

**Effect of Cephalexin at High Dose in Patients with Cellulitis****Ram Milan Prajapati<sup>1</sup>, Dinesh Kabre<sup>2</sup>, Ashok Khatri<sup>3</sup>**<sup>1</sup>Professor, Dept. of Surgery, Naraina Medical College & Research Centre, Panki, Kanpur<sup>2</sup>Professor, Dept. of Orthopaedic, Naraina Medical College & Research Centre, Panki, Kanpur<sup>3</sup>Professor, Dept. of Surgery, Naraina Medical College & Research Centre, Panki, Kanpur

Received: 14-12-2023 / Revised: 05-01-2024 / Accepted: 20-01-2024

Corresponding Author: Dr. Ram Milan Prajapati

Conflict of interest: Nil

**Abstract:**

**Introduction:** Cellulitis, a frequent bacterial skin illness caused by Streptococcus or Staphylococcus, provides varying dangers among groups. Redness, heat, swelling, and soreness are some of the signs of it. Cellulitis left untreated may cause abscesses, septicemia, lymphangitis, and recurrence. Cephalexin is routine antibiotic therapy; however, growing resistance necessitates greater dosages for improved effectiveness, requiring further study on cellulitis safety and results.

**Aims and Objective:** To evaluate the effects of a high-dose cephalexin regimen (1000 mg) compare to those of a conventional regimen (500 mg) in treating cellulitis.

**Method:** In a double-blind, randomized research, conducted in the hospital for one year period, the patients were given 7-day Cephalexin 1000 mg or 500 mg four times a day. Blinding and 1:1 computer-generated randomization reduced bias. Temperature, heart rate, discomfort, and erythema were assessed at days 3 and 7 after baseline vital signs. Blinding, adherence, adverse events, and satisfaction were surveyed. Using a 14-day follow-up, a multicenter study comparing high- and standard-dose Cephalexin established feasibility and sample size.

**Result:** The effectiveness of various cephalexin doses in the treatment of cellulitis is examined in this research. For cellulitis care, Cephalexin 1000 mg may be better than 500 mg at avoiding oral antibiotic treatment failure and lowering the requirement for a class change in 100 randomized individuals. However, both groups showed excellent clinical improvements by Day 3. It is important to carefully evaluate the study-specific elements before interpreting them.

**Conclusion:** The study has concluded that Cephalexin at a higher dose is significantly effective with minor adverse events that may be a little higher than the usual dose.

**Keywords:** Cellulitis, Bacterial Skin Illness, Streptococcus, Warmth.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

**Introduction**

Cellulitis stands as a prevalent bacterial skin infection penetrating the deeper layers of the dermis and subcutaneous tissues. Manifesting through redness, warmth, swelling, and tenderness, this condition arises when bacteria, notably Streptococcus or Staphylococcus, infiltrate the skin via wounds, cuts, or insect bites. While it can emerge across the body, its frequent occurrence on the lower legs marks a common trend [1-3].

Insights from diverse studies shed light on cellulitis incidence and its associated risk factors in distinct regions. Within the United States, a defined population revealed a cellulitis rate of 24.6 per 1000 person-years, while internationally, 15.78% of adults with chronic leg oedema reported cellulitis within a year. In Cameroon, obesity, skin disruption history, and toe-web intertrigo emerged as significant lower limb cellulitis risk factors. Similarly, across Africa, skin barrier disruption, neglected wounds, toe-web intertrigo, leg ulcers,

and oedema surfaced as local cellulitis risks. In India, 7.4% of hospitalized cirrhotic patients exhibited cellulitis. These varied prevalence rates underscore cellulitis as a widespread condition contingent on diverse population dynamics and risk factors [4-8].

Cellulitis typically reveals itself through distinctive symptoms: an affected area of skin marked by redness and inflammation, which might either remain localized or spread across a wider region. The skin might also show signs of swelling and feel notably warm to the touch, often accompanied by tenderness or pain. Additionally, the affected area might exhibit changes like a shiny appearance or tightness, indicative of the infection's impact on the skin. Occasionally, cellulitis might also bring on a fever. This condition is characterized by an acute bacterial infection causing inflammation in the deep dermis and subcutaneous tissues, lacking abscess formation or purulent discharge. The

primary culprits behind this infection are usually beta-hemolytic streptococci, predominantly group A streptococcus [1,9].

If left unaddressed, cellulitis can trigger severe complications, necessitating urgent medical attention. Among these complications is the potential for abscess formation, where pockets of infected fluid or pus may develop, often demanding surgical drainage to facilitate healing. In more serious cases, the infection might progress to the bloodstream, leading to septicemia, a critical and life-threatening condition requiring immediate medical intervention. Additionally, cellulitis can induce lymphangitis, causing inflammation and infection in the lymphatic vessels, often manifesting as red streaks extending from the infected area, warranting supplementary treatment. Moreover, recurrent cellulitis might arise, particularly when underlying causes or predisposing factors remain unmanaged. Addressing recurrent episodes can pose challenges, often requiring prolonged antibiotic prophylaxis for effective management [10].

