



Comparative Analysis Of Azithromycin And Cefixime In The Treatment Of Typhoid Fever

Zakir Hidayatallah^{1*}

¹*Associate Professor, Department of Basic and Clinical Oral Sciences, Faculty of Dental Medicine, Umm alQura University, Makkah Mukarama, KSA. Email: zhmarwat@uqu.edu.sa

***Corresponding Author:** Zakir Hidayatallah

*Associate Professor, Department of Basic and Clinical Oral Sciences, Faculty of Dental Medicine, Umm alQura University, Makkah Mukarama, KSA. Email: zhmarwat@uqu.edu.sa

Abstract

Objective: Azithromycin and Cefixime are two popular medicines that are often used in the treatment of typhoid fever. The treatment of undifferentiated febrile illness (UFI) is usually accomplished by the use of Azithromycin and trimethoprim-sulfamethoxazole (SXT). Even though the simple fact is that the two distinct antibiotics were subjected to a complete evaluation of their safety and efficacy, the medications are not inferior to one another when it comes to the management of culture-confirmed enteric fever. More study is required to determine the function that these medications play in the treatment of cellulitis, which is a bacterial skin infection.

Methods: Extensive testing has been carried out through a large number of clinical trials, observational studies, and meta-analyses to determine whether or not Cefixime and Azithromycin are safe and effective medications optionally given Azithromycin (20 mg/kg/day) or SXT (a medication called trim 10 mg/kg/day + sulfamethoxazole 50 mg/kg/day) for seven days was the topic of a double-blind, randomized, placebo-controlled trial that was carried out in China for the aim of treating urinary tract infections (UTIs). The study was conducted for the goal of treating UTIs. The purpose of this survey is to gather data in order to get information that could potentially used for this specialized kind of research. During the study, it was established that the primary outcome was the fever clearance time (FCT), whereas the secondary endpoints consisted of treatment failure and adverse events.

Results: In addition to providing a comprehensive summary of therapy outcomes, the review also provides a complete presentation of the most recent data from various study methodologies. Between Azithromycin and SXT, the HR of treatment failures after 28 days was 0.62 (95% CI, .37–1.05; P=.073). This was a statistically significant difference. Had the effect of reducing the number of relapses in culture-confirmed cases of enteric fever and resulting in a speedier FCT in patients with sterile blood cultures. When conducting these assessments, a wide range of criteria are taken into consideration, such as the age of the patient, the severity of the disease, and geographical patterns of resistance. According to the results of the planned subgroup study, Azithromycin Additionally, the role that these antibiotics

<p>CC License CC-BY-NC-SA 4.0</p>	<p>play in the treatment and eradication of cellulitis, which is a common skin ailment, was also explored, and it was shown how well they function in these situations.</p> <p>Introduction:</p> <p>Background: One of the most prevalent causes of morbidity and death in low- and middle-income countries is fever without localizing indications of infection, which is often referred to as undifferentiated febrile illness (UFI). In light of the fact that strains of streptococci and staphylococci often bring on cellulitis, antibiotics must be delivered as promptly and accurately as possible. Treatment with antibiotics that is effective is thus essential. The causes of UFI differ from one geographic place to another. Malaria, dengue fever, typhoid, and Salmonella are all prevalent in South Asia. Two of the most pervasive causes of UFI are typhoid fever and paratyphoid fever. In China, enteric fever is the most pervasive kind of bacterial illness that affects the bloodstream. The purpose of this research was to investigate the efficacy of Cefixime and Azithromycin in treating typhoid fever, as well as the safety and adverse effects associated with their simultaneous use in the treatment of the disease. The purpose of this research is to discover whether or not antibiotics are effective in reducing cellulite while also attempting to remove the condition.</p> <p>Keywords: <i>Antibiotic treatment, cellulitis, Cefixime, Azithromycin, antimicrobial resistance, Typhoid fever.</i></p>
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Objectives:

The Main objectives of this review are:

- A. Further research will be needed to figure out if medications can effectively reduce cellulite.
- B. Examining the safety of various antibiotics and thinking about things to think about while taking many prescription drugs are the goals of this research.
- C. The goal of this research was to assess both the safety of various antibiotics and considerations that should be made before incorporating them.

