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Original Research Article

Clarithromycin 500 mg extended-release in the management of patients with upper respiratory tract infection: results from a prospective, multicentre, single-arm and post-marketing observational study

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ABSTRACT

Background: Upper respiratory tract infections (URTI) are a leading cause of morbidity globally and frequently require antibiotic therapy. Clarithromycin extended-release (ER) formulation is widely used for treating URTI, and may improve adherence, gastrointestinal tolerability and outcomes. This study aimed to evaluate the effectiveness and safety of clarithromycin 500 mg ER in Indian patients with URTI.

Methods: This prospective, multicenter, single-arm, open-label, post-marketing observational study was conducted at six sites in India. Adults (20-70 years) with acute bacterial URTI (otitis media, sinusitis/pharyngotonsillitis) were enrolled. Patients received clarithromycin 500 mg ER once daily for 7 days, followed by a 5-day telephonic follow-up. Clinical improvement by day 7 (±2), changes in clinical symptom scores (CSS), and safety/tolerability were evaluated.

Results: Total of 227 were included in safety analysis set, with a mean (SD) age of 34.35 (11.09) years and a female predominance (129 females, 98 males). By day 7, 82.3% achieved clinical cure and 17.7% showed symptom improvement. Significant mean (SD) CSS reduction of 95.28% (±11.16) was observed ($p<0.0001$). Curative rates by diagnosis were 88.5% for pharyngotonsillitis, 78.3% for sinusitis, and 66.0% for otitis media. Symptom relief was reported by 76.1% of patients within 3 days. The treatment was well tolerated, and no serious adverse drug reactions (ADRs) were observed.

Conclusions: Clarithromycin 500 mg ER demonstrated high effectiveness and tolerability in treatment of URTI in Indian patients. It's reassuring safety profile and rapid symptom relief support its use in real-world primary care settings.

Keywords: Clarithromycin, Upper respiratory tract infection, Acute otitis media, Acute pharyngotonsillitis, Acute bacterial sinusitis

INTRODUCTION

Upper respiratory tract infections (URTIs) affect the mouth, nose, throat, larynx, and trachea, typically presenting with mild symptoms confined to the upper airway.[1,2] However, if unmanaged, they can progress to debilitating symptoms or lower respiratory tract infections (LRTIs), which carry the risk of higher morbidity and mortality.[3,4] This risk became more evident during the COVID-19 pandemic, where URTIs often preceded severe lower respiratory involvement.[5,6] URTIs are highly prevalent, with adults and children annually experiencing 2-5 and 7-10 episodes, respectively.[7] The economic burden, particularly from common cold-related absenteeism, is estimated to be in billions.[8] URTIs are the leading cause of acute illness globally, and despite their typically mild course, they pose a substantial burden on healthcare systems and productivity.[9-12] This is especially significant in primary care, where complications like otitis media remain a major reason for visits among children under five.[13]

URTI is a major global health concern and represents the most common communicable disease.[14] As of 2021, an estimated 12.8 billion episodes of URTIs were reported, along with approximately 19,600 URTI-related deaths. The highest mortality was observed in the newborns and adults aged 95 years and older.[14] Acute otitis media, a common complication of URTIs, occurs when inflammation and congestion in the nasal and nasopharyngeal mucosa allow pathogens to reach the middle ear via the eustachian tube.[15] It is typically characterized by fluid accumulation and ear pain.[16-18] In 2021, URTI and otitis media together accounted for 6.86 million years lived with disability, with the greatest burden seen in children aged 5-9 years, followed by those aged 10-14 years.[18-20] Acute sinusitis, another frequent URTI complication, involves inflammation of the nasal mucosa and sinuses, and approximately affects 1 in 7 adults per year.[1,21,22] Group A *Streptococcus* commonly causes pharyngitis, characterized by pharyngeal inflammation, and it is among the top 20 reasons for outpatient clinic visits, accounting for 15-30% of cases in children and 5-15% in adults.[1]

Antibiotic therapy may be recommended in certain URTI cases, such as those involving acute otitis media, pharyngitis, epiglottitis, or pertussis-associated bronchitis, as they can help prevent complications like rheumatic fever, reduce symptoms, and limit the spread of infection.[23-25] In cases of chronic, severe, or prolonged bacterial sinusitis, antibiotic treatment is also commonly used.[26,27] A 10-day course of penicillin has traditionally been the standard approach for treating URTIs. In cases like pharyngitis, initial therapy typically includes aminopenicillins or sometimes cephalosporins. However, rising resistance to these antibiotics has led to the growing use of macrolides, particularly in patients with beta-lactam allergy.[28] Clarithromycin, a newer macrolide developed after erythromycin and azithromycin, is approved for treating both URTI and LRTI. Its ER formulation offers improved effectiveness and patient adherence due to its once-daily dosing and better tolerability.[29-31] Clinical trials have shown clarithromycin to be effective in treating pneumonia, sinusitis, and pharyngitis/tonsillitis, with cure rates reaching up to 85%.[30-33] The ER formulation, in particular, supports ease of use and improved treatment compliance in patients with URTIs and LRTIs.