Treatment for cellulitis typically involves antibiotics, commonly penicillin or cephalosporins like dicloxacillin or Cephalexin, effective against common culprits like *Staphylococcus* and *Streptococcus* species. Yet, antibiotic resistance, particularly with methicillin-resistant *Staphylococcus aureus* (MRSA), poses a growing challenge. MRSA, resistant to many antibiotics, complicates treatment, often requiring alternative antibiotics. This resistance emergence emphasizes the importance of cautious antibiotic use and proper prescribing practices to curb further resistance development. Efforts to combat this issue include ongoing research into new antibiotics and strategies. While antibiotics remain pivotal in cellulitis treatment, responsible use and the pursuit of alternative options are vital in addressing antibiotic resistance's escalating threat [11-14].

Cephalexin, a first-generation cephalosporin, stands as a frontline antibiotic in treating skin infections, notably cellulitis, by impeding bacterial cell wall synthesis and effectively eliminating susceptible bacteria. With a broad spectrum targeting both gram-positive and some gram-negative bacteria, it effectively combats common pathogens like *Staphylococcus aureus* and *Streptococcus pyogenes*, causing skin infections. Clinical trials attest to its efficacy, showcasing comparable performance to other antibiotics like clindamycin and trimethoprim-sulfamethoxazole in managing uncomplicated cellulitis. Studies comparing it to cefuroxime axetil, cefadroxil, azithromycin, and cefdinir also confirm its effectiveness in skin infection treatment, maintaining clinical and bacteriological response rates. Notably, in community-associated methicillin-resistant

*Staphylococcus aureus* (MRSA) infections, Cephalexin demonstrates effectiveness akin to MRSA-active antibiotics like clindamycin, particularly in pediatric skin infections. Its longstanding use and consistent effectiveness position cephalexin as a reliable choice in managing skin infections, notably cellulitis, known for its tolerability and clinical efficacy [15-21].

Increased doses of Cephalexin present a promising avenue in cellulitis treatment, potentially yielding amplified bacterial elimination, accelerated symptom alleviation, and diminished chances of antibiotic resistance. Elevating cephalexin dosages may elevate its concentration within the body, bolstering its ability to eradicate bacteria effectively and hasten symptom resolution, possibly lowering treatment failure risks. Moreover, higher doses might curtail antibiotic resistance by ensuring a robust drug concentration, effectively targeting and eliminating the infecting bacteria. Nevertheless, extensive research is required to define the optimal dosage and assess the prolonged impact of heightened cephalexin doses on cellulitis therapy [16,22,23].

There exists a notable gap in the literature concerning the comprehensive evaluation of high-dose Cephalexin's efficacy, safety, and distinct outcomes in cellulitis management. Current studies predominantly focus on comparing high-dose Cephalexin against standard doses or alternative treatments, lacking comprehensive data on the exclusive outcomes of high-dose cephalexin administration. There is a pressing need for further investigation to comprehensively assess both the effectiveness and safety profiles of high-dose Cephalexin as an independent treatment approach for cellulitis [22,23].

## Method

**Research Design:** A double-blind, randomized pilot experiment was conducted in the hospital for one year. Trial participants got a 7-day prescription of cephalexin 1000 mg four times a day. Another group got a 7-day treatment of Cephalexin 500 mg four times a day. The patients, treating physician, and study team were blinded to each other. Blinding was crucial to reduce bias in reporting patient-relevant outcomes like pain and adverse events. The study team recruited eligible individuals for trial participation via integrative verbal consent. Participants were randomly assigned to high-dose or standard-dose arms (1:1). Computer-generated randomization sequences using a permuted block design with 4-length blocks. A research assistant recorded baseline clinical data during the index ED visit, including vital signs, comorbidities, infection site, erythema area, and pain level, using an 11-point NRS from 0 to 10. All participants were given disposable tape measures and temperature strips to record the

erythema area and temperature during follow-up visits. Follow-up appointments were arranged on days 3 (mid-therapy) and 7 (end-of-therapy). Patients who were unable or denied virtual follow-up were offered in-home or ED follow-up options. Data gathered at mid- and end-of-therapy visits included temperature, heart rate, pain level, and erythema area. On day 7, participants completed a questionnaire to measure blinding, medication adherence, adverse events, and integrated consent procedure satisfaction. After 14 days, research assistants called participants to check for any unscheduled doctor visits or adverse occurrences. The sample size for this pilot research was determined to demonstrate recruiting feasibility. We determined the sample size needed for the next major study. Based on a 20% standard-dose cephalexin failure rate, a multicenter trial would need 80 participants to detect a 5% difference in treatment failures between high-dose and standard-dose Cephalexin.

### Inclusion and Exclusion criteria

#### Inclusion

- Age 18 and above is required for participation.
- Non-purulent cellulitis should be brought to the ED.
- Outpatient oral antibiotic treatment requires approval by the emergency physician.

#### Exclusion

- Patients on oral antibiotics at presentation.
- Cellulitis with abscesses needs incision and drainage.
- Methicillin-resistant *Staphylococcus aureus* cellulitis instances.
- Cellulitis from animal or human wounds.

