Drug Corner

Exploring the Efficacy and Safety of Lincomycin 1000 mg SR Tablets in ENT Infections : A Clinical Investigation

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ENT conditions contribute to over 11% of the total cases in an accident and emergency department with acute ENT infections accounting for a significant portion of these presentations. Over the past decade, there has been a rise in hospital admissions for conditions like tonsillitis, peritonsillar abscess and deep neck space infections. Previous microbiology studies on admitted acute ENT infections have consistently identified Group A-beta-haemolytic Streptococcus (GABHS) (13.7%) as the most common isolate, followed by *Fusobacterium necrophorum* (13.6%) and *Staphylococcus aureus* (8.0%).

Lincomycin has shown its effectiveness in addressing a range of ENT infections[11-13]. A meta-analysis conducted by Desai, *et al* suggests that lincomycin has proven beneficial in treating various infections caused by gram-positive and anaerobic organisms.

This study aimed to evaluate the safety and effectiveness of a 1000 mg sustained-release tablet of lincomycin hydrochloride for the treatment of ENT infections caused by susceptible pathogens. The overall effectiveness of lincomycin treatment was evaluated using the PGA scale. A total of 460 (99.14%) patients achieved clinical success with lincomycin, while clinical failure was observed in only four (0.86%) cases. These findings support the idea that lincomycin is an effective and well-tolerated treatment option for diverse ENT indications.

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Key words **: Staphylococcus Aureus, Ent Infections, GABHS, Lincomycin, Tonsillitis.**

Infections affecting the Ear, Nose and Throat (ENT) or Upper Respiratory Tract Infection (URTI) are widespread and can affect individuals across all age groups, from children to adults. These infections, particularly those prevalent in children, necessitate early diagnosis and appropriate management to guarantee optimal growth and development. They can manifest as either acute or chronic conditions[1]. ENT constitutes a significant proportion of the cases seen by general practitioners, as well as by otorhinolaryngologists, both on an outpatient and an inpatient basis[2]. Common ENT infections that can be effectively treated with medications include Acute Rhinitis, Sinusitis, Adenoiditis, Tonsillitis, Pharyngitis, Acute and Chronic Suppurative Otitis Media (CSOM), Otitis externa, Laryngitis and Epiglottitis[3].

ENT conditions contribute to over 11% of the total cases in an accident and Emergency Department, with acute ENT infections accounting for a significant portion of these presentations. Over the past decade, there has been a rise in hospital admissions for conditions like Tonsillitis, Peritonsillar Abscess and Deep Neck Space Infections. Previous microbiology studies on admitted acute ENT infections have consistently identified Group A-beta-haemolytic streptococcus (GABHS) (13.7%) as the most common isolate, followed by *Fusobacterium necrophorum* (13.6%) and *Staphylococcus aureus* (8.0%)[4].

Most often, these infections are the primary cause for prescribing antibiotics, such that recovery usually occurs spontaneously. Some of these infections can progress to severe complications with a life-threatening potential. Swift therapeutic measures are necessary in these situations, involving hospitalization and the commencement of initial intravenous(IV) antibiotic therapy[5]. Several studies have demonstrated that patients who received antibiotics before admission exhibited a higher proportion of cultures with either no growth or normal flora. Additionally, there was a decrease in the number of isolates of Penicillin-susceptible organisms[2,6].

Risk factors associated with ENT infection include accidental aspiration or ingestion of foreign bodies, crowding, low socio-economic status, poor parental educational level, smoking, anaemia and poor nutrition[7,8]. The presentation of foreign bodies in the Ear, Nose and Throat is common in primary and emergency care settings[1,9].