Clinical trials provide critical data on treatment efficacy and safety, but real-world evidence is essential to understand outcomes in routine practice. Although clarithromycin ER has been evaluated internationally, data on its use in Indian patients with URTIs are limited. This prospective, multicenter, single-arm, post-marketing observational study aimed to assess the effectiveness and safety of clarithromycin 500 mg ER in Indian patients with acute bacterial URTIs, including otitis media, sinusitis, and pharyngotonsillitis.

METHODS

Study design

This prospective, multicenter, single-arm, open-label, post-marketing observational study was conducted from July 2024 to February 2025 (CTRI/2024/06/069427; date of registration 24 June 2024). The study evaluated the effectiveness and safety of Clarithromycin 500 Mg ER in Indian patients with URTI, over a period of 12 days (±2 days) (7 days of treatment and telephonic follow-up [Visit 3] for safety assessment, 5 days after the Visit 2 date).

The study was carried out in compliance with the international council for harmonization guidelines on good clinical practice (ICH-GCP), applicable local regulatory standards, and the ethical principles of the declaration of Helsinki. It also adhered to the new drugs and clinical trials rules, 2019, established by the ministry of health and family welfare, government of India, as well as relevant institutional standard operating procedures. Before study initiation, the protocol, informed consent documents, and any amendments were reviewed and approved by the appropriate ethics committee.

Participants

The study included patients aged between ≥20 to ≤70 years, diagnosed with acute URTI (acute bacterial sinusitis, acute pharyngotonsillitis, or acute otitis media) within the past 7 days of enrollment, and prescribed clarithromycin 500 mg ER once daily. Patients diagnosed with acute otitis media or acute pharyngotonsillitis may or may not have fever (>37° C). Diagnosis of acute otitis media required evidence of middle ear effusion indicated by bulging, limited or absent mobility, and air-fluid level behind the tympanic membrane, along with otorrhea. Additionally, evidence of middle ear inflammation, such

as marked erythema of the tympanic membrane or noticeable otalgia or irritability, was also required. For a diagnosis of acute pharyngotonsillitis, the presence of at least two characteristic clinical signs or symptoms-such as sore throat, redness of the pharynx, enlarged tonsils, pharyngotonsillar exudates, or tender cervical lymph nodes-was necessary. Acute bacterial sinusitis was diagnosed based on at least two clinical signs and symptoms (nasal discharge, nasal congestion, facial tenderness) persisting for 7 to 28 days, corresponding to mild to moderate cases. All patients included in the study provided written informed consent and were willing to adhere to the study-related procedures.

The exclusion criteria comprised patients who had been diagnosed and treated for an acute infection within 28 days before enrolment, and those likely to require hospitalization or ventilator support for their current symptoms. Patients with a history of clarithromycin or other antibiotic use within 1 month before study enrolment were excluded. Patients diagnosed with LRTIs, known hypersensitivity to macrolides, congenital or acquired QT prolongation, and a history of ventricular cardiac arrhythmia were not eligible. The use of systemic steroids, concurrent antibiotics, or any other medications contraindicated as per the approved prescribing information also led to exclusion. Additionally, pregnant or lactating women and patients with any condition deemed by the investigator to pose a safety risk or interfere with study participation were excluded. Patients diagnosed with acute otitis media who presented with complications such as having tympanostomy tubes in place or exhibited signs of otitis externa or chronic otitis media with cholesteatoma were excluded from the study.

Variables

The study evaluated the effectiveness and safety of once daily clarithromycin 500 mg ER tablets in the management of Indian patients with URTI.

The primary effectiveness outcome was the percentage of patients showing clinical improvements (cured [complete resolution of signs and symptoms] + improved [marked reduction in symptom severity without need for additional antimicrobial therapy]) based on clinical response to 7 days of treatment with clarithromycin 500 mg ER. Secondary effectiveness outcome evaluated the mean percentage change in CSS from baseline to end of the study at 7±2 days. Clinical score was calculated for each URTI diagnosis as presented in Table 1. The total CSS, calculated as the sum of all individual scores, gave the overall clinical findings and was considered a measure of clinical findings at each visit.

Table 1: Clinical symptom score used in the assessment of treatment effectiveness.