**Statistical Analysis:** The study has used SPSS 27 for effective analysis. All data was input into a

secure web-based system. Using descriptive statistics, baseline demographic and clinical variables were reported. Both primary and secondary feasibility and effectiveness results were presented using frequency and percentage. As a pilot experiment, no statistical significance testing was used to compare results across groups, per pilot study guidelines. Analysis followed an intention-to-treat procedure. MS Excel was used for creating graphs and other calculations. The continuous data were expressed as standard deviation, while the discrete data were expressed as frequency and its respective percentage. The level of significance was considered to be  $p < 0.05$ .

### Result

The screening process included 882 patients. However, 182 were not included because they showed up outside of normal business hours. At enrollment, 700 participants were evaluated for eligibility, excluding 600. Exclusions included not fulfilling inclusion criteria ( $n=500$ ), refusing to participate ( $n=81$ ), and missing cases (19). One hundred people were randomly from the pool. Due to alternative diagnoses, 15 for venous insufficiency and 1 for contact dermatitis, 16 were eliminated. Two groups of 42 subjects received Cephalexin 500 mg plus placebo and 1000 mg. Two individuals should have attended follow-up appointments. For treatment failure, 40 patients in the Cephalexin 500 mg and 1000 mg groups were examined. The flowchart in Figure 1 shows the study's allocation and inclusion procedure. This detailed breakdown shows the thorough screening, enrollment, and assessment methods, including the meticulous allocation of individuals into intervention groups and follow-up evaluations to evaluate treatment effects.

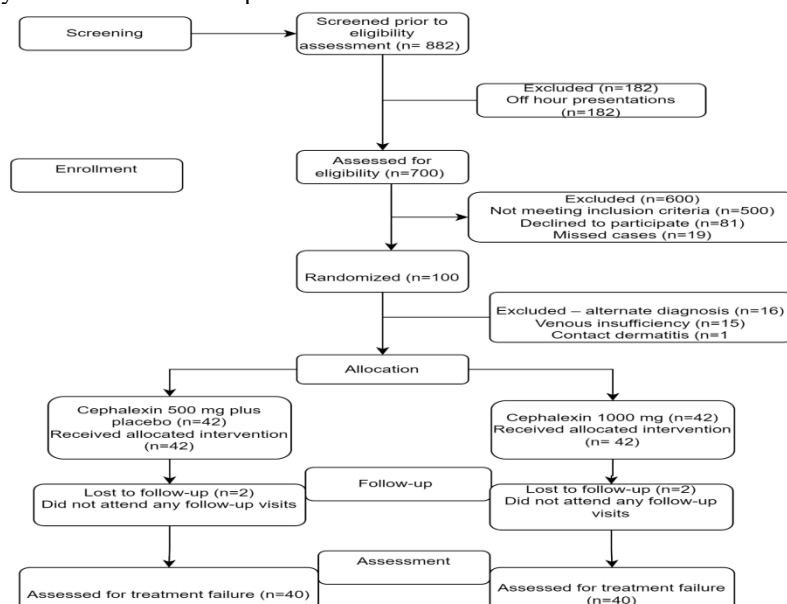


Figure 1: Flowchart showing allocation and inclusion of patients.

Table 1 outlines the baseline demographic characteristics of patients with cellulitis in the study, categorized by the two treatment groups - Cephalexin 500 mg plus placebo and Cephalexin 1000 mg. The median age for both groups is comparable, with 56 years (IQR: 40–68) for the former and 57 years (IQR: 35–70) for the latter. In terms of gender distribution, the percentage of female participants is slightly higher in the Cephalexin 1000 mg group (25.00%) compared to

the Cephalexin 500 mg plus placebo group (17.5%). The median Body Mass Index (BMI) shows a higher value for the Cephalexin 1000 mg group (31.6 kg/m<sup>2</sup>, IQR: 25.5–35.7) compared to the Cephalexin 500 mg plus placebo group (28.8 kg/m<sup>2</sup>, IQR: 22.3–30.7). While the differences in age, gender, and BMI seem relatively small, they are essential to consider when assessing the baseline characteristics of the study population.

**Table 1: Baseline demographic characteristics of patients with cellulitis in this study**

Baseline characteristic	Cephalexin 500 mg plus placebo N=40 (50.00%)	Cephalexin 1000 mg N=40 (50.00%)
Age (years), median (IQR)	56 (40–68)	57 (35–70)
Female sex, n (%)	7 (17.5%)	10 (25.00%)
Body Mass Index (kg/m <sup>2</sup> ), median (IQR)	28.8 (22.3–30.7)	31.6 (25.5–35.7)

Table 2 presents baseline comorbidities among patients with cellulitis in the Cephalexin 500 mg plus placebo and Cephalexin 1000 mg groups. Notably, the prevalence of obesity is higher in the Cephalexin 1000 mg group (50.00%) compared to the Cephalexin 500 mg plus placebo group (30.00%). Diabetes mellitus is more prevalent in the higher dosage group (22.5%) than in the lower dosage group (5.00%). Other comorbidities, such

as prior cellulitis in the past 12 months, chronic kidney disease, congestive heart failure, coronary artery disease, injection drug use, chronic venous insufficiency, and HIV, show varying prevalence between the two groups. These differences in baseline comorbidities highlight the importance of considering the patient's overall health status when analyzing treatment outcomes.

