative infections is routinely used to prevent resistance during prolonged ICU stays for burn patients. Consequently, cultures and ATB serum monitoring ensures optimization of serum levels to achieve the therapeutic goal with eradication of susceptible strains.

Objective: Antibiotic therapy based on infection and resistance was guided by therapeutic serum levels and MIC data for treatment selection against Gram-positive and Gram-negative nosocomial bacteria. Pharmacodynamics based on pharmacokinetic changes (PK/PD) was applied. Pharmacokinetics data related to ATBs prescribed was investigated. In addition, to support ATB therapy, inflammatory biomarkers NLR and c-RP were monitored daily to predict and prevent mortality in ICU.

Methods: A case report involved a 31-year-old male (160 kg, 171 cm) with severe burns (25% TBSA), multiple injuries, and morbid obesity following an engine explosion at work. ICU admission to the Burn Center started with medical history and injury details documented. Immediate care involved resuscitation, debridement, and management of respiratory and renal issues. Septic shock diagnosis used early microbiological tests and inflammatory biomarkers monitoring. Blood and site-specific cultures were taken before starting antibiotics, which were adjusted dose based on results monitored weekly related to pharmacodynamics based on pharmacokinetic changes tied to renal function. Initially, the recommended ATB protocol recommended in hospital infections was prescribed as a combined therapy, vancomycin against Gram-positive bacteria and piperacillin/tazobactam against Gram-negative bacteria. Daily NLR and c-RP measured ICU mortality risk.

Results: On ICU-day 3, the patient's condition deteriorated, leading to broad-spectrum antibiotics after cultures were obtained. Vancomycin and piperacillin/tazobactam were started; cultures identified *Staphylococcus epidermidis* (vancomycin/susceptible) and *Proteus mirabilis* (meropenem/susceptible). Consequently piperacillin/tazobactam was stopped, and meropenem, vancomycin, plus sodium colistinemethate against resistant *Acinetobacter baumannii* were given for 30 days, dosed by renal function and monitored with TDM and MIC data. A second shock occurred on day 21 with *Klebsiella pneumoniae* (meropenem/susceptible), so vancomycin and meropenem continued. On day 41, *Pseudomonas aeruginosa* (resistant to meropenem/amikacin, ciprofloxacin/susceptible) was isolated, and ciprofloxacin was prescribed. Cultures became negative on day 51; the patient was discharged from ICU on day 55 and hospital on day 60.

Conclusion: Antibiotic therapy was based on infections and resistance. ATBs doses were adjusted by TDM and target attainment including MIC data guiding treatment selection. PK-changes ensured therapeutic drug levels based on PK/PD targets recommended for prescribed antibiotics. Superiority of the NLR over c-RP in decision-making was demonstrated, as an early biomarker of death in the ICU.

Keywords: ICU major burn sepsis, immunosuppression-prolonged stay, inflammatory biomarker NLR in decision making, antibiotic related to dose adjusted by TDM, PK/PD target attainment

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Abbreviations: AKI, acute kidney injury; ARC, augmented renal clearance; ARDS, acute respiratory distress syndrome; $AUC^{ss}\tau$, Area under the curve at the steady state serum levels (C^{ss}) at the time dose interval (tau: τ) BAL, bronchoalveolar lavage (BAL) fluid; BSI, blood stream infection; CLSI, clinical & laboratory standard Institute, database USA; c-RP, c-Reactive Protein; CRRT, continuous renal replacement therapy; [CLT], total body clearance; [$t_{(1/2)\beta}$], elimination half-life/biological half-life; [Vd^{ss}], volume of distribution at the steady state; GNB, gram-negative bacteria; GPB, gram-positive bacteria; ICU, intensive care unit; MIC, minimum inhibitory concentration;

MV, mechanical ventilation; NLR, neutrophils to lymphocytes ratio; PK, pharmacokinetics; PK/PD, pharmacodynamics based on pharmacokinetics; PRF, preserved renal function; PTA, probability of target attainment; SAPS3, simplified acute physiology score 3; SIRS, systemic inflammatory response syndrome; SOFA score, sequential organ failure assessment score, known as the sepsis-related organ failure TBSA, total burn surface area; TDM, therapeutic drug monitoring.

