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# EFFECTIVENESS OF TELITHROMYCIN IN MANAGEMENT OF ACUTE PHARYNGITIS AND TONSILLITIS

1. **S. QAMAR ABBAS RIZVI**
2. **NAILA ZAHIR**

**ABSTRACT**

OBJECTIVE: *to evaluate the effectiveness of Telithromycin in the management of acute pharyngitis and tonsillitis.*
DESIGN & DURATION: *Prospective study conducted during Jan 2007 to Mar 2007.*
SETTING*: Outpatient department of Baitul Hikmah, Hamdard University and all irestigations & labouratory analysis was conducted at KMDC Karachi.*
MATERIAL AND METHODS: *This was a prospective and quasi experimental study. As far as the sample size is concerned, 40 patients fulfilling the inclusion criteria were included. A convenience sample from all consecutive patients clinically presenting with acute pharyngitis and tonsillitis were included. A six item questionnaire with various variables was used to record the parameters. The parameters included age (above 12 yrs), gender, dysphagia, inflammation of pharynx/tonsil, fever and cervical lymph node enlargement. Lactating and pregnant females were excluded from the study. Throat swab culture of all patients was assessed at day 0 and on 5the day after oral treatment with Telithromycin 800 mg once a day for five days.*
CONCLUSION: *Results of the study reveal that cure rate with Telithromycin for the treatment of bacterial pharyngitis and tonsillitis in our country is excellent as compared to those found treated with macrolides during other contemporary studies probably owing to development of resistance against them.*

**KEYWORDS :** Telithromycin, acute pharyngitis, tonsillitis

1. ***Assistant Professor***
**Dept. of Pharmacology & Therapeutics**
HAMDARD COLLEGE OF MEDICINE & DENTISTRY
HAMDARD UNIVERSITY, KARACHI
Contact: 03332216131
email: dr_qamar@hotmail.com
2. ***Associate Professor Pathology***
KARACHI MEDICAL AND DENTAL COLLEGE & ABBASI SHAHEED HOSPITAL, KARACHI.

***Correspondence to:***
House No. A-59, Paradise Homes, Abdul Hasan Isphani Road, Gulistan-e-Hijri, Karachi.
Contact:03332216131, 03333777513
email: dr_qamar@hotmail.com

## INTRODUCTION

The antimicrobial resistance to penicillins, cephalosporins, and non-beta-lactam antibiotics has markedly alarming rate [1-7]. The increased frequency of resistant isolates has made antimicrobial resistance a universal problem [8,9]. Currently, 30% to 44% of pneumococci in the United States have an intermediate or high-grade resistance to penicillin. Additionally penicillin-resistant *S pneumoniae* (PRSP) are often resistant to non-betalactam antibiotics, including macrolides, tetracyclines, chloramphenicol, and trimethoprim/sulfamethoxazole [10,11].

Consequently, the emergence of multidrug-resistant gram-positive isolates has made treatment more challenging, with geographic distribution also affecting susceptibility patterns of certain isolates [12]. In order to avoid such resistance, the ketolides that are semisynthetic derivatives of erythromycin of which telithromycin is the only one currently approved, have been introduced.

Telithromycin has the same basic 14 membered lactone (macrolide) ring structure. It differs from erythromycin in that there is replacement of ?-L-cladinose ring with a ketone group at position 3 (changing the structure from a macrolide to a ketolide) and the addition of an 11-12 cyclic carbamate [13].

The Telithromycin and macrolides have the same ribosomal target site. These sites are peptidyl transferase loop in domain V and and the Hairpin 35 in domain II [14,15].

The affinity for binding to these sites is increased in telithromycin, with a 6-10 folds higher affinity in wild-type organisms, compared with erythromycin or clarithromycin [16].

Typically, streptococcal resistance to antimicrobials is due to modification of the ribosomal drug-binding site through either methylation or mutation of the nucleotides involved [17,18,19]. Once modified, the binding affinity of the antimicrobial is decreased, leading to suboptimal inhibition of ribosomal activity and the development of resistance. All 14-

and 15-membered ring antimicrobials can induce methylase activity in streptococcal strains ($MLS_B$ resistance), with the exception of ketolides [20].

Furthermore, Telithromycin has a higher binding affinity for the 50S ribosomal subunit, allowing it to retain activity against pathogens with inducible methylase activity, making it a reasonable option for the treatment of resistant streptococcal respiratory infections.

The second mechanism of resistance involves active efflux of drug, which also confers resistance to all 14- and 15-membered ring macrolides [21,22,23]. It appears that telithromycin does not induce the efflux pump as effectively as do macrolides, allowing telithromycin to retain activity against strains [24,25,26]. Consequently, telithromycin has activity against strains that induce either methylase production or efflux pump activity, thereby bypassing common ways in which resistance is acquired by respiratory pathogens.

It is active in-vitro against streptococcus pyogens, Spneumoniae, S aureus, H influenza, Moraxella catarhallis, mycoplasmas, Legionella sp, Chlamydia sp, H pylori, N gonorrhoeae, B fragilis, T gondii and nontuberculosis bacteria. Many macrolide-resistant strains are susceptible to ketolides because the structural modification of these compounds renders them poor substrates for efflux pump – mediated resistance they bind to ribosomes of some bacterial species with higher affinity than macrolides.