**Table 2: Baseline comorbidities as found in this study**

Baseline Comorbidity	Cephalexin 500 mg plus placebo N=40 (50.00%)	Cephalexin 1000 mg N=40 (50.00%)
Obesity	12 (30.00%)	20 (50.00%)
Diabetes mellitus	2 (5.00%)	9 (22.5%)
Prior cellulitis in the past 12 months	5 (12.5%)	3 (7.5%)
Chronic kidney disease	2 (5.00%)	3 (7.5%)
Congestive heart failure	4 (10.00%)	2 (5.00%)
Coronary artery disease	7 (17.5%)	1 (2.5%)
Injection drug use	1 (2.5%)	2 (5.00%)
Chronic venous insufficiency	5 (12.5%)	2 (5.00%)
HIV	1 (2.5%)	0 (0.0%)

Table 3 outlines baseline vital signs and laboratory test results for patients in the Cephalexin 500 mg plus placebo and Cephalexin 1000 mg groups. Triage vital signs, including temperature, heart rate, respiratory rate, and systolic and diastolic blood pressure, exhibit some variations between the two groups. For example, the median temperature is higher in the Cephalexin 1000 mg group, as is the heart rate. Laboratory tests, such as white blood

cell (WBC) count and serum creatinine, also demonstrate differences, with higher values observed in the Cephalexin 1000 mg group. These variations in vital signs and laboratory values indicate potential differences in the severity of cellulitis or the patient's physiological response to the infection, which could impact treatment outcomes.

**Table 3: Baseline recordings of vital signs and laboratory tests**

Baseline Vital Signs and Lab Tests	Cephalexin 500 mg plus placebo N=40 (50.00%)	Cephalexin 1000 mg N=40 (50.00%)
Triage vital signs, median (IQR)		
Temperature (°C)	36.8 (36.6–36.8)	37.7 (37.137.1)
Heart rate (beats/min)	84 (71–92)	91 (78–98)
Respiratory rate (breaths/min)	17 (17–19)	19 (16–18)
Systolic blood pressure (mmHg)	138.5 (128–152)	135 (125–149)
Diastolic blood pressure (mmHg)	83 (72–91)	83 (72–87)

Laboratory tests, median (IQR)		
WBC count ( $\times 10^9/L$ )	6.8 (5.3–7.4)	8.8 (7.9–10.9)
Serum creatinine ( $\mu\text{mol/L}$ )	64 (51–98)	79 (65–109)

Table 4 provides information on the site of cellulitis among patients in the Cephalexin 500 mg plus placebo and Cephalexin 1000 mg groups. The majority of cases in both groups involve cellulitis on the lower limbs, with a higher percentage in the Cephalexin 1000 mg group (75.00%) compared to the Cephalexin 500 mg plus placebo group

(62.5%). The distribution of cellulitis on the upper limb, face, torso, and groin varies between the two groups. These differences in the site of cellulitis may be relevant when evaluating treatment responses, as the location of infection can impact the clinical course and outcomes.

**Table 4: Site of cellulitis as found among the patients**

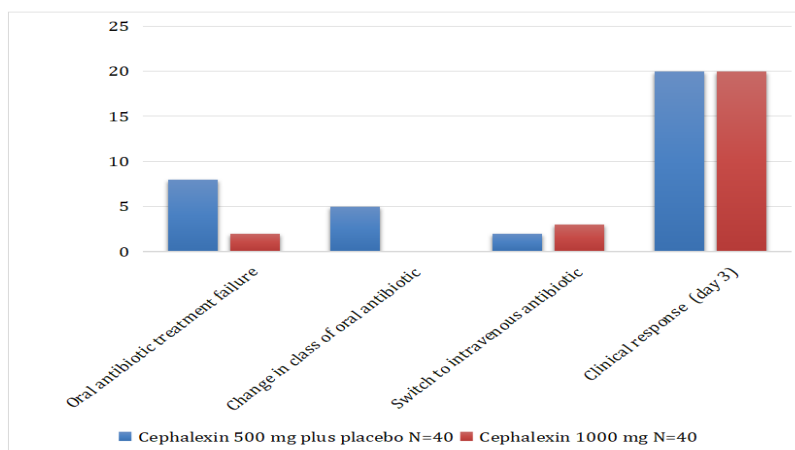
Site	Cephalexin 500 mg plus placebo N=40 (50.00%)	Cephalexin 1000 mg N=40 (50.00%)
Lower limb	25 (62.5%)	30 (75.00%)
Upper limb	10 (25.00%)	8 (20.00%)
Face	2 (5.00%)	2 (5.00%)
Torso	1 (2.5%)	5 (12.5%)
Groin	0 (0.0%)	2 (5.00%)

Figure 2 presents the outcomes of two groups receiving different dosages of Cephalexin (an antibiotic) in a clinical trial, with a sample size of 40 participants for each dosage group. The outcomes are categorized into various effectiveness measures. In the Cephalexin 500 mg plus placebo group, 8 participants experienced oral antibiotic treatment failure, while only 2 participants in the Cephalexin 1000 mg group had treatment failure. This suggests that the higher dosage of Cephalexin (1000 mg) may be more effective in preventing oral antibiotic treatment failure compared to the lower dosage. Regarding the change in the class of oral antibiotics, 5 participants in the Cephalexin 500 mg plus placebo group had a change.

plus placebo group and 3 participants in the Cephalexin 1000 mg group required such a switch. The difference is not substantial, but it suggests that a few participants in both groups needed escalation to intravenous antibiotics, with slightly more in the higher dosage group. The clinical response on Day 3 was similar in both groups, with 20 participants in each group exhibiting a positive clinical response. This indicates that both dosages of Cephalexin were effective in eliciting a clinical response by the third day of treatment.