Introduction

Infection is the most frequent complication and the leading cause of death among burn patients. The physiological changes that occur after a burn make these individuals especially vulnerable to infections and the development of burn wound sepsis. Accurate diagnosis and effective management of these infections depend on a combination of approaches, including a thorough physical examination and analysis of the pathological characteristics of the burn wound. Prolonged intensive care unit (ICU) admission frequently leads to a state of immunosuppression.[1] Patients with major burns are particularly susceptible to this phenomenon, such as ongoing critical illness, repeated surgical interventions, and persistent infection risks contribute to a weakened immune response. Extended ICU stays are often necessary for the management of severe complications, including recurrent infections and multiple organ dysfunctions. This immunosuppressed state further increases vulnerability to opportunistic fungal and yeast pathogens, complicating recovery and prolonging hospitalization. Management of burn sepsis requires a multifaceted approach that includes the use of local wound dressings, prompt surgical excision of the burn wound, and the administration of systemic anti-infective complex therapy.[2–6] Infection is a common complication and top cause of death in burn patients. Post-burn physiological changes increase vulnerability to infection and sepsis, making accurate diagnosis and management essential through physical exams and wound analysis. Prolonged ICU stays lead to immunosuppression, especially with severe burns, ongoing illness, surgeries, and recurrent infections, raising also the risk for opportunistic fungal and yeast pathogens.[1,7]

Study subject

Therapeutic Drug Monitoring (TDM) and culture data

The primary focus of the study was to evaluate antibiotic serum levels using therapeutic drug monitoring (TDM) alongside culture data. This approach aimed to assess the effectiveness of prescribed antibiotics by determining whether target attainment was achieved against Gram-positive and Gram-negative nosocomial bacteria isolated from cultures.

Clinical course and antibiotic therapy initiation

Following ICU admission and stabilization of the patient, antibiotic therapy was initiated in response to signs of sepsis. The pharmacodynamic effects of antibiotics initially prescribed were evaluated based on pharmacokinetic changes, particularly in the context of an extensive burn patient with acute kidney injury (AKI) requiring continuous renal replacement therapy (CRRT).

Guiding therapy with inflammatory biomarkers

To further guide antibiotic therapy, inflammatory biomarkers including the neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (c-RP) were monitored. These biomarkers were compared to predict ICU mortality, providing additional insight into the patient's response to treatment and overall prognosis.

Methods

ICU admission to the burn center of hospital: Medical history, comorbidities, injury details, and ICU admission were recorded. Resuscitation and surgical debridement were performed, with attention to respiratory and renal complications. Septic shock was diagnosed early through microbiological investigation and inflammatory biomarkers. Broad-spectrum anti-infective therapy began after clinical decline at ICU-day 3, following targeted culture analysis in blood, urine, BAL. Vancomycin and piperacillin/tazobactam addressed suspected Gram-positive and Gram-negative infections, respectively. Antibiotic dosing was adjusted using culture data weekly and serum monitoring. Neutrophil/Lymphocyte ratio (NLR) and C-reactive protein (c-RP) levels were measured daily to assess ICU mortality risk.

Medical history – Comorbidities - ICU admission and injury details: On January 15th, patient DMS (protocol 371), a 31-year-old morbidly obese male (171 cm, 160 kg), suffered burns over 25% of his body in a workplace accident. Admitted to a tertiary public hospital on January 16th, he was transferred to the ICU of Burn Center - Plastic Surgery, University of Sao Paulo/Sao Paulo/SP, Brazil. Injuries involved the face, neck, chest, scapular regions, forearms, both eyes, and upper airways with inhalation injury. On admission, he presented with hypovolemic/distributive shock, moderate ARDS, acute renal failure requiring dialysis, SAPS*3 score of 61 (49% mortality risk), and SOFA score of 9.

Immediate medical management - Resuscitation & surgical debridement: The patient presented with severe burns requiring rapid intervention. Cardiopulmonary resuscitation stabilized vital signs, and surgical debridement removed dead tissue to lower infection risk and support healing.

Airway, respiratory, and renal complications: Due to ongoing hypoperfusion, the patient required intubation and mechanical ventilation. Hypovolemic-distributive shock led to ARDS and acute kidney injury (creatinine clearance <25 mL/min), prompting CRRT for fluid and electrolyte management. Severe bilateral ocular injuries included a perforated, infected left eye ulcer needing ophthalmologic intervention.

