

Comparative Effect on Levels of C-Reactive Protein (CRP) and Other Inflammatory Markers by Empirical Antibiotic Therapy – A Prospective Observational Study

Sadaf Pervaiz^{1,2}, Ishrat Younus¹ and Sheikh Abdul Khaliq^{3*}

¹Department of Pharmacology, Faculty of Pharmacy, Hamdard University, Karachi, Pakistan

²Burns Unit, Dr. Ruth K M Pfau Civil Hospital, Karachi, Pakistan

³Department of Pharmaceutics, Faculty of Pharmacy, Hamdard University, Karachi, Pakistan

Abstract

Background: Burns trigger a vigorous inflammatory response to injury, which involves the release of various inflammatory mediators and the migration of inflammatory cells to the site of injury. Post-burn infection is also a significant issue.

Objective: The study aimed to compare the effects of two antibiotics, cefoperazone/sulbactam and co-amoxiclav, on inflammatory markers in burn patients.

Methods: A prospective observational study comparing the effects of antibiotics on inflammatory markers was conducted in a burns unit of a tertiary care hospital from April 2025 to June 2025. The end-point of the study was the reduction of C-reactive protein (CRP), leucocytes, neutrophils, and lymphocytes. 100 burn patients were divided into two groups, and each received either cefoperazone/sulbactam or co-amoxiclav. The ethics committee approved the study. Blood samples were collected on admission to obtain a baseline count of inflammatory markers and at 7 days post-treatment. SPSS-22 was used to assess a significant reduction in inflammatory markers.

Results: At day 7; cefoperazone/sulbactam (mean: 43.99 mg/dL) significantly lower ($p=0.001$) CRP levels compared to the coamoxiclav (mean: 94.55 mg/dL); leucocyte count was comparable ($p=0.820$) in cefoperazone/sulbactam (mean: $12.30 \times 10^9/L$) and coamoxiclav (mean: $12.50 \times 10^9/L$); neutrophil count was significantly lower ($p=0.014$) in cefoperazone/sulbactam (mean: 69.52%) compare to coamoxiclav (mean: 76.38%) and lymphocyte count was substantially lower ($p=0.035$) in coamoxiclav (mean: 14.44%) compare to cefoperazone/sulbactam (mean: 18.94%).

Conclusion: The outcomes of the study suggest that, overall, both antibiotics are effective in treating infections and inflammation in burn patients; however, cefoperazone/sulbactam might provide more effective control of systemic inflammation compared to coamoxiclav.

Keywords: Burn injury, inflammation, C-reactive protein, inflammatory markers, cefoperazone/sulbactam, coamoxiclav.

INTRODUCTION

Burns are considered one of the most devastating types of injuries since they cause damage to the epidermis and related soft tissues, which results in pain, severe edema, and vulnerability to infection and sepsis [1]. A burn wound infection fosters an environment that promotes bacterial growth and may increase the patient's risk of sepsis [2]. Moreover, scarring is inevitable, leading to both functional and cosmetic complications for patients [3]. In addition, immune suppression makes burn patients susceptible to invasive infections and inhalation injury, which increases their mortality risk [4]. New multi-drug-resistant bacteria included *Staphylococcus aureus*, *Enterococcus*, *Pseudomonas*, *Acinetobacter*, *Enterobacter*, and yeast spp. Challenge clinical care and require new medicines and antimicrobial therapy [4]. In such cases, the inflammatory response may worsen, and this can result in serious complications

such as failure of multiple organs or a state of shock due to sepsis; it reinforces the moral of the story that patients must be treated without delay [5].