Variables				
General clinical signs and symptoms				
Fever	[0] Absent	[1] 37.1-38°C	[2] 38.1-39°C	[3] >39°C
Chills	[0] Absent		[1] Present	
Headache	[0] Absent		[1] Present	
Cough	[0] Absent		[1] Present	
Rhinitis (Except for AS)	[0] Absent		[1] Present	
Vomiting	[0] Absent		[1] Present	
Inappetence	[0] Absent		[1] Present	
Specific clinical signs and symptoms				
Acute pharyngitis				
Sore throat	[0] Absent		[1] Present	
Pharyngeal erythema	[0] Absent		[1] Present	
Tonsillar enlargement	[0] Absent		[1] Present	
Tonsillopharyngeal exudates	[0] Absent		[1] Present	
Painful cervical lymphadenopathy	[0] Absent		[1] Present	
Acute sinusitis				
Nasal discharge	[0] Absent	[1] Serous	[2] Seromucous	[3] Mucopurulent
Nasal congestion	[0] Absent		[1] Present	
Facial tenderness	[0] Absent		[1] Present	
Acute otitis				
Bulging of tympanic membrane	[0] Absent		[1] Present	
Limited or absent mobility of tympanic membrane	[0] Absent		[1] Present	
Otalgia or irritability	[0] Absent		[1] Present	
Purulent otorrhea	[0] Absent		[1] Present	
Air-fluid level behind the tympanic membrane	[0] Absent		[1] Present	
Erythema of the tympanic membrane	[0] Absent		[1] Present	

Safety and tolerability assessment conducted post-treatment included the occurrence of ADRs and other pharmacovigilance relevant information (OPRI) throughout the study period that may or may not lead to treatment discontinuation. Significant changes in the electrocardiogram were also evaluated post-treatment as part of the safety and tolerability assessment.

Statistical methods

All safety assessments were conducted using the safety analysis set, which comprised participants who received at least one dose of the study medication. Those in the safety analysis set with post-baseline efficacy, comprised of the full analysis set (FAS). The FAS was utilized for the primary efficacy evaluations.

Subjects from the safety analysis set who completed the study without significant protocol deviations were included in the per protocol (PP) set, which was used for secondary efficacy analyses.

All data were processed, summarized, and analyzed using SAS® statistical software version 9.4. For quantitative variables, descriptive statistics included the number of non-missing values (n), mean, standard deviation (SD), median, and range. A paired t test at a 5% level of significance was used to determine statistical significance in quantitative variables. Qualitative variables were presented as the number (n) and percentage (%) of subjects. Where applicable, missing data were presented as a separate "Missing" category.

Percentages were calculated using the total number of patients in the relevant analysis population as the denominator, unless otherwise specified. The number and proportion of subjects achieving clinical effectiveness, clinical cure, clinical improvement, and clinical failure on day 7 (±2 days) were summarized, each accompanied by 95% confidence intervals (CIs) calculated using a large-sample normal approximation.

RESULTS

Demographics

A total of 237 patients were screened and enrolled in the study; 10 patients were lost to follow-up at visit 2 (7±2 days). Thus, 227 treated patients (male: female, 98: 129) with a mean (SD) age of 34.35 (11.09) were included in the safety analysis set.

The FAS had 226 patients, and as one of the patients in the safety analysis set discontinued due to "unsatisfactory therapeutic effect". The PP set also comprised 226 patients.

The majority of patients were diagnosed with acute pharyngotonsillitis (59%). Each patient received oral dose of clarithromycin 500 mg ER tablets, to be taken once daily with water for a period of 7 days, as per protocol. Demographic and baseline characteristics are detailed in Table 2.

Primary effectiveness outcome

Primary efficacy analysis was conducted on the FAS, and all subjects demonstrated clinical improvement. 186 (82.3%) patients experienced curative effect and 40 (17.7%) patients demonstrated improvement in symptoms, post 7 days of treatment with once daily clarithromycin 500 mg ER tablets. Results are summarized in Table 3.

Secondary effectiveness outcome

Compared to baseline (Day 1), the absolute mean (±SD) change in CSS by day 7 (±2 days) was -4.62 (±1.66), corresponding to a mean (±SD) percentage reduction of -95.28% (±11.16). This change was statistically significant ($p<0.0001$). Results are summarized in Table 4 and illustrated in Figure 1.

The highest percentage of cure response was reported in patients with Pharyngotonsillitis 119 (88.5%, 95% CI: 84.26, 94.69). The count and percentage of cure response in patients with otitis media was 31 (66.0%, CI: 52.41, 79.50), and in patients with Sinusitis, 36 (78.3%, CI: 66.34, 90.18). Results are summarized in Table 5.

CI is calculated using a large sample normal approximation.The mean (SD) percent change in the CSS from baseline to day 7 (±2 days) was -91.78 (13.77), -94.00 (12.29), and -96.95 (9.33) in patients with acute otitis media, acute bacterial sinusitis, and acute pharyngotonsillitis, respectively. The decrease in percentage change is statistically significant ($p<0.0001$) as illustrated in Figure 2.