Diagnosis, early microbiological investigation of septic shock followed by ATB therapy: On ICU- day 3, clinicians suspected septic shock collected blood and site-specific cultures before initiating antibiotics recommended against nosocomial strains, in a combined therapy including vancomycin and piperacillin-tazobactam against Gram-positive (Streptococcus spp, Staphylococcus spp) and Gram-negative (Enterobacteriaceae). Broad-spectrum testing was guided daily by c-RP and NLR, supporting a SIRS's diagnosis typical in severe burn infections. Cultures were done in the Microbiology Laboratory of Central Laboratories of hospital.

Biomarkers monitoring in hospital: Creatinine clearance was estimated by the Cockcroft-Gault equation based on serum creatinine levels and c-RP were monitored by the COBAS Analyzer 8000 series. Neutrophil-to-lymphocyte ratio (NLR - blood count) was measured using a Hematological Analyzer (SYSMEX brand). All results of the tests carried out in the hospital's Central Laboratory that were sent to the ICUs via the network, including cultures results.

Blood sampling for therapeutic ATB serum monitoring: Only two blood samples were required for TDM and PK-changes investigation, while MIC data from isolated strains were required for PK/PD target attainment measurements. Investigation started by

blood that was sampling at the steady state levels reached in a renal function dependently as follows: at the 3rd hr. of started ATB infusion (sample 1: 2.5 mL) and 1hr before the next dose (sample 2: 2.5 mL). Antibiotics prescribed were monitored by serum measurements once or twice a week by applying bioanalytical methods developed and validated in our laboratory at the Clinical Pharmacokinetics Center. Pharmacokinetic parameters estimated for a patient were compared to reference data reported previously in healthy volunteers.[8–11] Dosing was tailored to the patient's pharmacokinetics, optimizing effectiveness and reducing toxicity risk by measuring how long each antibiotic took to reach steady-state levels after the loading dose.[3–7,12,13]

Results and discussion

Septic shock episodes & infections management: On ICU-day 3, the patient's condition worsened, prompting initiation of broad-spectrum antibiotics after collecting blood and site-specific cultures. Then, vancomycin targeted Gram-positive bacteria, piperacillin/tazobactam against Gram-negative organisms. Cultures identified Staphylococcus epidermidis (vancomycin/susceptible, MIC 1mg/L) and Proteus mirabilis (piperacillin/tazobactam/resistant, MIC 32 mg/L) but susceptible to meropenem, MIC 0.25mg/L. Consequently, piperacillin/tazobactam was discontinued and meropenem was prescribed in a combined vancomycin therapy including also sodium colistinemethate against Acinetobacter baumannii/resistant to meropenem in the ICU Burn Center.

These antibiotics were administered for 30 days (ICU-day 3-33); dose was prescribed as a function of ideal body weight normalized (Table 1) and according to renal function (Figure 1). Pharmacokinetic changes based on renal function were guided by drug serum levels (TDM) and susceptibility by MIC data to optimize infection management.[1,3–7]

Table 1 Burn septic patient undergoing combined antimicrobial therapy - Dose regimen individualized according to renal function - PK/PD based on serum levels/MIC data