Burns cause a vigorous inflammatory response to injury, which involves the release of various inflammatory mediators that may include C-reactive protein (CRP), leucocytes, neutrophils, and lymphocytes [6]. These proteins are produced in the liver and are up-regulated by inflammatory cytokines; their levels are proportional to the degree of the inflammatory process [6]. Before the wound is dressed, CRP levels typically peak within 24 hours and remain above 30 mg/dL, suggesting a high risk of symptoms progressing to systemic infection and sepsis [6]. According to one researcher, the administration of antibiotics in burn management is a subject of ongoing debate. Researchers evaluated the influence of empirical antibiotic therapy on levels of C-reactive protein (CRP) and other inflammatory biomarkers such as leukocyte, neutrophil, and lymphocyte counts, as well as the neutrophil-lymphocyte ratio in patients with severe burns [7]. In this study, researchers found that over the 7-day course of empirical antibiotic treatment, no reduction in key inflammatory markers, including

*Corresponding author: Sheikh Abdul Khaliq, Department of Pharmaceutics, Faculty of Pharmacy, Hamdard University, Karachi, Pakistan, Email: drsheikh1974@gmail.com

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leukocytes, neutrophils, lymphocytes, or the neutrophil-lymphocyte ratio, occurred. In contrast, the antibiotic ceftazidime reduced CRP levels, but the decrease was not statistically significant [7]. Another study conducted by researchers on levels of CRP, white blood cells, and PCT (procalcitonin) in hospitalized burn wound patients; their findings indicate that conventional biomarkers—namely WBC, CRP, and PCT—hold little value for diagnosing or tracking infection in severe burn patients [8]. However, the combination of a third-generation cephalosporin and a beta-lactamase inhibitor is still commonly employed as an empirical antibiotic for prevention of microbial infections in burns or nosocomial-related complications in many clinical settings [9]. Simultaneously, the quantities of isolates exhibiting resistance to the penicillin antibiotics were as follows: 61(92%) isolates resistant to ampicillin, 54(82%) resistant to amoxicillin-clavulanic acid, and 24(36%) resistant to piperacillin-tazobactam [10]. The isolates were also assessed for resistance to the cephalosporins: cefazolin, cefuroxime, ceftazidime, ceftriaxone, cefepime, and ceftolozane-tazobactam; the corresponding number of resistant isolates were 60(91%), 60(91%), 39(59%), 48(73%), 42(64%), and 27(41%) [10]. These antibiotics, despite their resistance patterns, are still considered among the ideal choices for first-line management of burn wound infections [10]. One study examined whether antibiotic treatments have essential distinctions in lowering CRP levels and other inflammatory markers, providing evidence for better antibiotic use and response in burn patients by reducing these inflammatory mediators [11]. Consequently, detecting antibiotic therapy performance *via* inflammatory markers, including C-reactive protein (CRP), may be an essential factor in evaluating treatment outcomes and reducing infection-related complications [3, 12, 13].

Therefore, the objective of this investigation was to compare and observe the effects of commonly prescribed antibiotics in the burn ward of a tertiary care hospital, such as cefoperazone/sulbactam and amoxicillin/clavulanic acid, on levels of inflammatory markers, including CRP, leucocytes, neutrophils, and lymphocytes in burn patients. Antibiotics may influence the inflammatory response, and mismanagement could aggravate systemic inflammation or uncontrolled infection.

MATERIALS AND METHODS

This study was a prospective observational study held in the burn unit (inpatient) clinical setting of a tertiary care hospital. The hospital meets all requirements to manage patients with burn injuries and their related complications. Data was collected from April 2025 to

June 2025. The research procedures were approved by the Ethical Review Board (ERB) of Hamdard University with ethical approval reference number (ERB: 2025-03). Patients were included in the study after taking written informed consent if they were adult patients 18 years or older, had more than 10% of the Total Body Surface Area (TBSA) affected due to burn, and received either cefoperazone/sulbactam 4gm/day or coamoxiclav 1.2gm/6 hour within the first seven days of hospitalization based upon physician prescription. Antibiotics are prescribed as empirical therapy to prevent infection, which not only prevents disease but is also associated with inflammation. Antibiotic selection was based on the current history of burn patients, culture sensitivity results, and clinical experience. Patients were excluded from the study if they were less than 18 years of age, had co-existing medical conditions (co-morbidities) that could affect the inflammatory response, or had not received antibiotic treatment within the first 7 days post-admission, at the clinician's discretion.