Overall, 221 (97.4%) of patients were fully compliant with the study medication, with 172 (76.1%) patients reporting relief in URTI symptoms after 3 days of treatment, while 45 (19.9%) and 9 (4.0%) patients experienced symptom relief on the day 3 and 2, respectively.

Safety and tolerability

Safety assessment consisted of monitoring and recording all ADRs/OPRIs, serious ADRs/OPRIs, and those leading to discontinuation of treatment. One patient (0.4%) reported an OPRI (Unsatisfactory therapeutic response) and subsequently withdrew from the study.

Overall, the 7-day treatment with once-daily clarithromycin 500 mg ER tablets was well tolerated by patients with acute bacterial URTIs (acute bacterial sinusitis, acute pharyngotonsillitis, or acute otitis media).

Table 2: Demographics and medical history of safety analysis set (n=227).

Characteristics	N (%)
Total patients	227
Sex	
Male	98 (43.2)
Female	129 (56.8)
Age (in years)	
Mean (SD)	34.35 (11.09)
Median	32.00
Min, Max	18, 62
Height (cm)	
Mean (SD)	164.48 (8.01)
Median	164.00
Min, Max	146, 188
Weight (kg)	
Mean (SD)	68.44 (11.25)
Median	68.00
Min, Max	40, 98
BMI (kg/m^2)	
Mean (SD)	25.19 (3.42)
Median	24.98
Min and max	17.55, 41.6
Race	
Asian	227 (100)
Infection type	
Otitis media	47 (20.7)
Sinusitis	46 (20.3)
Pharyngotonsillitis	134 (59.0)

*N=Number of patients in safety analysis set; n=Number of patients with data available percentages are calculated using N as the denominator.

Table 3: Assessment of clinical response to clarithromycin 500 mg ER treatment (FAS, n=226).

Variables	N=226 (%)	95% CI
Clinical improvement	226 (100)	(100, 100)
Cure	186 (82.3)	(77.32, 87.28)
Improved	40 (17.7)	(12.72, 22.68)
Failure	0	

*N=Number of patients in FAS, n=Number of patients with data available. Percentages are calculated by using N as the denominator. CI is calculated using the large sample normal approximation.

Table 4: Assessment of change from baseline in clinical symptoms score (FAS, n=226).

Visits	Statistics	Clarithromycin 500 mg ER (n=226)
Baseline	N	226
	Mean (SD)	4.85 (1.66)
	Median	5.00
	Min, Max	2, 10
Day 7	N	226
	Mean (SD)	0.22 (0.51)
	Median	0.00
	Min, Max	0, 2
Day 7, mean change from baseline	N	226
	Mean (SD)	-4.62 (1.66)
	Median	-5.00
	Min, Max	-10, -1
	P value	<0.0001
	95% CI	(-4.8, -4.4)

Continued.

Visits	Statistics	Clarithromycin 500 mg ER (n=226)
Day 7, mean percent change from baseline	N	226
	Mean (SD)	-95.28 (11.16)
	Median	-100.00
	Min, Max	-100, -33
	P value	<0.0001
	95% CI	(-96.7, -93.8)

*N=Number of patients in FAS, n=Number of patients with data available, p value using one sample t test.

Table 5: Assessment of clinical response to clarithromycin 500 mg ER treatment as per URTI diagnosis at baseline (FAS, n=226).

Variables	Clarithromycin 500 mg ER (n=226) (%)	95% CI
Otitis media	47 (100)	
Clinical improvement	47 (100)	(100, 100)
Cure	31 (66.0)	(52.41, 79.50)
Improved	16 (34.0)	(20.50, 47.59)
Failure	0	
Sinusitis	46 (100)	
Clinical improvement	46 (100)	(100, 100)
Cure	36 (78.3)	(66.34, 90.18)
Improved	10 (21.7)	(9.82, 33.66)
Failure	0	
Pharyngotonsillitis	133 (100)	
Clinical Improvement	133 (100)	(100, 100)
Cure	119 (89.5)	(84.26, 94.69)
Improved	14 (10.5)	(5.31, 15.74)
Failure	0	

*N=Number of patients in PP analysis set, n=Number of patients with data available. Percentages are calculated by using the number of patients for the respective infection type as the denominator.