ATB therapy	**Dose regimen recommended**	**Predict daily dose (mg/kg)**
Therapeutic ATB Monitoring	**According to renal function**	**According to renal function**
Vancomycin (IBW/dose normalize)		
Loading dose 1g (1hr-infusion)	1g q8/6h 1hr-infusion	42.3-56.3 mg/kg (ARC)
Duration of therapy: 33 days	1g q12h 1hr-infusion	28 mg/kg (AKI-CRRT)
TDM: 33 days (ICU days D3-D36)	1g q24h 1hr-infusion	14 mg/kg (AKI)
TDM: D12, D14, D15, D17, D18, D23, D28, D32	1g q12h 1hr-infusion	28 mg/kg (PRF)
PK/PD target AUC/MIC: 400-600		**PTA attained up to MIC 2mg/L**
PTZ (IBW/dose normalize)		
Loading dose 4.5g (4hrs-infusion)	4.5g q8/6h 4hrs-infusion	190-254 mg/kg (ARC)
Therapy: 6 days (ICU days 2-7)	4.5g q8h 3hrs-infusion	190 mg/kg (PRF)
TDM: D3, D5 (Clcr 20-75 ml/min)	4.5g q24h 3hrs-infusion	63 mg/kg (AKI)
	4.5g q12h 3hrs-infusion	127 mg/kg (AKI- CRRT)
PK/PD target 100%fΔT>MIC		**PTA attained up to MIC 16g/L**
Meropenem (IBW/dose normalize)		
Loading dose 1g (4hrs-infusion)	1g q8h 4hrs-infusion	42 mg/kg daily (ARC)
Therapy: 40 days (ICU days 12-45)	1g q8h 3hrs-infusion	42 mg/kg daily (PRF)
TDM: D12, D14, D15, D17, D18, D23, D28, D32,	1g q24h 3hrs-infusion	14mg/kg daily (AKI)
D33, D37, D41	1g q12h 3hrs-infusion	28 mg/kg daily (AKI-CRRT)
PK/PD target 100%fΔT>MIC		**PTA attained up to MIC 2mg/L**
Ciprofloxacin (IBW/dose normalize)		
Loading dose 400mg (1hr-infusion)	400mg q12h 1hr-infusion	11.3 mg/kg daily (ARC)
Therapy 11 days (ICU days 48-59)	400mg q24h 1hr-infusion	5.6 mg/kg daily (AKI)
TDM: D43, D46, D47, D48, D50	400mg q12h 1hr-infusion	11.3 mg/kg daily (AKI-CRRT)
End of therapy on day 51	400mg q12h 1hr-infusion	11.3 mg/kg daily (PRF)
PK/PD target AUC/MIC>125		**PTA attained up to MIC 4mg/L**

Abbreviations: CLSI: Clinical Laboratory Standard Institute; TDM: therapeutic drug monitoring; IBW: ideal body weight; PK/PD: pharmacokinetic-pharmacodynamic approach; ICU: Intensive care unit; ARC: augmented renal clearance (vasopressors); RFP: renal function preserved; AKI: acute renal injury; CRRT: continuous renal replacement therapy

Citation: Santos SRCJ, Pires FR, Santos MJ, et al. Infection timeline guided by pharmacodynamics based on pharmacokinetics and inflammatory biomarkers during antibiotic therapy in burn patient – case report. *Pharm Pharmacol Int J.* 2026;14(2):31–37. DOI: 10.15406/ppij.2026.14.00491