The sample size of the study was determined using a power analysis, with a significance level of 5%, a confidence interval of 95%, a power of 80%, and a moderate effect size of 0.60 based on a previous study [14]. The G*Power software was used to calculate sample size [15]. The maximum sample size determined by this method was 96, which means 48 patients in the cefoperazone/sulbactam group and/or 48 in the co-amoxiclav group, based on the N1/N2 distribution. However, to maintain the study's power, attrition of study data was assessed in 100 patients.

Data for this study were generated from patients' files, medical records, and laboratory reports of the burn unit of a tertiary-care hospital. Data focused on measuring inflammatory markers, including CRP levels and complete blood count (CBC), including leucocyte, neutrophil, and lymphocyte counts. For this purpose, blood samples were collected by taking 2ml of venous blood on the day of admission (upon admission and at the start of antibiotic therapy as a baseline) and on day 7 after the burn incident. All patients in the study were informed of the study's purpose and assured that their medical information would be kept confidential.

The data was analyzed using SPSS software Version 22. The primary statistical tests were descriptive, and a parametric independent-samples t-test was applied because the data were normally distributed, as indicated by a bell-shaped curve. Data were in interval and ratio (continuous) forms, and the mean CRP, leucocytes, neutrophils, and lymphocytes levels were compared between burn patient groups treated with two antibiotics

through day 7, with a significance level of 5% ($p < 0.05$). Descriptive statistics, including mean reductions in CRP, leucocytes, neutrophils, and lymphocytes at day 7 of treatment, along with their standard deviations and standard errors, were calculated.

RESULTS

In the group of patients treated with cefoperazone/sulbactam, the mean age in males ($n=31$) was 28.48 ± 6.20 years, and in females ($n=19$), 29.58 ± 7.32 years. The TBSA affected was $26.45 \pm 5.49\%$ in males and $28.21 \pm 6.70\%$ in females. Similarly, in the group of patients treated with Coamoxiclav, the mean age in males ($n=32$) was 30.31 ± 6.35 years, and in females ($n=18$), 27.89 ± 5.55 years. The TBSA affected was $26.59 \pm 6.81\%$ in males and $24.88 \pm 6.28\%$ in females. In both groups,

the most common causes of burn injury are gas cylinder explosion, followed by acid burn or domestic violence, and then electric current shock (9%). Demographic characteristics of both groups were balanced, with no statistically significant differences (Table 1).

Mean reduction of CRP level, leucocytes count, neutrophil count, and lymphocyte count at day seven (07) of treatment by cefoperazone/sulbactam and Coamoxiclav was compared. CRP level and neutrophil count reduction were better in cefoperazone/sulbactam compared to Coamoxiclav; while lymphocyte count reduction was better in the Coamoxiclav group compared to cefoperazone/sulbactam (Table 2, Fig. 1).

Effect on CRP Level: An independent sample t-test results indicated a significant difference in the mean of

Table 1: Demographic parameters of the study in the cefoperazone/sulbactam group and the Coamoxiclav group.

Parameter	Gender	Cefoperazone/Sulbactam	Coamoxiclav	Significance
Mean Age and Standard deviation (Years)	Male	28.48 ± 6.20	30.31 ± 6.35	$p=0.234$
	Female	29.58 ± 7.32	27.89 ± 5.55	$p=0.106$
TBSA affected Mean and Standard deviation (%)	Male	$26.45 \pm 5.49\%$	$26.59 \pm 6.81\%$	$p=0.987$
	Female	$28.21 \pm 6.70\%$	$24.88 \pm 6.28\%$	$p=0.0765$
Mos common cause of burn injury in both groups (%)	Gas cylinder explosion	31 (61%)	30 (59%)	$p=0.062$
Second most common cause of burn injury in both groups (%)	Acid burn	6 (11%)	5 (9.66%)	$p=0.112$
Third most common cause of burn injury in both groups (%)	Electric current shock	5 (9%)	5 (10.6%)	$p=0.089$

Table 2: Comparative profile of inflammatory mediators (CRP, leucocytes, neutrophils, and lymphocytes) in both antibiotic groups at baseline.