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The initial guidance from the Groupe de Pathologie Infectieuse Pédiatrique de la Société Française de Pédiatrie (GPIP-SFP) and the Société de Pathologie Infectieuse de Langue Française (SPILF), as incorporated into the 2021 Haute Autorité de Santé (HAS) guidelines, emphasizes the recommendation against prescribing antibiotics for common cold, Non-streptococcal Tonsillopharyngitis, Laryngitis, Congestive Acute Otitis Media, or Otitis media with effusion[5]. Antimicrobial prescription patterns vary by location and are influenced by factors such as antimicrobial susceptibility, physician preferences, and costs. The irrational use of antimicrobials, including prescribing antibiotics for non-bacterial infections, administering inadequate dosages, and choosing improper routes, has resulted in ineffective treatment, prolonged illness, higher incidence of adverse drug reactions, suboptimal therapy, therapeutic failure, and polypharmacy. This eventually contributes to an increased burden of medical costs and the emergence of antibiotic resistance[3].

Lincomycin, the pioneering antibiotic in the lincosamide class, was initially discovered in 1964 in the actinomycete Streptomyces lincolnensis[10]. It has been extensively researched and applied in various outpatient and hospital-based settings and is available in both oral and injectable forms. Lincomycin is commonly prescribed for treating a spectrum of infections, including ENT and URTI, Skin and Soft Tissue Infections (SSTI) such as surgical wound infections, bone and joint infections (Osteomyelitis and septic arthritis), and oro-dental infections. Its antibacterial action targets gram-positive bacteria, such as *Staphylococcus, Streptococcus* (pyogenes, viridans, and pneumonia), *C diphtheriae*, and anaerobic bacteria, including *Clostridium Propionibacterium*[11].

Lincomycin has shown its effectiveness in addressing a range of ENT infections[11-13]. A meta-analysis conducted by Desai et al., suggests that lincomycin has proven beneficial in treating various infections caused by gram-positive and anaerobic organisms. It has demonstrated efficacy in managing Acute Upper Respiratory Tract and ENT infections, including Tonsillitis, Pharyngitis, Sinusitis and Acute Otitis Media (AOM)[11]. In another study trial, thirty-seven(100%) cases of gram-positive infections seen in an active general practice were treated successfully with lincomycin orally or intramuscularly[12].

Furthermore, the safety profile of lincomycin in a meta-analysis revealed that an oral dose of lincomycin (1-2 g/day) showed no signs of toxicity, with only mild transient adverse effects, including allergic contact dermatitis, anaphylaxis, bowel upset, occasional diarrhea, or other non-bothersome side effects[11]. Another study by Guslits showed that lincomycin 600 mg had no toxic effects with only a mild disruption of bowel function and occasional diarrhea being observed as side effects[12]. Therefore, this study was conducted to evaluate the effectiveness and safety of sustained released tablets of lincomycin 1000 mg in ENT infections.

Materials and Methods

Study Design :

This was an open-label, retrospective, observational study. This study aimed to evaluate the safety and effectiveness of a 1000 mg sustained-release tablet of lincomycin hydrochloride for the treatment of ENT infections caused by susceptible pathogens. Patients willing to follow the procedures as per the study protocol voluntarily signed an informed consent form.

Patient Criteria :

The study included individuals of age groups, from paediatric to elderly patients over 80 years of age and had been diagnosed with various infections, including URTI, such as Laryngopharyngitis, Tonsillitis, Bacterial Rhinosinusitis, Otitis Media and others. Participants who had not been part of a similar investigation within the preceding four weeks were included in the study.

Individuals who were pregnant, lactating, allergic to lincomycin antibiotics, had pre-existing renal, liver, or cardiac conditions, or other conditions as determined by the investigator (such as uncontrolled Diabetes and uncontrolled Hypertension), or who were already on antibiotic treatment or unable to follow the study procedures and protocol were excluded from the study.

Study Intervention :

A 1000 mg sustained-release tablet of lincomycin hydrochloride was administered once daily for 5 days.

Outcome Measures :

The primary outcome measures were adverse events and causality assessment.

The secondary outcomes were Total Symptom Score (TSS) and Physician's Global Assessment (PGA) scale. The TSS evaluated the clinical cure, while the PGA was used to assess the successful treatment outcome at the end of lincomycin treatment.

Data Analysis :

A sample size of 464 patients was considered appropriate. Categorical data were expressed as numbers and percentages. Effectiveness was tested

using the Wilcoxon signed-rank test. All adverse events were recorded and causality was evaluated using the causality assessment tool. Causality was categorized as definite, probable, possible, or unlikely.