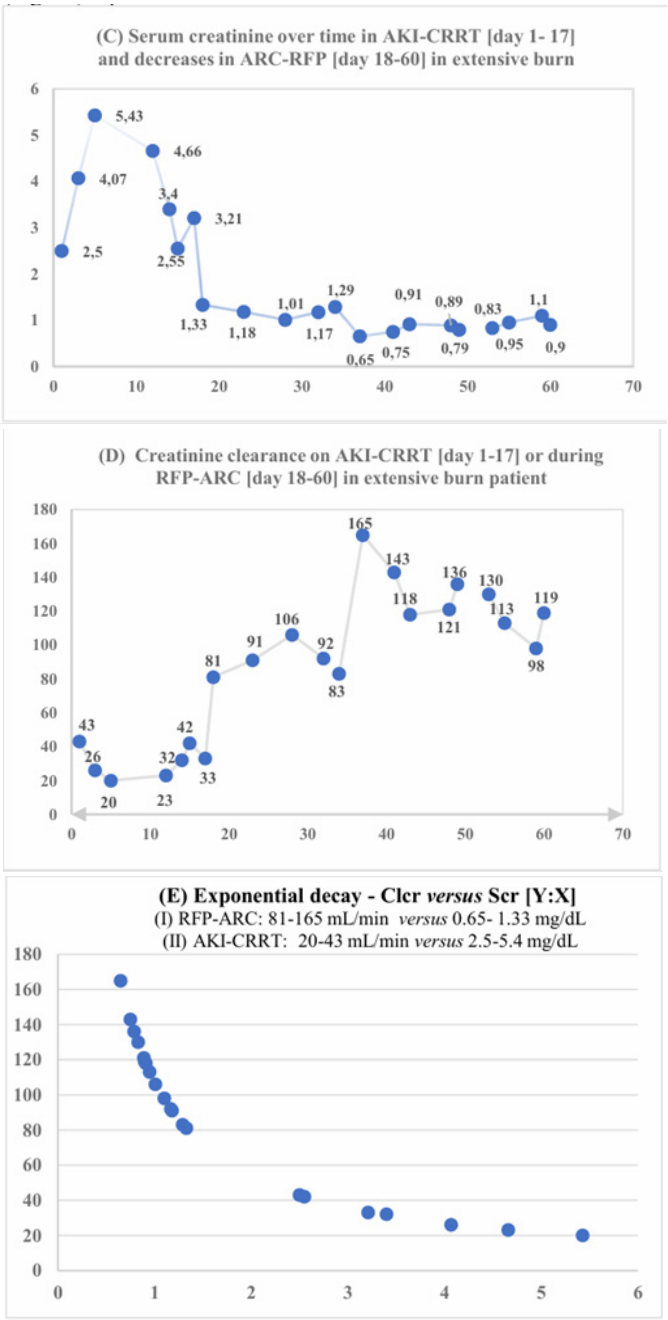

Figure 1 Timeline of renal clearance (Clcr) that in general occur in critically ill ICU patients as a function of pharmacokinetic changes occurring during the systemic inflammatory response syndrome (SIRS) in extensive burn patients. **(C)** Serum creatinine increases during acute kidney injury (AKI) but decreases in patients with renal function preserved (RFP), increasing in vasopressor requirements evidencing augmented renal clearance (ARC). **(D)** Clearance of creatinine decreases during AKI but increases in ARC patients. **(E)** Exponential decay was demonstrated by a reduction in Clcr (mL/min) on the Y-axis, as a function of the increase in Scr (mg/dL) represented on the X-axis.

Septic shock recurred on day 21 and day 33, with Klebsiella pneumoniae (meropenem/susceptible) isolated with MICs of 0.25 mg/L and 0.5 mg/L, respectively. Combined vancomycin-meropenem therapy continued until day 40. On day 41, Pseudomonas aeruginosa (resistant to meropenem/amikacin) susceptible to ciprofloxacin (MIC 0.5 mg/L) was found. In addition, Staphylococcus spp. (ciprofloxacin/susceptible, MIC 0.5 mg/L) appeared on days 41–45. Negative cultures on day 51 led to ICU discharge on day 55 and hospital discharge on day 60 (Table 1 & Figure 1).

Individualized Therapy by TDM/Cultures monitoring & PK/PD guided by PK-Changes: Medicine precision was implemented through individualized therapy with antibiotics guided by serum therapeutic drug monitoring (TDM) in ICU of Burn Center of a tertiary public hospital. Therapeutic target attainment was based on pharmacodynamics based on pharmacokinetics based on TDM and PK-changes renal dependently, while MIC data from isolated strains was required also for PK/PD target attainment results, by measuring how long each antibiotic took to reach steady-state levels after the loading dose, dosing was tailored to the patient's pharmacokinetics, optimizing effectiveness and reducing toxicity risk (Table 2).[3–7,12,13]

Vancomycin, piperacillin, meropenem and ciprofloxacin serum measurements were monitored once or twice a week by high performance liquid chromatography (Clinical Pharmacokinetics Center), and pharmacokinetic parameters in healthy volunteers were considered as reference data.[8–11] Pharmacokinetic changes based on renal function were guided by drug serum levels (TDM) and MIC data to optimize infection management (Table 3).

Inflammatory biomarkers and ICU mortality risk assessment: Previous study conducted by Setiawan et al.,[2] have demonstrated that certain biomarkers are reliable for assessing mortality risk in ICU patients, particularly those with extensive burns, by utilizing these biomarkers, clinicians can make timely adjustments to treatment protocols, thereby improving patient outcomes.[2]

Daily monitoring and comparative analysis of inflammatory biomarkers: Daily measurements of inflammatory biomarkers, including the neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (c- RP) were performed to guide patient management in the ICU. These biomarkers provided comparative insights into the patient's condition and response to interventions. It is well established that the NLR is a more efficient and cost-effective inflammatory biomarker compared to IL-6 or procalcitonin (PCT), which are often recommended for predicting short-term ICU mortality in critically ill patients with extensive burns.[5]