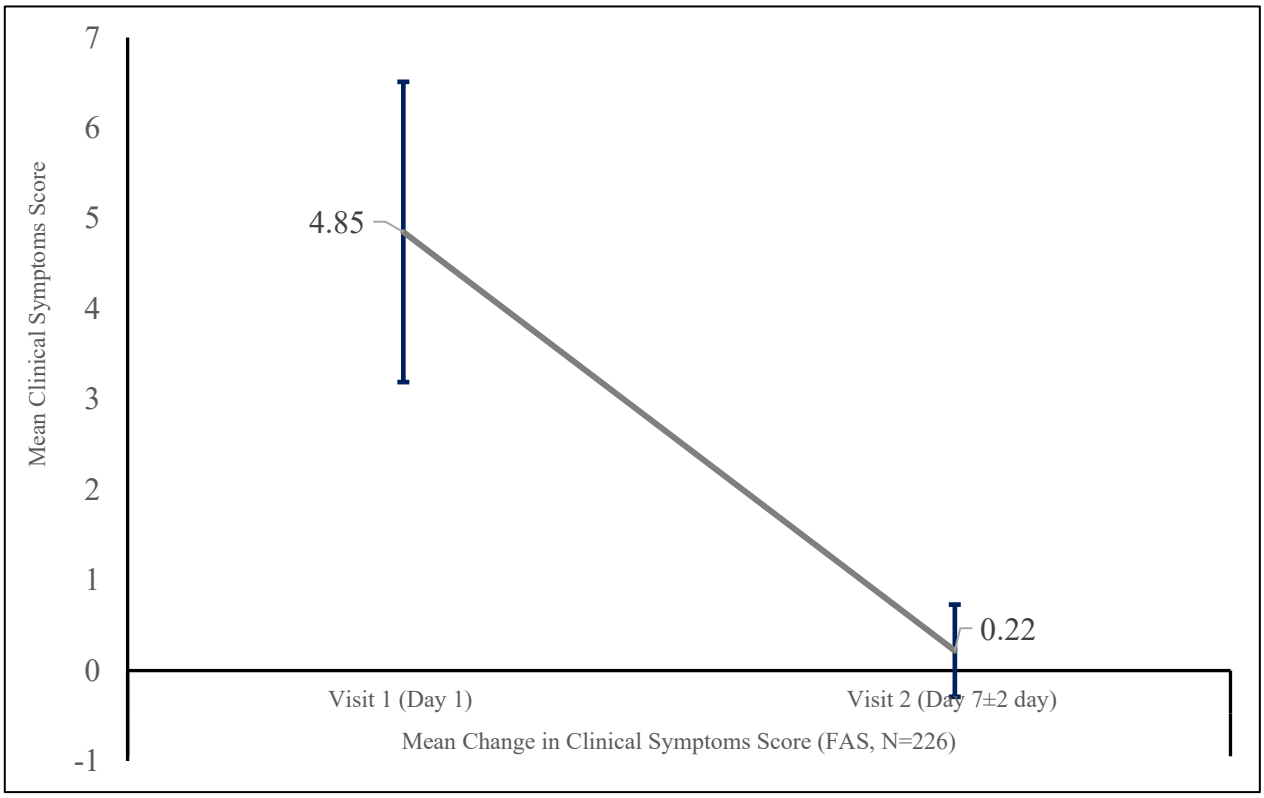

Figure 1: Mean (±SD) clinical symptoms score (FAS, n=226).