Results

Demographic Details :

A total of 464 patients were enrolled in the study, covering a broad spectrum of age groups, from paediatric to elderly patients over 80 years of age, all presenting with ENT infections. Most patients were male, accounting for 268 patients (57.76%). Individuals belonging to the 31-40 years (27.59%) age group contributed to the highest percentage of patients (Table 1).

Indications for Lincomycin :

This study included 39 ENT indications for which lincomycin was prescribed. Among these groups, patients diagnosed with Acute Pharyngitis, Cough, Csom, Throat Pain, Tonsillitis and URTI accounted for more than 5% each of the total indications (Fig 1). The other indications are summarized in Table 2.

Effectiveness of Lincomycin Based on Symptom Severity Score :

The effectiveness of lincomycin was assessed by using the total symptom severity score. The symptoms evaluated were ear pain, running nose, throat pain, nasal pain and discharge, deafness, voice hoarseness and painful swallowing. At baseline, 165(35.56%) and 248 (53.45%) patients had moderate and severe symptoms, respectively (Fig 2). A reduction in the average TSS score was observed on day 5 versus baseline (Fig 3). Following the 5-day lincomycin regimen, there was a notable decrease in the number of patients with moderate and severe symptoms (Fig 2), with a significant reduction in TSS (p=0.0000000092) (Table 3).

Overall Treatment Outcome of Lincomycin :

The overall effectiveness of lincomycin treatment was evaluated using the PGA scale. A total of 460 (99.14%) patients achieved clinical success with lincomycin, while clinical failure was observed in only four (0.86%) cases (Fig 4). Additionally, no fatal outcomes were observed throughout the study.

Table 1 — *Age distribution of patients involved in the study*

Age Group	No of Patients	Percentage
< 10 Years	8	1.72%
11-20 Years	27	5.82%
21-30 Years	127	27.37%
31-40 Years	128	27.59%
41-50 Years	93	20.04%
51-60 Years	51	10.99%
61-70 Years	23	4.96%
71-80 Years	5	1.08%
> 80 Years	2	0.43%
Total	464	100.00%

Safety Outcomes of Lincomycin Treatment :

After lincomycin treatment, 457 patients (98.49 %) reported no adverse reactions. Only a minority of patients, accounting for 7 (1.51%), experienced adverse drug reactions primarily related to Gastrointestinal (GI) disturbance, including Diarrhoea (0.22%), nausea (0.43%) and Abdominal pain (0.86%) (Fig 5).

Causality Assessment of Lincomycin Treatment :

The causality assessment scale employed in this study was used to determine the probability of adverse events associated with lincomycin administration. A total of 20 patients (46.51%) reported a causal relationship between lincomycin and GI disturbances as unlikely, while an equivalent percentage of patients (46.51%) reported it as certain.

Discussion

In the present study, the assessment of lincomycin's effectiveness demonstrated a significant

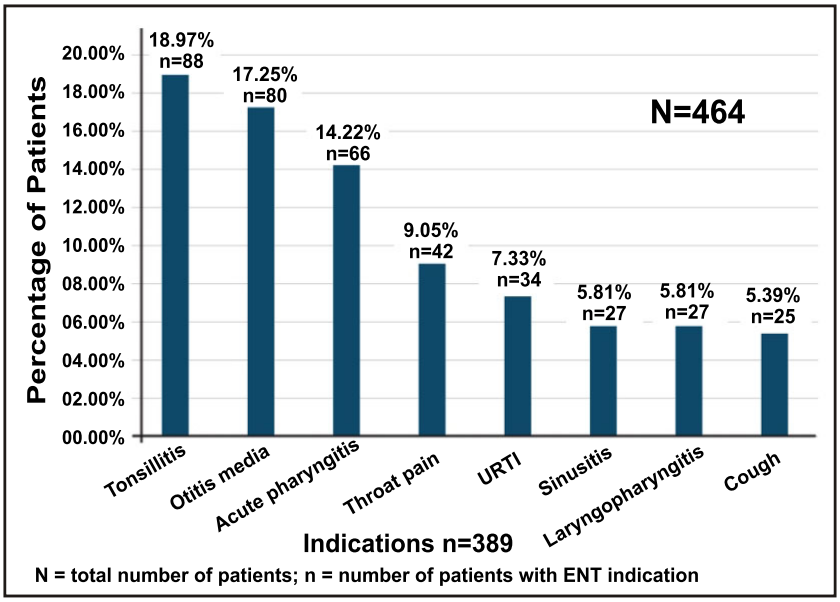

Fig 1 — ENT Indications in each group of patients contributing to more than 5% of the total population