Parameters	Cefoperazone/Sulbactam	Coamoxiclav	Significance*
CRP (mg/dL) 1 st Day	76.06 ± 55.51	94.55 ± 62.67	$p=0.002$
Leucocytes ($10^9/L$) 1 st Day	14.34 ± 7.52	14.41 ± 6.06	$p=0.106$
Neutrophils (%) 1 st Day	72.24 ± 14.11	76.38 ± 12.35	$p=0.055$
Lymphocytes (%) 1 st Day	18.94 ± 12.78	14.44 ± 7.44	$p=0.022$

*p-value is significant at <0.05

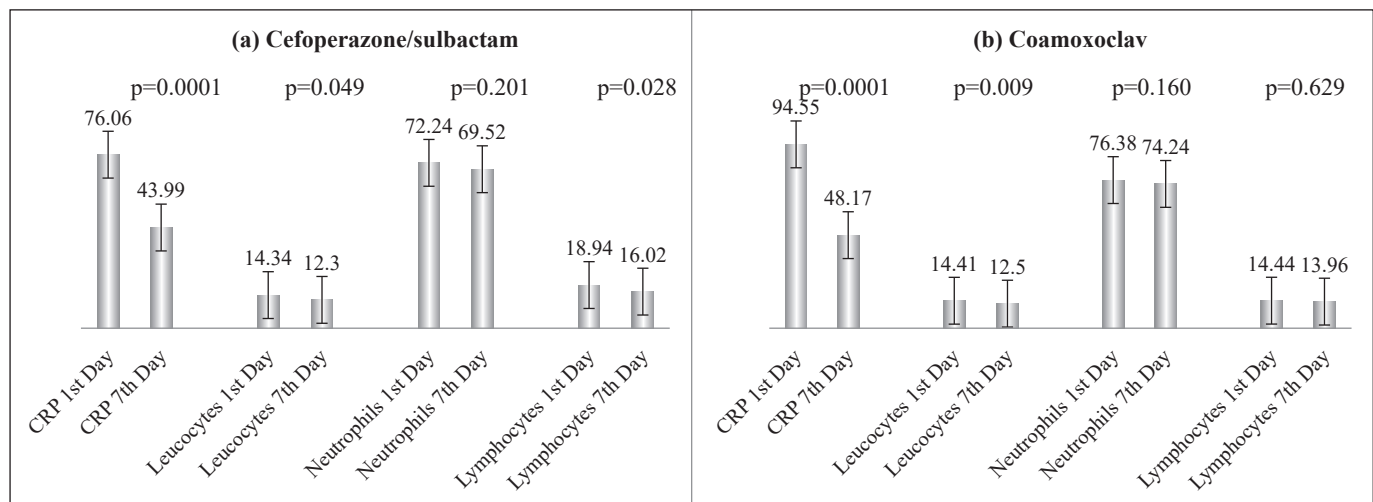


Fig. (1): Comparative effect of antibiotics on CRP, leucocyte, neutrophils, and lymphocyte before and after treatment: (a) Cefoperazone/Sulbactam, (b) Coamoxiclav.

Table 3: Comparative reduction of inflammatory mediators in both antibiotic groups at day 7 of treatment.

Parameters	Cefoperazone/Sulbactam	Coamoxiclav	Significance*
CRP (mg/dL) 7 th Day	43.99±37.64	48.17±39.13	p<0.001
Leucocytes (10 ⁹ /L) 7 th Day	12.30±4.45	12.50±4.66	p=0.820
Neutrophils (%) 7 th Day	69.52±14.92	74.24±12.81	p=0.014
Lymphocytes (%) 7 th Day	16.02±10.90	13.96±8.46	p=0.034

*p-value is significant at <0.05.

CRP levels between cefoperazone/sulbactam and Co-amoxiclav at day 1 ($t=6.29$; $p=0.002$) (**Table 2**) and at day 7 ($t=-4.89$; $p<0.001$) (**Table 3**); this shows that cefoperazone/sulbactam has a relatively lower CRP level than Co-amoxiclav. From the baseline, CRP is also significantly reduced in cefoperazone/sulbactam ($t=4.92$; $p<0.001$) and Co-amoxiclav ($t=8.77$; $p<0.001$) groups at day 7 (**Fig. 1**).