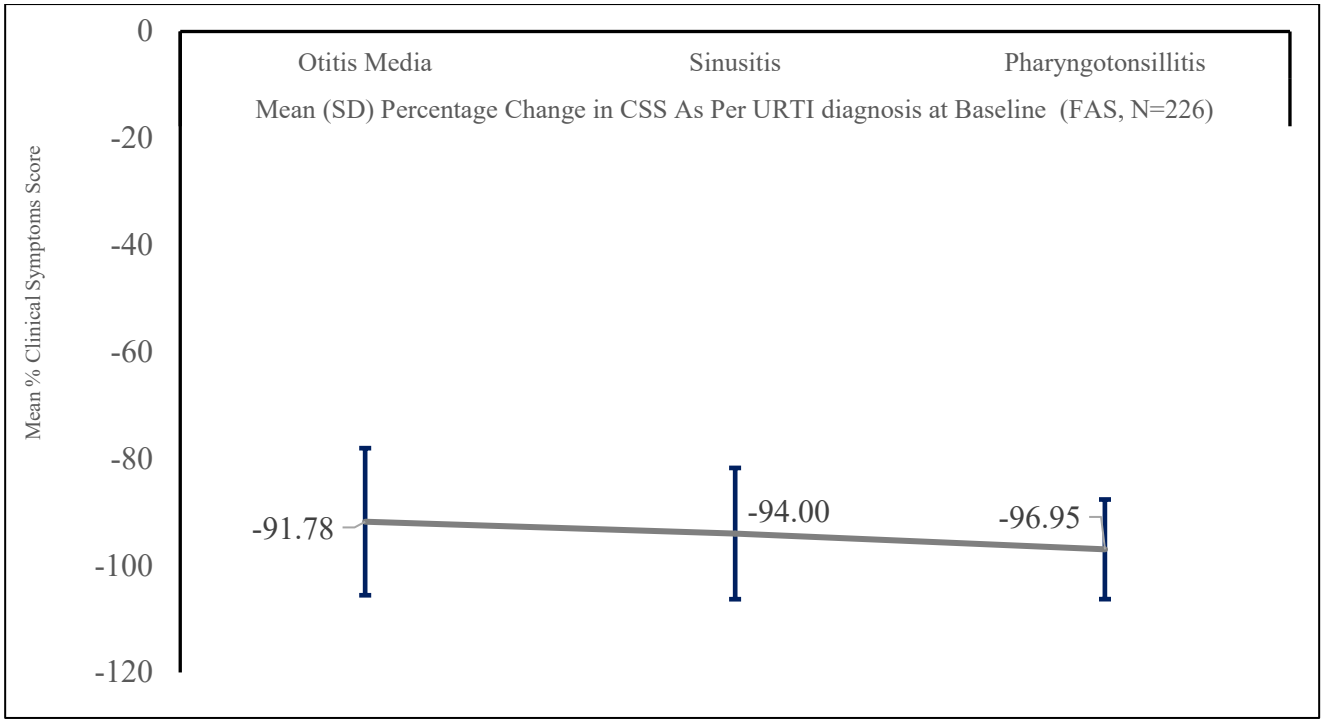

Figure 2: Mean (±SD) percentage change in CSS as per URTI diagnosis at baseline in (FAS, n=226).

DISCUSSION

URTIs remain a major cause of morbidity globally and are frequently encountered in primary care.[4–6] While typically self-limiting, URTIs such as acute bacterial sinusitis, acute pharyngotonsillitis, or acute otitis media may require antibiotic treatment to prevent complications and reduce symptom burden.[23,24] Macrolide antibiotics, particularly clarithromycin, are widely recommended due to their broad-spectrum activity and favorable safety profile. Clarithromycin is an orally active, advanced-generation macrolide that has been reformulated as an ER tablet, allowing convenient once-daily administration. The availability of an ER formulation of clarithromycin offers additional advantages in terms of dosing convenience and adherence.[30-33] The present prospective, multicenter, single-arm, open-label, observational cohort study was undertaken to assess the real-world utility of clarithromycin in Indian patients, where local data on clinical outcomes in URTI management remain limited. The observation period spanned 12 (±2) days, including 7 days of treatment and a telephonic follow-up conducted 5 days after the treatment period for safety assessment. To the best of our knowledge, this is the first real-world study in India to evaluate the effectiveness and safety of once-daily clarithromycin 500 mg ER tablets in patients with acute bacterial URTIs.

After 7 days of treatment, 82.3% of patients experienced a curative effect, while the remaining showed symptom improvement. A similar cure rate of approximately 84% was observed in a randomized clinical trial in the South African population on clarithromycin 500 mg ER, which supports our outcome. Further randomized trials in the USA population with acute bacterial sinusitis reported up to an 85% cure rate with clarithromycin 1000 mg ER after 14-day treatment regimen, suggesting that the dosage used in the present study is optimal, as a higher dose did not result in a significantly better outcome.[34,35] The study also reported that clarithromycin 500 mg ER was effective against streptococcal pharyngitis/tonsillitis and in the treatment of acute exacerbation of chronic bronchitis.[35]

Significant improvements in CSS were observed at day 7 (±2 days). The curative response was highest for acute pharyngotonsillitis (88.5%), followed by acute bacterial sinusitis (78.3%) and acute otitis media (66.0%). Previous investigations have demonstrated cure rates of up to 88% for community-acquired pneumonia over a 7-day treatment regimen and up to 85% for acute maxillary sinusitis with a 14-day clarithromycin 1000 mg ER course.[34] Another study conducted in the USA found clarithromycin to be effective in 90% of pharyngitis and sinusitis cases.[36]

To ensure successful treatment and reduce the risk of antibiotic resistance, antibacterial medications should not only reach effective levels at the infection site but also help lower bacterial carriage.[37] Poor adherence to antibiotic regimens is a common cause of treatment failure and resistance.[34] It is well known that longer treatments and multiple daily doses often reduce patient compliance.[38,39] In infections like streptococcal pharyngitis, symptoms usually improve within 3-4 days of starting antibiotics, which can lead patients to stop medication early.[40] Clarithromycin 500 mg in its ER form was developed to support once-daily dosing, making it

easier for patients to stick to treatment.[34] In this study, 97.4% completed the full treatment course, and 4% and 19.9% patients reported relief from URTI symptoms at day 2 and 3, respectively, and 76.1% of patients reported relief from URTI symptoms after 3 days of starting clarithromycin 500 mg ER. Only one patient discontinued the study due to unsatisfactory therapeutic response, while the remaining subjects did not report any ADRs or OPRIs. Comparative clinical trials have shown that the ER formulation of clarithromycin offers improved gastrointestinal tolerability over the immediate-release version and is better tolerated than amoxicillin or clavulanic acid, with a safety profile comparable to that of levofloxacin, aligning with the findings of our study.[35]