In contrast, none in the Cephalexin 1000 mg group required such a change. This implies that the higher dosage group had a more stable course of treatment without the need to switch to a different class of oral antibiotics. For the switch to intravenous antibiotics, 2 participants in the Cephalexin 500 mg

plus placebo group and 3 participants in the Cephalexin 1000 mg group required such a switch. The difference is not substantial, but it suggests that a few participants in both groups needed escalation to intravenous antibiotics, with slightly more in the higher dosage group. The clinical response on Day 3 was similar in both groups, with 20 participants in each group exhibiting a positive clinical response. This indicates that both dosages of Cephalexin were effective in eliciting a clinical response by the third day of treatment.



**Figure 2: Outcome of patients in each group**



Figure 3 displays the clinical cure rates for two different dosages of Cephalexin (an antibiotic) in a clinical trial with a sample size of 40 participants for each dosage group. The clinical cure rates are reported at two different time points, Day 7 and Day 14. For the Cephalexin 500 mg plus placebo group, the clinical cure rate on Day 7 was 7 participants out of 40, and this rate remained the same on Day 14. This suggests that, by Day 7, seven participants in this group had achieved clinical cure, and this level of cure was sustained through Day 14. In

the Cephalexin 1000 mg group, the clinical cure rate on Day 7 was also 7 participants out of 40. However, by Day 14, the clinical cure rate increased to 15 participants out of 40. This indicates that while both dosage groups had the same clinical cure rate on Day 7, the higher dosage of Cephalexin (1000 mg) led to an increase in the number of participants achieving clinical cure by Day 14 compared to the Cephalexin 500 mg plus placebo group.

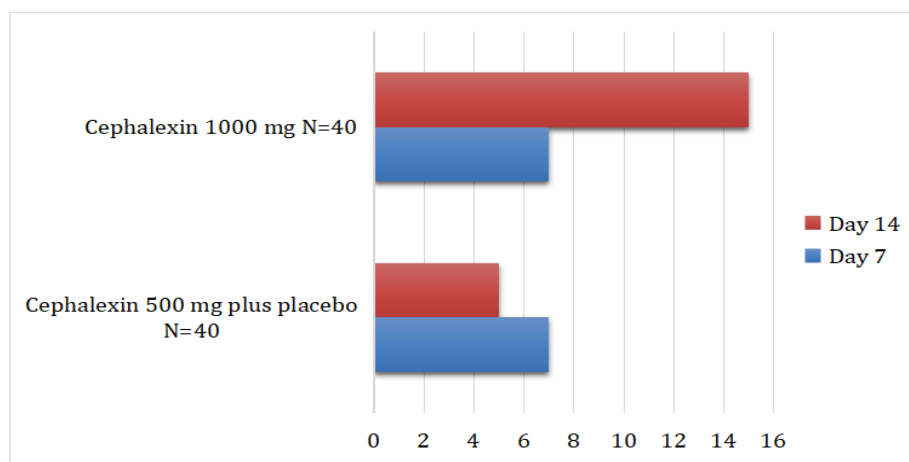


Figure 3: Condition cured at follow-up study in each group

Figure 4 presents data on adverse events associated with two different dosages of Cephalexin (an antibiotic) in a clinical trial, with a sample size of 40 participants for each dosage group. The adverse events are categorized, and the number of occurrences is provided for each category, along with the corresponding p-values for statistical significance. For the Cephalexin 500 mg plus placebo group, the number of participants experiencing nausea or vomiting was 6; diarrhoea was reported by 1 participant, abdominal pain by 2 participants, and other adverse events by 1 participant. No participants in this group reported experiencing a rash. The total number of adverse events in this group was 10, and the p-value for all adverse events combined was 0.054. In the Cephalexin 1000 mg group, the number of participants experiencing nausea or vomiting

was 7; diarrhoea was reported by 4 participants, abdominal pain by 3 participants, and a rash by 1 participant. One participant in this group reported other adverse events. The total number of adverse events in this group was 16, and the p-value for all adverse events combined was 0.054. The p-values indicate the level of statistical significance for the observed differences in adverse events between the two dosage groups. Notably, some specific adverse events, such as abdominal pain, diarrhoea, and the total number of adverse events, show p-values below the conventional significance threshold of 0.05, suggesting a potential difference between the two dosage groups in these aspects. However, it's important to interpret these results cautiously and consider the clinical relevance of the observed differences in addition to statistical significance.