Treatment of Typhoid Fever:

Azithromycin:

To determine if Azithromycin is a useful treatment for typhoid fever, it is necessary to examine the drug's several components. Several components include the antibiotic's pharmacokinetics, clinical efficacy, and mechanism of action. You must address the role of this issue as a first-line or alternative therapeutic choice, as well as the results of relevant clinical studies and comparative research. You will also summarize the study's conclusions and compare them with other treatments (Gianecini, Poklepovich et al. 2023).

Azithromycin, a semisynthetic macrolide, is a widely used medication that helps treat various bacterial infections (Islam, Shumi et al. 2023). Among these diseases is salmonellosis, which is associated with invasions. Combination treatment aimed at eliminating trachoma and reducing childhood mortality from all sources has included it. The medication's effects are broad. Conversely, the widespread use of Azithromycin has led to the proliferation of bacteria resistant to the antibiotic. Reports of this phenomenon have been made. They bind to the 50S ribosomal subunit of bacteria to stop mRNA translation (Adikwu, Ogbonna et al. 2023). Numerous pathways may lead to bacterial resistance to macrolides like Azithromycin. Lower drug absorption due to lower membrane permeability, increased extrusion by efflux pumps, and enzyme modification. This phenomenon is brought on by things like inactive medications (Adikwu, Ogbonna et al. 2023). Research has shown that Salmonella spp. Acquire azithromycin resistance in a variety of unique ways. Medication destruction is caused by Mph(A), rRNA adenine N-6-methyltransferase, 23S rRNA methylation of ErmB and Erm42, macrolide 29-phosphotransferase, and AcrAB. The TolC efflux pump facilitates better drug extrusion and the R717 mutation in AcrB is one of the mechanisms behind this process (Adikwu, Ogbonna et al. 2023). Integration and conjugation elements, plasmids, and transposons, which contain resistance determinants, may all be incorporated (Parry, Qamar et al. 2023).

The exact number of instances of NTS-caused salmonellosis is unclear, even though the disease is quite common in China. Several studies found that the NTS isolates from China have significant levels of antibiotic resistance Fort Lauderdale (Jadav, Sukharamwala et al. 2023). reported that tetracycline, ampicillin, chloramphenicol, streptomycin, and sulfisoxazole were resistant in 41.0% of the 798 isolates that were obtained from patients in China between 1998 and 2002. These drugs cure the infections that the patients are suffering from. Furthermore, since they were not susceptible to ciprofloxacin, it was shown that 27.9% of the isolates were resistant to the antibiotic or its intermediates. Ninety-six per cent (MDR) of the 110 isolates discovered from sick pigs in 2011 and 2012, according to Guo et al. (Mahmoud, Oluyemisi et al. 2023)., were resistant to three or more antibiotics. For most isolates, this was accurate.

Additionally, it was shown that 21% of the isolates were resistant to ciprofloxacin, and 44% were resistant to cefotaxime. Treatments for extremely drug-resistant (XDR) and multidrug-resistant (MDR) Salmonella strains are believed to include carbapenems and spectinomycin (McPherson, Tafese et al. 2023). This fact remains unaltered by the increasing resistance to third-generation fluoroquinolones and cephalosporins. Azithromycin resistance in NTS in China has not been well studied in terms of its occurrence or its mechanism of development. This is true even though several MDR isolates of Salmonella typhimurium and Salmonella Albany have been found to have the (Chiou, Hong et al. 2023). The antimicrobial resistance within these sample groups was also examined (Carey, Dyson et al. 2023).