Despite the encouraging outcomes, this study has certain limitations. Being a single-arm observational study without a comparator group, it does not allow direct comparison with other antibiotics or placebo. The open-label design may also introduce bias in outcome assessment. However, the sample size was statistically powered for this study, and this should be adequate for the inference-drawing ability of this study. Moreover, the study used validated scales/scores to evaluate the primary and secondary objectives, which establishes the precision of results. Additionally, evaluating the drug in regular clinical practice offers the potential to bring research closer to practice and audit. Further studies are needed to define the optimal long-term roles for the use of clarithromycin ER 500 mg in URTI patients. The results of this study will be useful for providing preliminary data and guidance for designing large-scale, long-term randomized controlled and/or open-label studies using larger sample sizes. Such future studies can corroborate the findings of this study and establish the long-term effectiveness and safety of clarithromycin ER 500 mg.

CONCLUSION

This prospective, multicenter observational study demonstrated that clarithromycin 500 mg ER, administered once daily, is effective and well tolerated in the treatment of URTI, including acute bacterial sinusitis, acute pharyngotonsillitis or acute otitis media in Indian patients. High rates of clinical cure, rapid symptom resolution, and excellent treatment adherence were observed over a 7-day treatment regimen. It was also demonstrated that the study medication was well-tolerated with an acceptable safety profile and an effective therapeutic option in the management of URTI. These findings support the real-world utility of clarithromycin ER as a convenient and efficacious treatment option in Indian outpatient URTI management.

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REFERENCES

1. Grief SN. Upper Respiratory Infections. Prim Care. 2013;40(3):757-70.
2. Mifsud EJ, Kuba M, Barr IG. Innate Immune Responses to Influenza Virus Infections in the Upper Respiratory Tract. Viruses. 2021;13(10):2090.
3. King D, Mitchell B, Williams CP, Spurling GK. Saline nasal irrigation for acute upper respiratory tract infections. Cochrane Database of Sys Rev. 2015;2015(4):CD006821.
4. Jain N, Lodha R, Kabra SK. Upper respiratory tract infections. Indian J Pediatr. 2001;68(12):1135-8.
5. Sungnak W, Huang N, Bécavin C, Berg M, Queen R, Litvinukova M, et al. SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes. Nat Med. 2020;26(5):681-7.
6. Mulay A, Konda B, Garcia G, Yao C, Beil S, Villalba JM, et al. SARS-CoV-2 infection of primary human lung epithelium for COVID-19 modeling and drug discovery. Cell Rep. 2021;35(5):109055.
7. Chang AB, Harrhy VA, Simpson J, Masters IB, Gibson PG. Cough, airway inflammation, and mild asthma exacerbation. Arch Dis Child. 2002;86(4):270-5.
8. Bramley TJ, Lerner D, Sarnes M. Productivity Losses Related to the Common Cold. J Occup Environ Med. 2002;44(9):822-9.
9. Vos T, Barber RM, Bell B, Bertozzi-Villa A, Biryuko S, Bolliger I, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. The Lancet. 2015;386(9995):743-800.
10. Duan KI, Birger M, Au DH, Spece LJ, Feemster LC, Dieleman JL. Health Care Spending on Respiratory Diseases in the United States, 1996-2016. Am J Respir Crit Care Med. 2023;207(2):183-92.
11. Fendrick AM, Monto AS, Nightengale B, Sarnes M. The Economic Burden of Non-Influenza-Related Viral Respiratory Tract Infection in the United States. Arch Intern Med. 2003;163(4):487.
12. Dixon RE. Economic costs of respiratory tract infections in the United States. Am J Med. 1985;78(6):45-51.
13. Klein JO. The burden of otitis media. Vaccine. 2000;19(1):S2-8.
14. Sirota SB, Doxey MC, Dominguez RMV, Bender G, Vongpradith A, Albertson SB, et al. Global, regional, and national burden of upper respiratory infections and otitis media, 1990-2021: a systematic analysis