Effect on Leucocyte Count: An independent sample t-test indicated that both antibiotics (cefoperazone/sulbactam and Co-amoxiclav) did not differ significantly with respect to mean reduction of leucocyte count at day 1 ($t=5.29$; $p=0.106$) (**Table 2**) and at day 7 ($t=-0.288$; $p=0.820$) (**Table 3**). From the baseline, the leucocyte count is also significantly reduced in cefoperazone/sulbactam ($t=1.96$; $p=0.049$) and Co-amoxiclav ($t=2.72$; $p=0.009$) groups at day 7 (**Fig. 1**).

Effect on Neutrophil Count: Independent sample t-test results indicated that there is a significant difference in mean count of neutrophil at day 7 ($t=-2.503$; $p=0.014$) (**Table 3**); however, at the baseline day 1, there was no significant difference between the two groups of antibiotics ($t=16.25$; $p=0.055$). This shows that cefoperazone/sulbactam has significantly reduced neutrophil counts compared to the Co-amoxiclav group in burn patients at day 7. The baseline neutrophil count is non-significantly reduced in cefoperazone/sulbactam ($t=1.29$; $p=0.201$) and Co-amoxiclav ($t=1.42$; $p=1.60$) groups at day 7 (**Fig. 1**).

Effect on Lymphocyte Count: For Lymphocyte count, independent sample t-test statistics at day 7 ($t=2.154$; $p=0.034$) and at day 1 were ($t=14.54$; $p=0.022$), suggesting differences and significantly higher mean count of lymphocytes in cefoperazone/sulbactam group as compared to Co-amoxiclav group in burn patients. From the baseline, the lymphocyte count is reduced considerably in the cefoperazone/sulbactam ($t=1.71$; $p=0.028$) group and non-significantly reduced in the Co-amoxiclav ($t=1.50$; $p=0.629$) group at day 7 (**Fig. 1**).

DISCUSSION

Infection is a common complication following burns, imposing considerable strain on both patients and the

healthcare system. Burn injury results in loss of skin, the body's first line of defense against infections, leading to the potential for internal infections and significantly increasing the risk of morbidity and mortality [16]. CRP is a recognized indicator of systemic inflammation [17]. CRP is a well-established marker of systemic inflammation [18]. Elevated CRP levels indicate substantial inflammation in the body, typically due to infection or tissue damage [17]. In burn victims, high CRP levels indicate an intensified immunological response to the injury or an infection [19]. The elevated CRP values seen in patients treated with amoxicillin/clavulanic acid (Coamoxiclav) indicate a heightened inflammatory response. This may have multiple clinical ramifications: sepsis is a critical illness in which the body's reaction to infection induces extensive inflammation, resulting in organ failure. Although Coamoxiclav successfully targets a wide range of infections, the elevated immune response indicated by elevated CRP levels may lead to severe systemic inflammation. The mortality rate has significantly declined over the past decade; however, ongoing efforts in timely management and infection prevention remain crucial [20].

This study identified trends in antibiotic use for burn patients. Existing research on the efficacy of prophylactic antibiotics for debridement in burn patients has yielded conflicting results, creating a lack of consensus among surgeons. Although a single pre-operative dose is recognized for reducing infection risk in conventional autografting, there is insufficient data on its application in modern minimally invasive debridement and grafting procedures [21]. The third-generation cephalosporin ceftriaxone is the most frequently prescribed antibiotic in many burn care practices [22]. A study evaluating single-dose pre-operative antibiotics for burn debridement found that intravenous piperacillin/tazobactam (4.5g) maintained concentrations above the MIC for *Pseudomonas aeruginosa* for a mean of only 1.15 hours [21].