Neutrophil-to-Lymphocyte Ratio (NLR) as an inflammatory biomarker in ICU burn patients: The neutrophil-to-lymphocyte ratio (NLR) was selected as the primary inflammatory biomarker for predicting short-term ICU mortality in critically ill patients. NLR proved to be more effective than C-reactive protein (c-RP) in this context, as it offers real-time insight into inflammatory status and the risk of ICU death. This enables clinicians to promptly identify systemic inflammatory response syndrome (SIRS), particularly in cases of septic shock, and to adapt investigations and treatment strategies to the individual needs of each patient.[3–7] NLR provides real-time information regarding inflammation and the risk of mortality in the ICU, supporting the identification of septic shock cases and facilitating personalized investigations and treatments tailored to each patient. Importantly, analysis revealed no correlation between NLR and c-RP (r^2: 0.0811), further supporting the preference for NLR as the biomarker of choice for clinical decision- making in the Burn Center (Figure 2).

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Table 2 Microbiology of Isolates from Cultures – ATBs Therapy Day 3 – Day 55

Cultures MIC data (CLSI database)	Microbiology	MIC data
Vancomycin [Target AUC_{24}/MIC>400-600]	*Gram positive bacteria (n=4)*	
D3	*S. aureus/S (n=1)*	1 mg/L
D3 **Coverage extended up to MIC 2 mg/L**	*Staphylococcus epidermidis (n=3)*	1 mg/L
Piperacillin [Target 100%fT>MIC]	*Enterobacterales (n=1)*	
D0-D3 Target Attainment up to MIC 16 mg/L	*Proteus mirabilis/PTZ Resistant*	>32 mg/L
D3 Enterobacterales Meropenem/S MIC 0.25 mg/L		
Meropenem [Target 100%fΔT>MIC]	***Enterobacterales (n=5)***	MIC data
D3	*P. mirabilis (1)*	0.25 mg/L
D11- D21	*K pneumoniae (3)*	0.25 mg/L
D33	*K pneumoniae (1)*	0.5 mg/L
Coverage extended up to MIC 2 mg/L/Susceptible	Not isolated strain	2 mg/L
MIC 4 mg/L/Intermediate susceptibility	Not isolated strain	NAP
MIC 8 mg/L/ Intermediate susceptibility	Not isolated strain	NAP
Ciprofloxacino [Target AUC^{ss}_{24}/MIC> 125]	***Non-Enterobacterales***	**MIC data**
GNB isolated	*Gram-negative bacteria (n=3)*	
D41	*Pseudomonas aeruginosa (n=1*	0.5 mg/L
D43	*Pseudomonas aeruginosa (n=1)*	0.5 mg/L
D45	*Pseudomonas aeruginosa (n=1)*	0.5 mg/L
Coverage extended up to MIC 4 mg/L/Susceptible	Not isolated strain	NAP
GPB isolated	***Gram positive bacteria (n=3)***	**MIC data**
D41	*S. aureus (n=1)*	1 mg/L
D43	*Staphylococcus epidermidis (n=1)*	1 mg/L
D45	*Staphylococcus epidermidis (n=1)*	1 mg/L
Coverage extended up to MIC 4 mg/L/Susceptible	Not isolated strain	NAP

Timeline of Therapy of Infections (days 1-60)

Abbreviations: CLSI, clinical laboratory standard institute; ICU, intensive care unit; MIC, minimum inhibitory concentration; IS, intermediate susceptible strain; NAP, not applied

Table 3 Pharmacokinetic-Changes based on Renal Function - ATB therapy in ICU (51 days) Med (IQ)