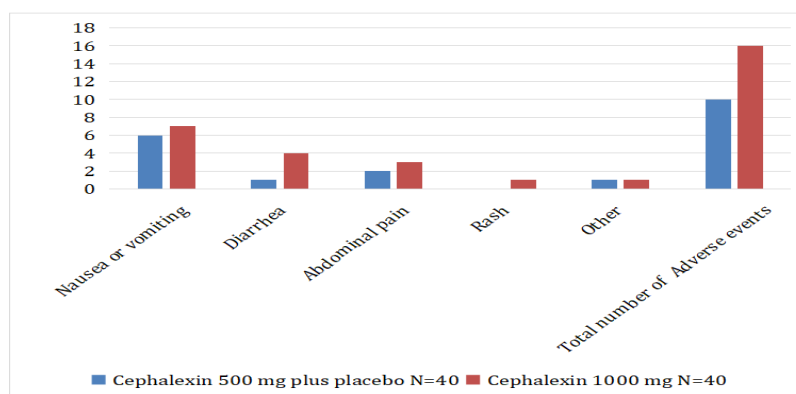


Figure 4: Number of adverse events

## Discussion

In the realm of Emergency Departments (EDs), skin and soft tissue infections like non-purulent cellulitis contribute to around 3% of all visits, with a treatment failure rate hovering at roughly 20%. There needs to be more clear evidence on the best outpatient management for cellulitis, prompting an exploration into a potential solution. The primary aim was to ascertain the viability of a randomized trial comparing high-dose (1000 mg) versus standard-dose (500 mg) cephalexin for treating ED-presenting cellulitis. In a dual-site, double-masked pilot trial by Yadav et al. (2023) across Canadian EDs, 69 out of 134 eligible participants (51.5%, 95% CI 43.1 to 59.8%) were successfully recruited and randomized. After exclusions, 33 participants were allocated to each arm, with 19 eligible cases (14.2%) inadvertently overlooked. The follow-up loss was marked at 6.1%. Treatment failure figures stood at four patients (12.9%) in the standard-dose group versus one patient (3.2%) in the high-dose cohort. Notably, minor adverse effects were more prevalent in the high-dose arm. Encouragingly, there were no unplanned hospitalizations within 14 days [22].

In a retrospective cohort study by Trottier et al. (2022) focusing on children treated for moderate cellulitis at the emergency department (ED), a specific guideline emphasizing high-dose (HD) oral Cephalexin was employed over 2 years. Among 123 included children, 117 were administered HD oral cephalexin following the guideline. Impressively, the treatment showed a success rate of 89.7% (105 out of 117). However, 12 children (10.3%) experienced treatment failure, with 10 necessitating admission, 1 requiring IV antibiotics at the medical day hospital (MDH), and 1 revisiting the ED without admission. Notably, there were no reported severe complications, although drainage was required for four abscesses, and one patient developed a rash. On average, each child had 1.6 visits (SD 1.0) to the MDH. These findings suggest that HD oral cephalexin exhibits effectiveness and safety in managing moderate cellulitis among children, potentially curbing hospitalization rates and diminishing the need for intravenous interventions [23].

Various studies have highlighted adverse effects associated with cephalexin usage. Commonly reported gastrointestinal disturbances like diarrhoea, nausea, and vomiting have emerged as frequent side effects observed in studies. Interestingly, these effects manifest irrespective of whether standard or high doses of Cephalexin are administered. Allergic reactions, indicated by manifestations like rash, itching, and hives, have also been documented in cephalexin use, demonstrating occurrence across both standard and high doses. Additionally, less common side effects

encompassing symptoms such as headache, dizziness, and alterations in taste perception have been noted in certain instances of cephalexin administration [24,25].

The exploration of high-dose Cephalexin's impact on bacterial eradication and antibiotic resistance development is ongoing. Studies have pointed to Cephalexin's efficacy in combating streptococcal and staphylococcal skin infections, showcasing cure rates surpassing 90%. Moreover, its successful application in managing uncomplicated skin abscesses, even in cases involving methicillin-resistant *Staphylococcus aureus* (MRSA), further underlines its effectiveness [26,27].

Determining the optimal dosing for high-dose Cephalexin revolves around identifying the most potent and safe dosage regimen to attain desired treatment outcomes. High-dose Cephalexin involves administering a higher quantity of the antibiotic compared to the standard dosage. For instance, it was found in a trial for cellulitis treatment compared 1000 mg of Cephalexin was taken four times daily for a week to the standard 500 mg dosage taken four times daily. The findings revealed that while high-dose Cephalexin showcased fewer treatment failures, it also correlated with a higher occurrence of minor adverse effects in contrast to the standard dosage. This indicates a potential for increased efficacy in treating cellulitis with high-dose Cephalexin, yet it also raises concerns about a higher risk of adverse effects [22].