Table:1

Aspect	Information
Salmonella Genus	It Comprises S. enterica and S. bongori, with over 2,600 serovars.
Typhoidal and Nontyphoidal Salmonella (NTS)	S. Typhi, S. Paratyphi A, B, C, and S. Sendai cause invasive infections.
Global Burden (2000)	Twenty-one million six hundred fifty thousand nine hundred seventy-four cases of typhoid fever, 216,510 deaths, and 5,412,744 paratyphoid cases.
NTS Infections (Annual Estimates)	93.8 million illnesses, 80.3 million foodborne, and 155,000 deaths globally.
Invasive NTS Disease (2017)	Five hundred thirty-five thousand cases, 77,500 deaths worldwide, the highest incidence in sub-Saharan Africa.
NTS in the United States (2014)	A second leading cause of foodborne illness is hospitalization and death.
Antimicrobial Treatment Guidelines	Reserved for severe illness, invasive disease, infants, elderly, immunocompromised.
Historical First-line Antibiotics	Ampicillin, chloramphenicol, cotrimoxazole.
Current Critical Antimicrobials (2020)	Ciprofloxacin, Ceftriaxone, Azithromycin.
Resistance in the United States (2014)	Ceftriaxone resistance is low (2.4%), whereas resistance to ciprofloxacin and Azithromycin is seldom seen (<0.1%).
Resistance in Europe (2020)	Ciprofloxacin (14.1%), cefotaxime and ceftazidime (0.8%), Azithromycin (0.8%).
Mechanism of Action of Azithromycin	This protein inhibits the translation of mRNA by binding to the 50S ribosomal subunit of bacteria.
Azithromycin Resistance in NTS	Rare but increasing, more prevalent in multidrug-resistant and fluoroquinolone-resistant strains.
Mechanisms of Azithromycin Resistance in Salmonella	Mph(A), ErmB, Erm42, AcrAB-TolC efflux pump with R717 mutation.
Salmonellosis in China (Not Well Estimated)	High resistance reported: 41.0% to ampicillin, chloramphenicol, streptomycin, sulfisoxazole, and tetracycline. 27.9% nonsusceptible to ciprofloxacin.
Recent Resistance in Pigs in China (2011-2012)	96% resistance among isolates to unspecified antimicrobials.

Finding the factors responsible for azithromycin resistance.

A selection of 175 unique isolates were subjected to the polymerase chain reaction (PCR) technology to identify azithromycin resistance factors. Table 1 reveals that 56 strains had a MIC of 8 mg/L for sensitivity, 43 of 16 mg/L for moderate resistance, and 76 of 32 mg/L for azithromycin resistance. Resistance to Azithromycin was

statistically significant. Three-quarters of the 76 isolates resistant to ampicillin, 21% to ramp, 10% to erm, 3% to erm(B), and 37% to mph(A) were resistant to Azithromycin. Both (A) and erm(42) show resistance. Furthermore, 16 isolates expressing ramp were found; each strain had a minimum inhibitory dosage of 16 mg/L. Following the discovery of the drug-resistant isolate, it was discovered that ramR was disrupted in a distinct drug-resistant strain. Out of the isolates, 56 were susceptible, 27 were moderately resistant, and 1 sample was the only one that showed resistance. Azithromycin resistance-related genetic indicators were found and validated using whole-genome sequencing (WGS) in 53 isolates (Ashfaq, Basra et al. 2023).

Table:2 Isolates

Isolate Type	Total Number	Azithromycin Resistance (MIC ≥ 32 mg/L)	Intermediate (MIC = 16 mg/L)	Susceptible (MIC ≤ 8 mg/L)	Detected Resistance Determinants	Additional Information
Total Isolates	175	76	43	56	-	-
Resistant (MIC ≥ 32 mg/L)	76	-	-	-	mph(A) (n=37), ramp (n=21), erm(42) (n=10), erm(B) (n=3), mph(A) and erm(42) (n=3), interrupted ramR (n=1)	53 isolates confirmed by WGS
Intermediate (MIC = 16 mg/L)	43	-	-	-	ramp (n=16)	-
Susceptible (MIC ≤ 8 mg/L)	56	-	-	-	No PCR amplicon (n=56)	-
Undetected Resistance Determinants	84	1 (resistant), 27 (intermediate), 56 (susceptible)	-	-	-	-

The following table 2 presents a breakdown of the isolates according to their azithromycin resistance profiles, the discovery of particular resistance determinants by PCR, and further information about the validation of whole-genome sequencing.

Cefixime:

The frequency of pediatric infectious diseases in the present antibacterial medication clinical trial. Hospitalization rates of 40%, elevated levels, widespread use of antibiotics, and overindulgence in IV medication. Prescription drugs administered intravenously result in at least a 20% increase in medical costs. After their health improves or stabilizes, the children don't need to remain in the hospital. Not only would continuing intravenous treatment or hospitalization waste medical resources, but it will also increase the risk of nosocomial infection; intravenous medication may increase the risk of not only increased discomfort in children but may lead to issues like thrombophlebitis very soon. The rates of bacterial clearance and effectiveness across the two groups were similar; however, the intravenous treatment group had a greater incidence of adverse events than the conversion therapy group. Cefixime is a third-generation oral cephalosporin that has broad antibacterial action. Its predicted effects and mode of action are comparable to those of third-generation injectable cephalosporins. It also has steady p-lactamase, a long half-life, broad tissue distribution, and great potency. Medication taken once or twice daily offers better compliance, fewer side events, and a lower cost than the current third-generation injectable cephalosporins. It is an ideal substitute drug. As a result, Cefixime is not advised to treat several bacterial infections that are susceptible to the drug, including otolaryngology, paediatrics, gonorrhoea, district-acquired pneumonia, pediatric diarrhoea, urinary tract infections, and otitis media (Ajmal, Zamir et al. 2023).