Vancomycin - Reference data[9]		**AKI**	**CRRT installed**	**ARC**	**RFP**
$t_{(1/2)\beta}$	*3.7-5.1 (hrs.)*	14 (13-21)	10 (6-12)	4 (3-5)	9 (5-12)
CLt	*4.7-6.6 (L/h)*	1.0 (0.9-1.2)	1.8 (0.8-1.9)	4.5 (3.9-4.8)	1.8 (0.9-2.9)
Vd^{ss}	*30-42 (L)*	21 (17-30)	21 (18-28)	25 (20-28)	21 (18-28)
Comments: Vancomycin PK-changes impacting coverage against GPB vancomycin susceptible MIC 1mg/L and dose adjustment was done for efficacy and safety					
• Prolongation of biological half-life was higher in AKI >CRRT >RFP, and in ARC was reduced by vasopressors.					
• Reduction on total body clearance was higher in AKI>CRRT>RFP, while parameter was augmented in ARC.					
• Volume of distribution was maintained unchanged, independently of renal function.					
Piperacillin - Reference data[8]		**AKI**	**CRRT installed**	**ARC**	**RFP**
$t_{(1/2)\beta}$ *(hrs.)*	*0.7 -0.9*	5 (4-8)	4 (3-5)	NA	NA
CLt	*10-12 (L/h)*	1.3 (1.0-1.5)	6.5 (3.4-6.8)	NA	NA
Vd^{ss}	*10-14 (L)*	10 (6-11)	34 (23-44)	NA	NA
Comments: Piperacillin PK-changes impacting coverage against GNB Piperacillin susceptible up to MIC 16 mg/L. Dose adjustment was done for efficacy and safety					
• Prolongation of biological half-life was major in AKI compared with CRRT installed.					
• Reduction in total body clearance was major in AKI compared with CRRT installed.					
• Volume of distribution was reduced in AKI, but it was increased by trice in CRRT.					
Meropenem - Reference data[10]		**AKI**	**CRRT installed**	**ARC**	**RFP**
$t_{(1/2)\beta}$ *(hrs.)*	*0.5 -0.6*	5 (4-6)	4 (3-5)	1.5 (1.4-1.6)	2.2 (1.9-2.6)

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Table 3 Continued....

CLt	*12-13 (L/h)*	3.3 (2.4-4.1)	5.5 (4.8-6.1)	9.7 (9.1-10.3)	7.8 (7.5-9.2)
Vd^{ss}	*9-10 (L)*	27 (13-35)	31 (27-37)	21 (19.2-23)	22 (18-29)

Comments: Meropenem PK-changes impacted coverage against GNB susceptible strains up to MIC 2 mg/L. Coverage was extended up to MIC 4-8 mg/L, strains of intermediate susceptibility. Dose adjustment was required for safety.

- Prolongation of biological half-life was higher in AKI >CRRT >RFP, and in ARC was reduced by vasopressors.
- Reduction on total body clearance was higher in AKI>CRRT>RFP, while parameter was augmented in ARC.
- Volume of distribution was maintained unchanged, independently of renal function.

Ciprofloxacin - Reference data[11]		**AKI**	**CRRT installed**	**ARC**	**RFP**
$t_{(1/2)\beta}$ *(hrs.)*	*3.2-4.1*	NA	NA	3.5 (3.1-3.7)	5.4 (4.5-7.8)
CLt	*33 - 54 (L/h)*	NA	NA	42 (38- 45)	33 (30-38)
Vd^{ss}	*119-179 (L)*	NA	NA	89 (75-105)	97 (90-134)

Comments: Ciprofloxacin PK-changes occurred in a few days by vasopressors requirements once acute kidney injury or CRRT installed weren't required at ICU-days 41-44 of therapy.

In addition, coverage increases against GNB and GPB susceptible strains up to MIC 4 mg/L in this patient with preserved renal function. Then, prescription 400mg q12h 1hr-infusion was maintained, once the total body clearance did not change during therapy up to ICU-day 55 with coverage guaranteed.

Abbreviations: NA, Not Applied; Reference pharmacokinetics data, healthy volunteers 8-11; MIC, minimum inhibitory concentration; PK/PD, pharmacodynamics based on pharmacokinetics; ICU, Intensive care unit; ARC, augmented renal clearance (vasopressors requirements); RFP, renal function preserved; AKI, acute renal injury; CRRT, continuous renal replacement therapy; $t_{(1/2)\beta}$, biological half-life; CLt, total body clearance; Vd^{ss}, volume of distribution at the steady