Oral bioavailability of telithromycin is 57%, and tissue and intracellular penetration is generally good. Telithromycin is metabolized in the liver and eliminated by a combination of biliary and urinary routes of excretion. It is administered as a once –daily dose of 800 mg, which results in peak serum concentrations of approximately 2mcg/mL. Telithromycin is indicated for treatment of respiratory tract infections, including community-acquired bacterial pneumonia, acute exacerbations of chronic bronchitis, sinusitis and streptococcal pharyngitis. It is reversible inhibitor of the CYP3A4 enzyme system and may slightly prolong the QT interval. Rate cases of hepatitis and liver failure have been reported [27].

OBJECTIVE:

To evaluate the effectiveness of the Telithromycin in pharyngitis and tonsillitis.

**MATERIAL & METHOD:**

This study was carried out in the out-patients department of Baitul Hikmat, Hamdard University, Karachi upon 40 consecutive clinically diagnosed cases of acute pharyngitis and tonsillitis and investigates & laboratory analysis was conducted along the colobration of department of Pathology Karachi Medical & Dental College, Abbasi Shaheed Hospital, Karachi Patients were required to be above the age of 12 years. Both male and female sex were included.

Female patients with pregnancy and lactation were excluded.

The assessment of clinical signs and symptoms included dysphagia, Pharyngeal inflammation alongwith inflammation of tonsils, Lymphoid hypertrophy, fever As far laboratory assessment is concerned throat swab culture was carried out in all cases.

TREATMENT AND ASSESSMENT:

All the 40 patients were kept on telithromycin with a dosage of 800mg oral once per day for 05 days.

Throat swabs for culture were taken both at base line i.e. at 0 day of treatment and at followup i.e. at 5th day of the treatment. Clinical assessment was made at base line i.e. at 0 day of treatment and at follow up i.e. at 5th day of the treatment.

**RESULTS:**

Among 40 patients, 18 were found suffering from both dysphagia and inflammation of tonsils and pharynx, 16 with fever alongwith dysphagia and inflammation of tonsils and pharynx, whereas 6 were found suffering from fever alongwith dysphagia and inflammation of tonsils and pharynx and lymphoid hypertrophy as shown in Table I.

Throat swab cultures of 28 patients out of 40 were found positive whereas samples of 12 patients were found negative as depicted in Table II.

However all the patients were treated with telithromycin with an oral dosage of 800mg once per day for 05 days.

At the end of the treatment all the patients were found cured both clinically and bacteriologically.

**TABLE I:**
**SIGN & SYMPTOMS AT BASE LINE**

| SIGNS/SYMPTOMS | NUMBER OF PATIENTS |
|---|---|
| Dysphagia + Inflammation of Tonsills & Pharynx | 18 |
| Fever + Dysphagia + Inflammation of Tonsills & Pharynx | 16 |
| Fever + Dysphagia + Inflammation of Tonsills & Pharynx + lymphoid hypertrophy | 6 |

**TABLE II:**
**LABORATORY INVESTIGATION AT BASE LINE**

| LABORATORY INVESTIGATION | NUMBER OF PATIENTS |
|---|---|
| Throat Swab Culture positive | 28 |
| Throat Swab Culture Negative | 12 |

**DISCUSSION:**

In Japan, telithromycin has been approved since December 2003 for the treatment of respiratory tract infections, such as pneumonia, bronchitis, pharyngitis, tonsillitis and sinusitis[28].

In 2004, however, telithromycin resistance emerged rapidly in H. influenzae in Japan. In this report the mechanisms conferring telithromycin resistance have been partially characterized. Multiple mutations in 23S rDNA from domains I to VI were identified, as well as an amino acid mutation in the L4 ribosomal protein. To determine genetic traits associated with the emergence of telithromycin resistance, however, relationships between alterations in 23S rDNA and/or ribosomal proteins and telithromycin resistance require more definitive characterization [29].

Previously in two separate studies, a 05-day course of Telithromycin 800 mg/day was compared with a 10-day course of Penicillin or Clarithromycin for patients with tonsillitis or pharyngitis. Clinical cure was reported in 84-91% of Telithromycin treated patients. However adverse effects were more frequent in Telithromycin group than in Penicillin group [30,31].

In comparison to the outcome of above mentioned studies, in our study we considered 40 patients with pharyngitis or

tonsillitis.

Patients taken for the study were above the age of 12 years. The eldest patient was 45 years old whereas the youngest one was 14 years old. The mean age was 31 years. Patients below the age of 12 years were not considered in order to keep the study focused on adult segment of the populace.

As far as gender was concerned, among 40 patients, 19 male and 21 female patients were there. However no discernable variations were found in results of the study in relation to the gender.

Results of positive throat swab culture patients showed the presence of streptococcus.

At the end of the treatment all were found cured both clinically and bacteriologically with negligible adverse effects.

Owing to the lack of adequate number of similar studies, it is not possible to develop a comprehensive comparative data to establish the conclusive notions and make them public.

**CONCLUSION:**

Results of the study reveal that cure rate with telithromycin for the treatment of pharyngitis and tonsillitis (bacterial) in our country are excellent as compared to those found treated with macrolides during other contemporary studies probably owing to development of resistance against them. However studies conducted on such smaller scale cannot be declared conclusive. Therefore it is imperative to conduct such studies on larger scale in same environment and milieu.

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