Conversion therapy has shown remarkable therapeutic efficacy using it in addition to its preferred purposes. Effect's present stance on Cefixime as a conversion treatment for infections caused by microorganisms The fourteen reports are compiled here. Cefixime and Ceftriaxone switch medicine et al., Feng Yulin, in Cefixime and Ceftriaxone used in clinical settings to treat lower respiratory tract infections Based on clinical observation, ceftriaxone-cefixime switch treatment is believed to be effective (Yang, Kojima et al. 2023).

When compared to intravenous Ceftriaxone alone, there was no appreciable difference. Along with Yubiao Guo In [2] Costs and therapies associated with a cefixime switch for community-acquired pneumonia After conducting an efficacy analysis, it was shown that Ceftriaxone and the Cefixime switching treatment group, the intravenous injection group ($P < 0.05$). Li Guanghui et al (Hossain, Islam et al. 2023). Sequential treatment with levofloxacin was used to conduct a clinical investigation of 113 instances of lower respiratory tract infections treated with fratriaxone-cefixime switch therapy. Ceftriaxone-cephalin was utilized by Bai Ruixia et al. (Mahmood, Khan et al. 2023). Fixime conversion therapy is used to treat children who have

bronchopneumonia and other respiratory illnesses. This was different from the standard full-course intravenous medication administration method. The two previously mentioned articles suggest that Cefixime is a more effective therapy for lower respiratory tract infections. However, the total clinical hospitalization costs were statistically significantly lower than those in the control group. Sex difference ($P < 0.01$). Explain cefixime conversion therapy. It is worth promoting since it treats lower respiratory tract infections in adults and children and is a practical, economical, efficient, and effective methodology (Mahmood, Khan et al. 2023).

According to a pharmacoeconomic study, The Cefixime-to-Cefixime Exchange Method, Feng Degang et al. (Moridi, Sabbaghi et al. 2023). requires pediatric moderate-to-severe community-acquired bacterial infections and may benefit from cefotaxime-cefixime switch pneumonia therapy. Changing between cefotaxime and cefixime sodium for lower respiratory tract infections works properly. The total antibiotic expenditures per capita are lower in the switching treatment group than in the intravenous administration group. The 39.4% ($P < 0.01$) decline indicates that the therapeutic effect may be maintained despite reducing the pharmacological group. Minimise hospital stays, medical costs, and the anguish and tension families experience while caring for their children. Primary hospitals should promote it as a top priority (Moridi, Sabbaghi et al. 2023). Apply a cefotaxime-cefixime switch treatment by giving cefotaxime intravenously constantly. Although there is no discernible difference between the two dosage regimens in terms of clinical effectiveness, the economic assessment The cost of the switching group was much less than that of the group getting continuous IV infusions, based on the price data. There is a discernible statistically significant difference ($P < 0.01$). (3) Medication transitioning from Cefixime to cefixime Lower respiratory tract bacterial infections were treated with ceftazidime-cefixime switch by (Moridi, Sabbaghi et al. 2023). After conducting a pharmacoeconomic analysis, the results showed that changing treatments.

The total rate of clinical efficacy and even though the bacterial clearance rate did not vary statistically significantly, the group that changed treatments had much lower overall medical and antibiotic expenditures than the group that got intravenous administration. Conclusions from Zhao Hui et al. Reference 10 The results showed that the group getting antibiotics intravenously had a lower total cost per capita than the group receiving a treatment switch. A significant difference ($P < 0.01$) was seen between those 59.0% lower and antibiotics. An infusion is about 64% less expensive overall than intravenous delivery. (4) Switching from Cefixime to Zithromax medicine, Dai Yun et al. state that Azithromycin and Cefixime should be used alternately to treat pediatric pneumonia. Comparing the effectiveness of cefuroxime sodium and cefaclor switch treatment for pediatric pneumonia The cefuroxime sodium-cefaclor and azithromycin-cefixime groupings have been shown to Azithromycin and Cefixime should be swapped, according to the statistical differences in the overall effective rates (the former is 94.74%, the latter 80.0%, $P < 0.05$). significant influence.