Table 2 — *Indications in each group of patients contributing to less than 5% of the total population*

ENT Indications (N=464)	Other indications(N=464)
Respiratory tract infection (n=14, 3.03%)	Acute vestibular pain (n=1, 0.22%)
Rhinitis (n=13, 2.8%)	Granuloma (n=1, 0.22%)
Folliculitis (n=7, 1.51%)	Headache (n=5, 1.08%)
Dysphagia (n=4, 0.86%)	Furunculitis (n=3, 0.65%)

N=total number of patients; n=number of patients with ENT indication

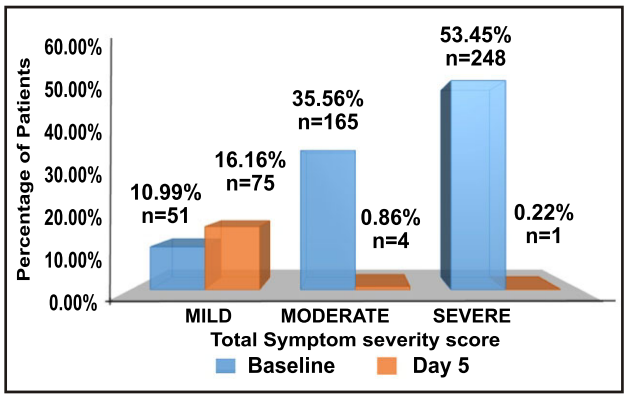

Fig 2 — Total symptom severity score of patients at baseline versus 5 days of lincomycin treatment

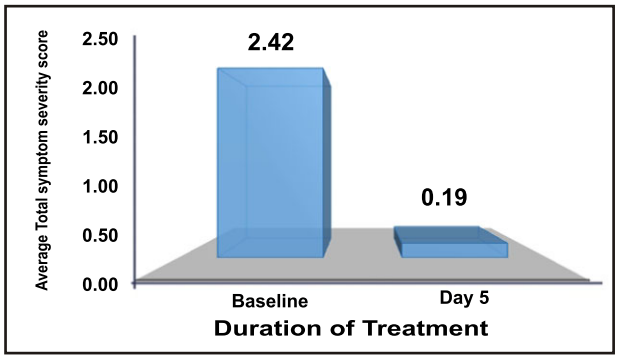

Fig 3 — Average total symptom score of patients at baseline versus day 5 of lincomycin treatment

reduction in symptoms by day 5 versus baseline. This finding is consistent with that of a recent Indian study indicating the prompt and effective action of lincomycin in alleviating ENT symptoms[13]. A multicentre postmarketing study evaluated the comparative efficacy and safety of multidose treatments using 500 mg capsules of lincomycin hydrochloride versus 200 mg tablets of cefpodoxime proxetil in 41 patients with tonsillitis and sinusitis. The