The utilization of Cephalexin for cellulitis encounters multifaceted challenges. Evolving antibiotic resistance poses a significant concern, particularly with the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA). Despite Cephalexin's effectiveness against numerous bacterial strains, its limitations in addressing MRSA or other resistant organisms raise apprehensions. Determining the optimal cephalexin dosage remains a debated subject for cellulitis treatment. While some studies delve into high-dose Cephalexin, determining the most potent dosing regimen necessitates further investigation. Treatment failure persists as a potential outcome despite Cephalexin's efficacy. Various factors, including the cellulitis severity, concurrent health conditions, and patient adherence to treatment, contribute to this possibility. Given the escalating antibiotic resistance, exploring alternative options for cellulitis treatment becomes imperative. Antibiotics like trimethoprim-sulfamethoxazole and clindamycin, exhibiting efficacy against community-associated MRSA, emerge as potential preferences in specific cases [22,23,28,29].

Future research avenues on Cephalexin's role in cellulitis management encompass expansive comparative trials, contrasting its efficacy and safety against trimethoprim-sulfamethoxazole or clindamycin. Delving into optimal dosing strategies, including treatment duration and frequency, aims to refine the most effective and convenient regimens. Assessing Cephalexin's influence on antibiotic resistance in cellulitis-causing bacteria, notably methicillin-resistant *Staphylococcus aureus* (MRSA), informs prudent antibiotic stewardship. Tailoring treatment for specific demographics like children, elderly individuals, pregnant women, or those with coexisting conditions, such as diabetes, is vital for personalized care. Exploring combination therapies involving Cephalexin and other agents targeting resistant bacteria seeks potential synergies to bolster cellulitis management strategies [11,16,22,26,29,30].

### Conclusion

The study has concluded that Cephalexin at a higher dose is significantly effective, with minor adverse events that may be a little higher than the usual dose. In summary, the study results suggest that a higher dosage of Cephalexin (1000 mg) may be more effective in preventing oral antibiotic treatment failure and reducing the need for a change in the class of oral antibiotics compared to the lower dosage (500 mg plus placebo). However, the clinical response on Day 3 appears comparable between the two dosage groups, indicating that both dosages effectively elicit an early positive response. Furthermore, the clinical cure rates on Day 14 demonstrate a notable advantage for the higher dosage group, with a significant increase compared to both groups' similar cure rates on Day 7. This implies that the 1000 mg dosage leads to a more sustained and improved clinical cure throughout the study. Examining adverse events, while there are numerical differences in specific occurrences between the groups, the statistical significance (p-values) suggests caution in interpreting these differences. Although some events show potential significance, the overall context of the study and the clinical relevance of observed variations should be considered.

In conclusion, these findings provide valuable insights into the effectiveness, cure rates, and safety profiles associated with different dosages of Cephalexin for cellulitis treatment. The higher dosage appears advantageous in certain aspects, emphasizing the need for careful consideration of the study context and potential confounding factors when interpreting the results. This study contributes to ongoing discussions on optimal cephalexin dosages for cellulitis treatment, paving the way for further exploration and refinement of treatment strategies.

### References

1. H. Buck B, Akhtar N, Alrohim A, Khan K, Shuaib A. Stroke mimics: incidence, aetiology, clinical features and treatment. *Annals of Medicine*. 2021;53(1):420-36.
2. Raff, A. B., & Kroshinsky, D. Cellulitis: A review. *JAMA: The Journal of the American Medical Association*, 2016;316(3):325-37.
3. Gunderson, C. G. Cellulitis: Definition, aetiology, and clinical features. *The American Journal of Medicine*, 2011;124(12):1113–1122.
4. Ellis Simonsen, S. M., Van Orman, E. R., Hatch, B. E., Jones, S. S., Gren, L. H., Hegmann, K. T., & Lyon, J. L. Cellulitis incidence in a defined population. *Epidemiology and Infection*, 2006;134(2):293–299.
5. Burian, E. A., Karlsmark, T., Franks, P. J., Keeley, V., Quéré, I., & Moffatt, C. J. Cellulitis in chronic oedema of the lower leg: an international cross-sectional study. *The British Journal of Dermatology*, 2021; 185(1):110–118.
6. Njim, T., Aminde, L. N., Agbor, V. N., Toukam, L. D., Kashaf, S. S., & Ohuma, E. O. Risk factors of lower limb cellulitis in a level-two healthcare facility in Cameroon: a case-control study. *BMC Infectious Diseases*, 2017;17(1):418.
7. Tianyi, F.-L., Mbang, C. M., Danwang, C., & Agbor, V. N. Risk factors and complications of lower limb cellulitis in Africa: a systematic review. *BMJ Open*, 2018;8(7):e021175.
8. Sanglodkar, U., Jain, M., Jothimani, D., Parida, S. Balajee, & Venkataraman, J. Cellulitis in liver cirrhosis – a series of 25 cases from southern India. *Clinical and Experimental Hepatology*, 2018;4(3):201–204.
9. Boettler, M. A., Kaffenberger, B. H., & Chung, C. G. Cellulitis: A review of current practice guidelines and differentiation from pseudocellulitis. *American Journal of Clinical Dermatology*, 2022;23(2):153–165.
10. Bystritsky, R. J. Cellulitis. *Infectious Disease Clinics of North America*, 2021;35(1):49–60.
11. Bailey, E., & Kroshinsky, D. Cellulitis: diagnosis and management: *Cellulitis. Dermatologic Therapy*, 2011;24(2):229–239.
12. Muhaj, F. F., George, S. J., & Tying, S. K. Bacterial antimicrobial resistance and dermatological ramifications. *The British Journal of Dermatology*, 2022;187(1):12–20.
13. Spellberg, B. The future of antibiotics. *Critical Care (London, England)*, 2014;18(3):228.
14. Rrapi, R., Chand, S., & Kroshinsky, D. Cellulitis. *The Medical Clinics of North America*, 2021;105(4):723–735.
15. Parish, L. C., Routh, H. B., Miskin, B., Fidelholtz, J., Werschler, P., Heyd, A.,