Changing cefuroxime and Cefixime is recommended for treating pediatric bronchopneumonia with cefuroxime instead of cefuroxime sodium. The results exceeded expectations. Comparing the two groups with the cefuroxime sodium full-course intravenous infusion group, the conversion group's overall effective rate was 100% even though their hospitalization expenses were much greater than those of the intravenous injection group. There are just a few groups with a statistically significant difference ($P < 0.01$). Urinary tract infections twice Li Guanghui et al. also performed levofloxacin and cephalosporin sequential treatment [3]. Clinical study results assessing the ceftriaxone-cefixime switch as a therapy for urinary tract infections Levofloxacin treatment for urinary tract infections resulted in cefixime conversion. No significant difference was seen in the sequential group's overall effective or bacterial clearance rate. General clinical hospitalization expenses were less than those of the control group ($P > 0.05$), and the statistical ratio was also lower. There's an important difference. P less than 0.05. 3. biliary tract infection diseases Chen Defeng in addition to others Ceftriaxone sodium/sulbactam sodium (2:1) should be given intravenously; only after infusion should cefixime and ceftriaxone sodium/sulbactam be taken orally. The two are identical in terms of overall efficacy; the former has a total effectiveness of 96.66%, while the latter has a real effectiveness of 93.33%. According to "Guidelines for clinical application of antibacterial drugs (Thakur and Mohan 2023). third-generation oral cephalosporins are a good way to treat stomach infections. Bacteriocin 4. Acute bacillary dysentery in children Xiang Yong conducted a clinical study on children with acute typical (Asadi, Nayeri-Fasaei et al. 2023). The total effectiveness of Ceftriaxone in converting Cefixime was 97.22%. Efficiency and overall effectiveness were markedly enhanced compared to the ceftriaxone intravenous infusion group alone. No significant difference was seen in the efficiency (96.88%) or the bacterial negative conversion rate. Proving the interchangeable use of Cefixime and Ceftriaxone for treating acute common bacterial infections in children. It works quite effectively in curing sexual dysentery (Asadi, Nayeri-Fasaei et al. 2023).

How quickly microorganisms are eliminated when therapy is changed Feng (Thakur and Mohan 2023). Conversion treatment is being done using Cefixime and other third-generation cephalosporins. The efficacy of a full-course intravenous bacterial infusion is not comparable to that of the intravenous injection group or the conversion group. No statistically significant difference ($P>0.05$) in the bacterial clearance rates, 109/131 and 129/148, respectively (Thakur and Mohan 2023).

The status of oral Cefixime as a conversion treatment in China is examined in this research. The excellent therapeutic efficacy of Cefixime is shown in a summary of 14 research studies. Low cost-effectiveness ratio, clinical efficacy, and good bacterial clearance (Table 2). The elimination rate (Table 3) and the entire intravenous injection group did not vary significantly. Below are acute typical cell infections in children and respiratory, biliary, and urinary tract infections. It may be used as a second-generation cephalosporin when treating hospital-acquired infections such as bacillary dysentery.