from the Global Burden of Disease Study 2021. Lancet Infect Dis. 2025;25(1):36-51.
15. Heikkinen T, Chonmaitree T. Importance of Respiratory Viruses in Acute Otitis Media. Clin Microbiol Rev. 2003;16(2):230-41.
16. Cetinkaya E. A., Topsakal V., Acute Otitis Media. In: Cingi C, Arısoy ES, Muluk B, eds. Pediatric ENT Infections, Springer, Cham. 2022;381-92.
17. Nokso-Koivisto J, Marom T, Chonmaitree T. Importance of viruses in acute otitis media. Curr Opin Pediatr. 2015;27(1):110-5.
18. Lieberthal AS, Carroll AE, Chonmaitree T, Ganiats TG, Hoberman A, Jackson MA, et al. The Diagnosis and Management of Acute Otitis Media. Pediatrics. 2013;131(3):e964-99.
19. Chonmaitree T, Trujillo R, Jennings K, Alvarez-Fernandez P, Patel JA, Loeffelholz MJ, et al. Acute Otitis Media and Other Complications of Viral Respiratory Infection. Pediatrics. 2016;137(4):e20153555.
20. Kutter JS, Spronken MI, Fraaij PL, Fouchier RA, Herfst S. Transmission routes of respiratory viruses among humans. Curr Opin Virol. 2018;28:142-51.
21. Mandal R, Patel N, Ferguson BJ. Role of antibiotics in sinusitis. Curr Opin Infect Dis. 2012;25(2):183-92.
22. Aring AM, Chan MM. Acute rhinosinusitis in adults. Am Fam Physician. 2011;83(9):1057-63.
23. Zoorob R, Sidani MA, Fremont RD, Kihlberg C. Antibiotic use in acute upper respiratory tract infections. Am Fam Physician. 2012;86(9):817-22.
24. Centor RM, Allison JJ, Cohen SJ. Pharyngitis Management: Defining the Controversy. J Gen Intern Med. 2007;22(1):127-30.
25. Bisno AL, Gerber MA, Gwaltney JM, Kaplan EL, Schwartz RH. Practice Guidelines for the Diagnosis and Management of Group A Streptococcal Pharyngitis. Clin Infect Dis. 2002;35(2):113-25.
26. Ahovuo-Saloranta A, Borisenko OV, Kovanen N, Varonen H, Rautakorpi UM, Williams Jr JW, et al. Antibiotics for acute maxillary sinusitis. Cochrane Database of Sys Rev. 2008;16(2):CD000243.
27. Chow AW, Benninger MS, Brook I, Brozek JL, Goldstein EJC, Hicks LA, et al. Executive Summary: IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults. Clin Infect Dis. 2012;54(8):1041-5.
28. Sécurité AFD, Santé SDPD. Systemic antibiotic treatment in upper and lower respiratory tract infections: official French guidelines. Clin Microbiol Infect. 2003;9(12):1162-78.
29. Peters DH, Clissold SP. Clarithromycin. A review of its antimicrobial activity, pharmacokinetic properties and therapeutic potential. Drugs. 1992;44(1):117-64.
30. Adler JL, Jannetti W, Schneider D, Zhang J, Palmer R, Notario G. Phase III, randomized, double-blind study of clarithromycin extended-release and immediate-release formulations in the treatment of patients with acute exacerbation of chronic bronchitis. Clin Ther. 2000;22(12):1410-20.
31. Murray JJ, Solomon E, McCluskey D, Zhang J, Palmer R, Notario G. Phase III, randomized, double-blind study of clarithromycin extended-release and immediate-release formulations in the treatment of adult patients with acute maxillary sinusitis. Clin Ther. 2000;22(12):1421-32.
32. Weiss K, Vanjaka A. An open-label, randomized, multicenter, comparative study of the efficacy and safety of 7 days of treatment with clarithromycin extended-release tablets versus clarithromycin immediate-release tablets for the treatment of patients with acute bacterial exacerbation of chronic bronchitis. Clin Ther. 2002;24(12):2105-22.
33. Anzueto A, Fisher Jr CL, Busman T, Olson CA. Comparison of the efficacy of extended-release clarithromycin tablets and amoxicillin/clavulanate tablets in the treatment of acute exacerbation of chronic bronchitis. Clin Ther. 2001;23(1):72-86.
34. Snyman JR, Schoeman HS, Grobusch MP, Henning M, Rabie W, Hira M, Parshotam K, et al. Generic versus Non-Generic Formulation of Extended-Release Clarithromycin in Patients with Community-Acquired Respiratory Tract Infections. Clin Drug Investig. 2009;29(4):265-74.
35. Darkes MJM, Perry CM. Clarithromycin extended-release tablet: a review of its use in the management of respiratory tract infections. Am J Respir Med. 2003;2(2):175-201.
36. Block SL. Comparative tolerability, safety and efficacy of tablet formulations of twice-daily clarithromycin 250 mg versus once-daily extended-release clarithromycin 500 mg in pediatric and adolescent patients. Clin Pediatr (Phila). 2006;45(7):641-8.
37. Dagan R, Klugman KP, Craig WA, Baquero F. Evidence to support the rationale that bacterial eradication in respiratory tract infection is an important aim of antimicrobial therapy. J Antimicrob Chemother. 2001;47(2):129-40.
38. Rudd P, Lenert L. Pharmacokinetics as an Aid to Optimising Compliance with Medications. Clin Pharmacokinet. 1995;28(1):1-6.
39. Bloom BS. Daily regimen and compliance with treatment. BMJ. 2001;323(7314):647.
40. Shaw E, Anderson JG, Maloney M, Jay SJ, Fagan D. Factors associated with noncompliance of patients taking antihypertensive medications. Hosp Pharm. 1995;30(3):201-7.

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