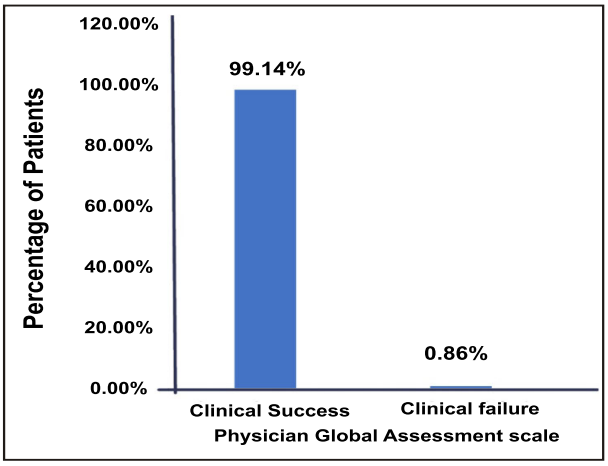

Fig 4 — Outcome assessment of lincomycin treatment using the PGA scale

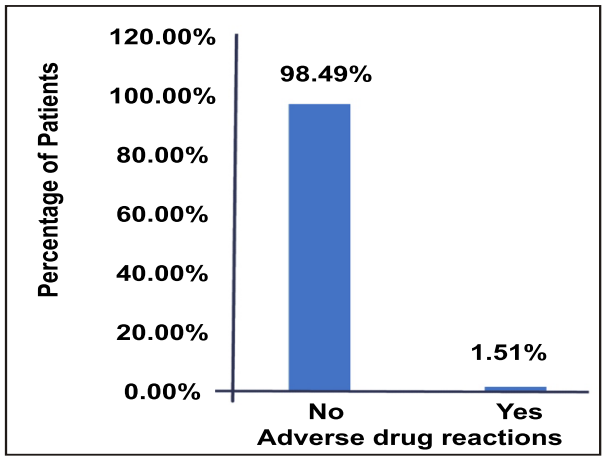

Fig 5 — Incidence of adverse drug reactions due to lincomycin treatment

results revealed that 67.89% and 52.27% of the patients in the lincomycin and cefpodoxime groups, respectively, achieved complete relief from all clinical symptoms. The findings suggest that lincomycin hydrochloride capsules, a conventional antibiotic, demonstrate effective treatment for alleviating tonsillitis and sinusitis compared to the newer third-generation antibiotic[13]. The minimal incidence of clinical failure observed in our study further serves as a testament to the overall effectiveness of lincomycin in the treatment of ENT infections.

The impact of ENT infections extends beyond specific age groups and influences both adults and children. This prevalent issue often leads to substantial disruptions in the daily lives of affected individuals, posing a growing health concern.

Table 3 — *Summary of total symptom scores of patients at baseline versus 5 days of lincomycin treatment*

TSS	Mean	N	Median	SD	SE	Wilcoxon W	P-Value	% Effect	Result
Baseline	2.42	464	3.00	0.68	0.0317	-18.911[b]	0.0000000092	92.36	Significant
Day 5	0.19	464	0.00	0.43	0.0198				

A study focusing on pediatric ENT disorders in India revealed that otitis media was most commonly observed in male children (53.2%). The majority of these affected children were from lower socio-economic backgrounds, living in combined-family setups and had mothers with limited educational backgrounds[14,15].

A crucial aspect of our findings pertains to the safety profile of lincomycin. The low frequency of reported adverse reactions is a noteworthy observation, emphasizing the favorable safety profile associated with lincomycin use in the context of ENT infections. Among the reported adverse reactions, gastrointestinal disturbances emerged as the singular event, consistent with the well-documented side effect profile of lincomycin. The causality assessment indicated a well-balanced perception among patients concerning the probability of these occurrences being linked to lincomycin treatment, with an equal number of patients reporting no connection between lincomycin use and adverse events. In conclusion, the collective evidence presented in this study significantly adds to our understanding of the effectiveness and safety of lincomycin in the treatment of ENT infections.

Limitations of the Study and Prospects :

This study had some limitations, including the assessment period of 5 days for lincomycin's effectiveness is relatively short, potentially not capturing any long-term effects or complications that may arise with its extended use. To gain a more comprehensive understanding, further research, including randomized controlled trials, long-term follow-up, and comparative studies with other antibiotics, is necessary to provide additional insights into the sustained effectiveness and safety of lincomycin.

Conclusion

Our study highlights the broad applicability of a 1000 mg lincomycin sustained-release tablet in the management of ENT infections, with significant improvements in symptom severity, clinical success rates, and minimal adverse reactions. These findings support the idea that lincomycin is an effective and well-tolerated treatment option for diverse ENT indications.

Declaration : Article is not published / submitted in any other journal.

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Conflict of Interest : No

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