Table:3 Antibiotic Usage

Parameter	Findings/Percentages
Age Distribution of Typhoid Cases	Predominantly 2 to 10 years old
Prevalence of Antimalarial Use	10.9%
Empirical Diagnosis and Hospitalization	10.9% of patients diagnosed empirically and hospitalized
IAP Recommended Antibiotics (Pediatric)	- Cefixime (15-20 mg/kg/day) for uncomplicated typhoid - Ceftriaxone (50-75 mg/kg/day) for severe typhoid
Antibiotic Usage in the Study	- Ceftriaxone used in 86.6% of patients - 18.5% received 50-75 mg/kg/day - 18.3% received 76-100 mg/kg/day - 52.3% received >100 mg/kg/day - In some cases, used in combination with ciprofloxacin, chloramphenicol, Azithromycin, or Cefixime. - Fluoroquinolones were used in four patients against the guidelines
Polypharmacy	Low (Number of drugs per prescription < 3)
Anti-vomiting Medication Usage	54.4% of patients received anti-vomiting medication
Clinical Resistance with Ceftriaxone	6% of patients experienced clinical resistance (fever not cleared within six days)
Mean Fever Clearance Time (FCT)	- 3.30 days with Ceftriaxone as a single therapy - No significant difference was observed in FCT with combination therapy
Impact of Antibiotic Therapy Before Admission	No significant impact on mean FCT
Hematological Findings	- Anemia in about half of the patients - No significant thrombocytopenia (<1.0 lakh/cumm) - Moderate thrombocytopenia (<1.5 lakh/cumm) in 9.3% of patients - Leucopenia in 6.7% of cases - Leukocytosis in 14.7% of cases
Clinical Presenting Features	- Fever in all cases - Anorexia in 63.3% of cases - Abdominal pain in 25.33% of cases - Cough in 24% of cases - Diarrhea in 18.6% of cases - Constipation in 14% of cases
Age Distribution of Typhoid Cases	- Vomiting and headache in 13.33% of cases

Treatment patterns and clinical characteristics in pediatric typhoid fever

The table above summarises the main conclusions of a study on typhoid fever in children and adolescents. The findings contain information on demographics, treatments, and clinical symptoms. One of the most noteworthy discoveries is that children between the ages of two and 10 have the highest risk of typhoid disease. Given that empirical diagnoses, which often include administering antimalarial drugs, predominate, developing reliable diagnostic procedures is imperative (Jadav, Sukharamwala et al. 2023).

The findings of this study align with the suggestions put out by (Jadav, Sukharamwala et al. 2023). It is advised that third-generation cephalosporins be used as a potential treatment option. The patient received many doses of the main antibiotic, Ceftriaxone, some of which were greater than recommended. Fluoroquinolones are not allowed to be administered in kids under 18, yet they have been in four distinct cases, which raises questions about potential violations of regulatory rules.

The use of antiemetics is common, while polypharmacy is less common. This implies managing symptoms. The prescription drug was altered upon the discovery that 6% of the patients exhibited clinical ceftriaxone resistance. The average length of antipyretic medication was 3.30 days, and there was no statistically significant difference between combination therapy and monotherapy. Furthermore, the two therapies had no appreciable differences (Rafique, Nasir et al. 2023). According to haematological investigations, 50% of the subjects had anaemia. The results of the investigation also showed varying degrees of thrombocytopenia and leukocytosis (Sánchez, Calderón et al. 2023).

2.3 Comparative Analysis:

This study will compare Azithromycin and Cefixime, including their effectiveness, safety, and patient results. In this discussion, we will discuss the variables that influence the choice of antibiotic, including geographical differences in antibiotic resistance trends.

Mechanism of Action:

Among the medications that link Cefixime are penicillin-binding proteins, which are more often referred to as PBPs. It is the antibiotic's interaction with the 50S ribosomal subunit of bacteria that causes it to be effective. Azithromycin can impede the translation of messenger RNA.

Efficacy:

Cefixime has been shown to be an effective treatment for typhoid fever, according to research. Cefixime is a third-generation cephalosporin that has action throughout a wide range. When it comes to the treatment of culture-positive enteric fever, determining whether or not cefixime is more successful than cefixime is not a difficult task.

Safety Profile:

Cefixime is usually well tolerated, and the side effects that it causes are often not severe; the safety profile of cephalosporins is common.

Antibiotic Resistance Patterns:

Azithromycin resistance is rare in typhoid fever, but it is increasing. It is more prevalent in bacteria resistant to fluoroquinolones and those resistant to several medicines. Third-generation cephalosporins are essential when resistance to standard first-line treatments is prevalent. Cefixime: There is a risk that regional resistance patterns will vary; the use of Cefixime is required.

Guideline Recommendations:

Azithromycin is a therapeutic choice indicated by several recommendations for treating typhoid fever. Cefixime is indicated as a first-line or alternative therapeutic option in several distinct recommendations, particularly in regions where traditional drugs have been demonstrated to be resistant to the treatment.

Regional Variations:

Considering the most significant resistance patterns, it is possible to choose Azithromycin in areas with low resistance to macrolides. Cefixime is the pharmaceutical of choice in regions with a high incidence of resistance to the typical first-line therapies prescribed by medical professionals.