In contrast, cefalotin (1g) remained above the MIC for *Staphylococcus aureus* for a mean of 6.49 hours [21]. As debridement surgeries lasted 2.25 to 8.5

hours, no patients in the piperacillin/tazobactam group were adequately protected, compared with only 4 of 9 patients in the cefalotin group [21]. Unfortunately, in burn patients, hypermetabolism accelerates hepatic drug clearance, reducing plasma concentrations of cefotaxime; consequently, higher cefotaxime doses are necessary to maintain adequate antimicrobial levels [21]. In the current study, a comparative analysis of cefoperazone/sulbactam and co-amoxiclav on inflammatory markers in burn patients revealed significant differences in their effects, findings supported by another study [23]. The current study also found that cefoperazone/sulbactam is associated with lower baseline CRP levels and higher lymphocyte counts, suggesting a potentially better outcome in managing systemic inflammation. The same findings are also reported by Putra *et al.* in 2023 [7]. Conversely, coamoxiclav led to higher neutrophil counts, which may reflect a more robust and immediate immune response but is also associated with higher CRP levels, suggesting increased systemic inflammation; however, from baseline, the coamoxiclav groups also show a significant reduction in CRP and leucocyte count.

Regarding the lymphocyte count, cefoperazone/sulbactam was significantly better in reducing the count, while coamoxiclav was not significantly different from baseline. Therefore, cefoperazone/sulbactam was more effective at reducing inflammation associated with lymphocytes. The inflammatory markers mentioned in the current study may guide clinicians and researchers to determine the effects of antibiotics on inflammation and immune functions of the body. They may lead to better antibiotic selection, particularly in burn patients, to achieve ultimate clinical, humanistic, and economic outcomes [24, 25].

This study further provides information on the careful selection of antibiotics, as another researcher suggested using cefoperazone/sulbactam in burn patients to reduce inflammation [18]. The elevated CRP level in the co-amoxiclav group may indicate an increased risk of inflammation and infection, as the immune system is focused on repairing damaged tissue rather than controlling infection. On the other hand, a decrease in neutrophil levels in the cefoperazone/sulbactam group could help prevent inflammation and repair damaged cells [21-23]. Patients in the co-amoxiclav group have elevated CRP levels, suggesting an increased inflammatory response [15].

One of the studies analyzed the antibiotic sensitivity patterns of the primary pathogens, *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, in 624

patients with severe burns at a tertiary burn center; key findings on antibiotic sensitivity revealed that *P. aeruginosa* was most susceptible to imipenem, meropenem, and amikacin, and least vulnerable to amoxicillin-clavulanate, aztreonam, and fluoroquinolones, while *A. baumannii* was most sensitive to polymyxin, cefoperazone-sulbactam, and doxycycline [26].

CONCLUSION

To put it in a nutshell, it is suggested that cefoperazone/sulbactam may be more effective than coamoxiclav in controlling CRP and neutrophils in patients with burn injuries. However, co-amoxiclav is more effective at controlling lymphocyte counts, and both groups have similar effects on leucocyte counts. Additionally, the main limitation of the current study is its small sample size, short duration, and single-center design; therefore, a larger sample, a longer duration, and multi-center data with more antibiotics will further validate its findings. To improve prophylactic antibiotic use for burn debridement, hospitals must establish specific surgical guidelines. It is recommended to use narrow-spectrum antibiotics to combat microbial resistance. The study findings are vital for informing future policy, which should focus on educating staff, aligning with national guidelines, and implementing continuous monitoring.

ETHICAL APPROVAL

This study was undertaken as part of an MPhil research project. The research protocol was initially reviewed and approved by the Ethical Review Board (ERB) of Hamdard University, where the degree was being pursued (Ethical Approval No. ERB: 2025-03). Subsequently, permission to conduct the study and collect data was obtained from the participating institution before the commencement of data collection. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and the Helsinki Declaration.

CONSENT FOR PUBLICATION

Written informed consent was taken from the participants.

AVAILABILITY OF DATA

The data set may be acquired from the corresponding author upon a reasonable request.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Declared none.

AUTHORS' CONTRIBUTION

SP: Study concept, design, data collection, initial drafting; IM: Study critical review and revision of the initial draft; SAK: critical review, results analysis, and statistical analysis. All authors have critically reviewed, revised, and approved the final version of the manuscript.

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