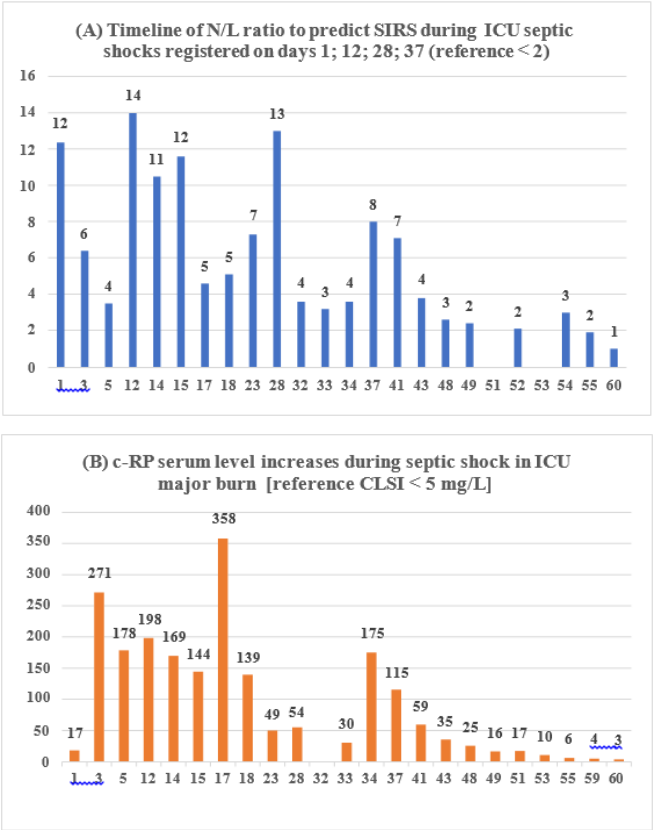

Figure 2 Inflammatory biomarkers of septic shock and of systemic inflammatory response syndrome (SIRS) in an extensive burn patient: **(A)** Neutrophils/Lymphocytes ratio is a sensitive biomarker to predict ICU mortality in extensive burn patient applied to guide and individualize the anti-infective therapy of septic shock in a real time. **(B)** c-Reactive protein is the older biomarker of septic shock.

Conclusion

Antibiotic therapy was tailored according to infection type and resistance patterns, guided by serum therapeutic monitoring and minimum inhibitory concentration (MIC) data, which informed the selection of treatment. Adjustments in renal function monitoring facilitated the optimization of serum antibiotic levels and attainment of therapeutic targets. Ciprofloxacin demonstrated efficacy, yielding negative culture results by the fifty-first day of treatment, with subsequent discharge from the intensive care unit on the fifty-fifth day. The neutrophil-to-lymphocyte ratio (NLR) demonstrated greater efficiency than C-reactive protein (c- RP) in predicting short-term mortality in the ICU and offered real-time assessments of inflammation and septic shock risk, thereby supporting personalized patient management. Consequently, the NLR was selected as an inflammatory biomarker to enhance decision-making in the ICU Burn Center.

Limitations

This clinical study is a Case Report conducted in the ICU with a patient with several sepsis infections during the treatment of each septic shock, with a single-center design. Microbiological confirmation was done from day 3 in the ICU up to day 51 confirmed by negative cultures. Prolonged hospitalization was expected especially for the surviving patient in the ICU due to the extent of total body surface area burned (TBSA), several surgical interventions followed by septic shocks. A total of 11 isolates from cultures in a period by negative cultures up to 51 days followed by patient ICU discharge at day were distributed as follows: Gram-positive bacteria, Gram-negative bacteria, invasive fungal yeasts as function of a patient with an extended ICU period of immunosuppression at the Burn Center of the tertiary public hospital.

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Authors' contributions: All authors contributed equally to this work based on their specialty. DSG contributed to the study related to ethical approvals at the hospital and the Brazilian Platform for clinical projects, data acquisition, interpretation, and critical review of the manuscript content. SRCJS contributed to the conception and design of the study, acquisition and interpretation of data, writing of the manuscript with critical review for intellectual content. DCSP, EDC, EMSJ, FRP and JMSJ contributed to clinical data acquisition, interpretation, and critical review of clinical data in the manuscript for important intellectual content. ASGA, GAF, TCO contributed to the critically ill patients care in the ICU, blood collection of viable samples for antibiotics serum measurements, and blood collection for laboratorial data acquisition related to biomarkers were done. MJS contributed to the revision of detailed information of articles included and especially in the last revision related to references included. PR, NJCD and NMS contributed to the critical revision of data for important intellectual new contents. PRA and MSS contributed to the discussion on anti-infectives prescription. All authors read and approved the final manuscript version.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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None.

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