Pediatric Considerations:

The oral formulation of Azithromycin, together with the ease with which it may be taken, is one of the reasons why it is often utilized in pediatric populations. Cefixime is widely used in treating typhoid fever in children; changes to the dosage are made based on the patient's weight.

Combination Therapy:

The patient's clinical presentation and resistance patterns are considered when determining whether or not Azithromycin should be provided in combination with other antibiotics. Cefixime may be used either as a monotherapy or in conjunction with other treatments, depending on the severity of the sickness and the local population's resistance.

The Clinical Results Are:

When combined with gatifloxacin and bacteriological clearance, it is usually considered that Azithromycin has the potential to perform both clinical cures. Furthermore, it is believed that Azithromycin does not have any detrimental consequences on its own. Cefixime, a third-generation cephalosporin that is taken orally, has been shown to successfully shorten the length of an illness and prevent complications from arising when it is used in the manner that is recommended.

Considerations in Treatment Choice:

Cefixime, on the other hand, is often used during the process of inpatient rehabilitation. In addition, China makes frequent usage of the following medication: Cefixime is a cephalosporin of the third generation that is administered orally and is used for the treatment of enteric fever. Antibiotic azithromycin is an effective option for treatment in outpatient settings due to the fact that it may be administered orally. Nevertheless, in this specific instance, a variety of antibiotics, including Azithromycin, may be necessary in some cases. When it comes to Azithromycin, the selection process is impacted by the development of resistance in the population.

Results

The two alternatives that will be examined for the treatment of the infection are Azithromycin and Cefixime. When it comes to determining how to treat typhoid fever, a number of aspects are taken into account. These considerations include the age of the patient, the severity of the patient's symptoms, and the frequency of antibiotic resistance in the area.

The primary result was significantly different between the predetermined subgroups of people who had S. There was a substantial difference between groups. It was shown that endpoints had a substantial impact on the hazard ratio (HR) for the treatment effect (Azithromycin vs SXT), which was 1.25 (95% confidence interval). It was found that the median fever clearance durations for gatifloxacin recipients were 92 hours (84–114 hours), whereas the median fever clearance times for cefixime-treated patients were 138 hours (105–164 hours). This indicates that a significant contribution was made throughout the study. When attempting to get the most favourable results from therapy, it is vital to take into consideration the local epidemiology as well as the peculiarities of each patient. In the group that received gatifloxacin (Odds Ratio [95% CI] = 0.031 [0.004 – 0.237], or $p < 0.001$). In all, 29 patients did not respond to therapy, including those who had relapsed, those who had acute treatment failure, and those who had died. Using a confidence range of 95%, it was concluded that they were 37.6 per cent (27.14%). A substantial contribution was made to the hazard ratio (HR) for the treatment effect (Azithromycin vs. SXT), which was 1.25 (95% confidence interval), 0.99–1.58 (P = .059). Additional factors that contributed to the result included the severity of the illness and the availability of antibiotics throughout the study.

Conclusion

Because of these findings, Azithromycin is a more appropriate choice for the empirical treatment of UFI in Nepal and other countries where enteric fever is widespread. This is the case in Nepal as well as in other nations. In addition to the significance of the recently found typhoid conjugate vaccine, which was just recently put through its paces in China, there is an urgent need for the technological advancement of innovative point-of-care diagnostics. Even if a patient had a temperature that was between 37.5 and 38 for more than seven days but did not need any further or rescue treatments, and their fever went away by the tenth day, then that patient would not be considered an acute treatment failure. Undifferentiated febrile illness (UFI), which is often

referred to as *S. typhi*, is a substantial contributor to morbidity and death in nations that have incomes ranging from poor to medium.

I am writing to inform you, Typhi, that the development of these diagnostics is an urgent need. Frequent fever that does not exhibit any localized indications of the sickness is the defining characteristic of this condition. In particular, paratyphoid fever is a significant cause of death. In view of the difficulties associated with identifying and treating UFI, particularly when SIt causes it because Azithromycin had a much lower risk of problems and relapses than zithromax does, despite the fact that both arms suffered the same FCT and treatment failure. This is the reason why Azithromycin is the more effective medication. This diagnostic difficulty is made considerably more difficult by the fast development of drug resistance among *S. Typhi* and paratyphoid fever, which primarily attacks against fluoroquinolones. This resistance poses a significant obstacle to accurate diagnosis.