- Haverstock, D., & Church, D. Moxifloxacin versus Cephalexin in the treatment of uncomplicated skin infections. *International Journal of Clinical Practice*, 2000;54(8):497-503.
16. Moran, G. J., Krishnadasan, A., Mower, W. R., Abrahamian, F. M., LoVecchio, F., Steele, M. T., Rothman, R. E., Karras, D. J., Hoagland, R., Pettibone, S., & Talan, D. A. Effect of Cephalexin plus trimethoprim-sulfamethoxazole vs Cephalexin alone on clinical cure of uncomplicated cellulitis: A randomized clinical trial. *JAMA: The Journal of the American Medical Association*, 2017; 317(20):2088-2096.
  17. Tack, K. J., Littlejohn, T. W., Mailloux, G., Wolf, M. M., & Keyserling, C. H. Cefdinir versus Cephalexin for the treatment of skin and skin-structure infections. *Clinical Therapeutics*, 1998; 20(2):244-256.
  18. Gooch, W. M., III, Kaminester, L., Cole, G. W., Binder, R., Morman, M. R., Swinehart, J. M., Wisniewski, M., Yilmaz, H. M., & Collins, J. J. Clinical comparison of cefuroxime axetil, Cephalexin and cefadroxil in the treatment of patients with primary infections of the skin or skin structures. *Dermatology (Basel, Switzerland)*, 1991;183(1):36-43.
  19. Kiani, R. Double-blind, double-dummy comparison of azithromycin and Cephalexin in the treatment of skin and skin structure infections. *European Journal of Clinical Microbiology & Infectious Diseases: Official Publication of the European Society of Clinical Microbiology*, 1991;10(10):880-884.
  20. Giordano, P. A., Elston, D., Akinlade, B. K., Weber, K., Notario, G. F., Busman, T. A., Cifaldi, M., & Nilius, A. M. Cefdinir vs. Cephalexin for mild to moderate uncomplicated skin and skin structure infections in adolescents and adults. *Current Medical Research and Opinion*, 2006; 22(12): 2419-2428.
  21. Murphy SJ, Werring DJ. Stroke: causes and clinical features. *Medicine*. 2020; 48(9):561-6
  22. Yadav, K., Eagles, D., Perry, J. J., Taljaard, M., Sandino-Gold, G., Nemnom, M.-J., Corrales-Medina, V., Suh, K. N., & Stiell, I. G. High-dose cephalexin for cellulitis: a pilot randomized controlled trial. *CJEM*, 2023; 25(1):22-30.
  23. Trottier, E. D., Farley St-Amand, B., Vincent, M., Chevalier, I., Autmizguine, J., Tremblay, S., & Gouin, S. Outpatient management of moderate cellulitis in children using high-dose oral Cephalexin. *Paediatrics & Child Health*, 2022; 27(4):213-219.
  24. Browning, A. K. The efficacy of twice daily Cephalexin. *PharmacoTherapeutic*, 1981; 2(9): 559-64.
  25. Bathini, L., Jandoc, R., Kuwornu, P., McArthur, E., Weir, M. A., Sood, M. M., Battistella, M., Muanda, F. T., Liu, A., Jain, A. K., & Garg, A. X. Clinical outcomes of failing to dose-reduce cephalosporin antibiotics in older adults with CKD. *Clinical Journal of the American Society of Nephrology: CJASN*, 2019; 14(2):197-205.
  26. Derrick, C. W., & Reilly, K. The role of Cephalexin in the treatment of skin and soft-tissue infections. *Postgraduate Medical Journal*, 1983;59 Suppl 5:43-6.
  27. Rajendran, P. M., Young, D., Maurer, T., Chambers, H., Perdreau-Remington, F., Ro, P., & Harris, H. Randomized, double-blind, placebo-controlled trial of Cephalexin for treatment of uncomplicated skin abscesses in a population at risk for community-acquired methicillin-resistant *Staphylococcus aureus* infection. *Antimicrobial Agents and Chemotherapy*, 2007;51(11):4044-4048.
  28. Khawcharoenporn, T., & Tice, A. Empiric outpatient therapy with trimethoprim-sulfamethoxazole, Cephalexin, or clindamycin for cellulitis. *The American Journal of Medicine*, 2010;123(10):942-950.
  29. Kaufman, K. R., Thurber, K. M., O'Meara, J. G., Langworthy, D. R., & Kashiwagi, D. T. Evaluation of cephalexin failure rates in morbidly obese patients with cellulitis. *Journal of Clinical Pharmacy and Therapeutics*, 2016; 41(4):409-413.