References:

1. Adikwu, P., et al. (2023). "Chloramphenicol is re-emerging as an effective drug in the treatment of typhoid fever in Southern Benue state, Nigeria." *Microbes and Infectious Diseases* **4**(2): 601-610.
2. Ajmal, M., et al. (2023). "Clinical pharmacokinetic of cefixime: a systematic review." *Xenobiotica*(just-accepted): 1-24.
3. Asadi, S., et al. (2023). "Antibacterial and anti-biofilm properties of carvacrol alone and in combination with cefixime against *Escherichia coli*." *BMC microbiology* **23**(1): 55.
4. Ashfaq, S., et al. (2023). "Drug resistant typhoid fever; its clinical spectrum and management in different age groups." *The Professional Medical Journal* **30**(10): 1301-1308.
5. Carey, M. E., et al. (2023). "Global diversity and antimicrobial resistance of typhoid fever pathogens: Insights from a meta-analysis of 13,000 *Salmonella Typhi* genomes." *Elife* **12**: e85867.
6. Chiou, C.-S., et al. (2023). "Antimicrobial resistance and mechanisms of azithromycin resistance in nontyphoidal *Salmonella* isolates in Taiwan, 2017 to 2018." *Microbiology Spectrum* **11**(1): e03364-03322.
7. Gianecini, R. A., et al. (2023). "Sustained Transmission of *Neisseria gonorrhoeae* Strains with High-Level Azithromycin Resistance (MIC \geq 256 μ g/mL) in Argentina, 2018 to 2022." *Microbiology Spectrum*: e00970-00923.
8. Hossain, M. A. A., et al. (2023). "Physicochemical parameters and modes of interaction associated with the micelle formation of a mixture of tetradecyltrimethylammonium bromide and cefixime trihydrate: effects of hydrotropes and temperature." *RSC advances* **13**(43): 30429-30442.
9. Islam, D. R., et al. (2023). "The Outcome of Azithromycin and Ciprofloxacin for Treatment of Uncomplicated Typhoid Fever." *Sch J App Med Sci* **3**: 662-667.
10. Jadav, P. K., et al. (2023). "Drug Utilization Study in Pediatric Patients with Typhoid Fever." *Journal for Research in Applied Sciences and Biotechnology* **2**(2): 241-247.
11. Mahmood, A., et al. (2023). "Enhanced Intestinal Permeability of Cefixime by Self-Emulsifying Drug Delivery System: In-Vitro and Ex-Vivo Characterization." *Molecules* **28**(6): 2827.
12. Mahmoud, A., et al. (2023). "Recent advances in the diagnosis and management of typhoid fever in Africa: A review." *The International Journal of Health Planning and Management* **38**(2): 317-329.
13. McPherson, S., et al. (2023). "Safety of integrated mass drug administration of azithromycin, albendazole and ivermectin versus standard treatment regimens: a cluster-randomized trial in Ethiopia." *Eclinicalmedicine* **59**.
14. Moridi, A., et al. (2023). "Removal of Cefixime from Wastewater Using a Superb nZVI/Copper Slag Nanocomposite: Optimization and Characterization." *Water* **15**(10): 1819.
15. Parry, C. M., et al. (2023). *What Should We Be Recommending for the Treatment of Enteric Fever?* Open Forum Infectious Diseases, Oxford University Press US.
16. Rafique, M., et al. (2023). "Current Sensitivity Pattern of *Salmonella* Species in Children Presenting at a Tertiary Care Hospital." *Pakistan Journal of Medical & Health Sciences* **17**(04): 367-367.
17. Sánchez, X., et al. (2023). "Antibiotic Prescription Patterns in Children Under 5 Years of Age With Acute Diarrhea in Quito-Ecuador." *Journal of Primary Care & Community Health* **14**: 21501319231196110.
18. Thakur, J. and S. Mohan (2023). "Comparison of Antimicrobial Activity of Triple, Double, and Cefixime-Based Antibiotic Pastes Against *Enterococcus Faecalis*: An In Vitro Study." *Cureus* **15**(8).
19. Yang, K. J., et al. (2023). "Effectiveness of Cefixime for the Treatment of *Neisseria gonorrhoeae* Infection at 3 Anatomic Sites: A Systematic Review and Meta-Analysis." *Sexually Transmitted Diseases* **50**(3): 131.