

The Place of Macrolides in the Treatment of Upper Respiratory Tract Infections

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Summary

The majority of all acute upper respiratory tract infections (URTIs) are viral in aetiology. Bacterial infection, either as a prime cause or secondary to the initial viral infection, can be effectively eradicated with appropriate drug therapy. A course of penicillin is usually effective in cases of acute tonsillitis, pharyngitis, otitis media and sinusitis. Macrolide antibiotics may be prescribed as an alternative, especially if β -lactamase-producing strains are present. Roxithromycin achieves high tissue concentrations, and cure rates between 85 and 100% have been reported in various URTIs.

1. Incidence of Upper Respiratory Tract Infections

Acute respiratory infections are recognised internationally as the most common group of diseases causing sickness and morbidity. A worldwide mortality rate of 1 death every 2 seconds in children under 5 years of age has been derived from demographic data. Furthermore, 92% of these 15 million deaths occur in developing countries. Not surprisingly, the Mexican Ministry of Health has placed the prevention and management of acute respiratory diseases on its priority list.

Most acute upper respiratory tract infections (URTIs) are viral in aetiology (e.g. the common cold) and do not benefit from routine use of antibacterial drugs (Soyka et al. 1975; Taylor et al. 1977). However, some patients present with a progression of symptoms suggestive of secondary bacterial infection. For these patients, antibacterial agents may be beneficial.

A study conducted in Guatemala has shown that otherwise healthy children in rural and urban areas

may suffer from 6.4 and 9 URTIs per year, respectively. In other words, a child may suffer from URTIs every 4 to 6 weeks even without any underlying immunological weakness.

This paper will cover various URTIs and review current treatments, with emphasis on the role of macrolide antibiotics.

2. Common Rhinitis

Viruses are the main cause of rhinitis. Among the viruses stated to be responsible are

- rhinovirus (30 to 35% of cases)
- coronavirus (\geq 10% of cases)
- respiratory syncytial virus
- parainfluenza
- adenovirus.

60 to 70% of rhinitis is caused by these viruses, the remainder being attributed to unidentified viruses.

Pathogenic bacteria do not have a primary specific role in rhinitis. This is one disease, therefore, where management is difficult, as specific antiviral

Table I. Therapeutic efficacy of roxithromycin (ROX) in the treatment of ear, nose and throat infections

Reference	Type of infection	Study design	Treatment groups	Treatment duration (days)	Clinical response rate (%)	Bacteriological response rate (%)
D'Enfert & Fiessinger (1988)	Pharyngitis	Open	ROX 150mg bid	5-10	371/384 (96.6)	(93)
	Otitis	Open	ROX 150mg bid	5-10	33/35 (94)	(91)
Grassi et al. (1988)	Pharyngotonsillitis	mc	ROX 150mg bid	5-20	7/7 (100)	(100)
	Ear, nose and throat	mc	ROX 150mg bid	5-20	31/37 (84)	11/12 (92)
Herron (1987)	Streptococcal throat infections	Open	ROX 300mg od	10	76/76 (100)	(84)
Matsumoto & Hara (1987)	Otitis media	Open, mc	ROX 100-300mg bid	4-14	59/100 (59)	
Melcher (1988)	Pharyngitis	Open	ROX 150mg bid	10	9/9 (100)	

Abbreviations: od = daily; bid = twice daily; mc = multicentre.

treatment is generally lacking. Aerosolised ribavirin, however, has been shown to decrease the length of viral shedding in infants with cardiopulmonary disease who have been hospitalised with respiratory tract infection due to respiratory syncytial virus (Hall et al. 1983).

3. Acute Tonsillitis and Pharyngitis

Many sore throats are of viral aetiology, especially in children under 5 years of age. For these patients, antibacterial therapy is, of course, inappropriate and relief of symptoms with throat irrigations, lozenges and analgesics are the only supportive therapies that can be offered.

Lancefield's type A β -haemolytic streptococci are the most prevalent cause of bacterial sore throat. Over 60 to 65 serotypes are known; thus, it is possible for an individual to fall victim to this species many times. Other possible bacterial pathogens are *Neisseria gonorrhoeae* and *Corynebacterium diphtheriae*.

Some experts stress the need for prompt treatment of symptoms of bacterial pharyngitis or tonsillitis in order to avoid complications. Treatment should be initiated very early, (e.g. in streptococcal sore throat infections) to eliminate the risk of rheumatic fever.

Antibacterial drugs are effective not only in pre-

venting such rheumatic sequelae, but also in early symptomatic relief of bacterial pharyngitis (Krober et al. 1985). The usual therapy is phenoxymethylpenicillin (penicillin V) for 10 to 14 days. Sometimes streptococci may persist in the tonsils after penicillin treatment because of the emergence of β -lactamase-producing strains of *Haemophilus influenzae*, *Staphylococcus aureus* and *Bacteroides* spp. (Brook et al. 1981). For this reason, macrolide antibiotics are a valuable second option in tonsillitis and pharyngitis. Clinical cure rates of between 90 and 100% have been reported with roxithromycin, partly due to its excellent enteral absorption and resulting high tissue concentrations (table I).

4. Otitis Media and Acute Sinusitis

Inflammation of the middle ear is a common problem in infants. Indeed, 25% of 120 million antibiotic prescriptions written yearly in the USA are directed mainly at the treatment of otitis media in children. Worldwide, bacteria can be found in about 75 to 80% of acute otitis ears. The more common bacteria are *Streptococcus pneumoniae*, *H. influenzae* and group A *Streptococcus*. *Branhamella (Moxarella) catarrhalis* has been isolated with increasing frequency in recent years; most strains appear to be β -lactamase-producing (fig. 1; Jackson et al. 1987).

Secondary bacterial infection occurs frequently, not only in otitis media but also in sinusitis. Nasal congestion over 7 to 10 days with the appearance of purulent discharge indicates the need for systemic antibacterial therapy (Jackson et al. 1987). The same pathogens involved in otitis media are implicated in sinusitis. *Chlamydia pneumoniae* is also regarded as an important pathogen.

In both otitis media and sinusitis, treatment is mostly empirical and based on β -lactam antibiotics as traditional first-choice therapy. Macrolide antibiotics are also recommended (Jackson et al. 1987), and impressive cure rates of 95% for otitis media and 85% for sinusitis have been calculated for roxithromycin (table I; Young et al. 1989).

5. Laryngitis and Laryngotracheitis

Laryngitis or laryngotracheitis may be suspected if a sore throat is accompanied by hoarseness and cough in adults and croup with some breathing difficulties in children. In most instances, the causal

infecting agents are viruses. The influenza virus is responsible for about 40% of acute laryngotracheitis in both adults and children. A bacterial aetiology should be expected in only 10% of patients, a probable pathogen being *Mycoplasma pneumoniae*, against which macrolide antibiotics such as roxithromycin have proven antibacterial activity (Young et al. 1989).

6. Conclusions

The main causative bacteria in URTIs are *H. influenzae* and *S. pneumoniae*. Pathogenic bacteria may be the prime source of infection or may colonise susceptible tissues after initial viral infection. In either case, antibacterial therapy including cephalosporin, penicillin, sulphonamide and macrolide antibiotics, may be indicated.

Macrolide antibiotics have an acknowledged place in URTI therapy. Roxithromycin has demonstrated good efficacy and tolerability in the treatment of URTI infections.

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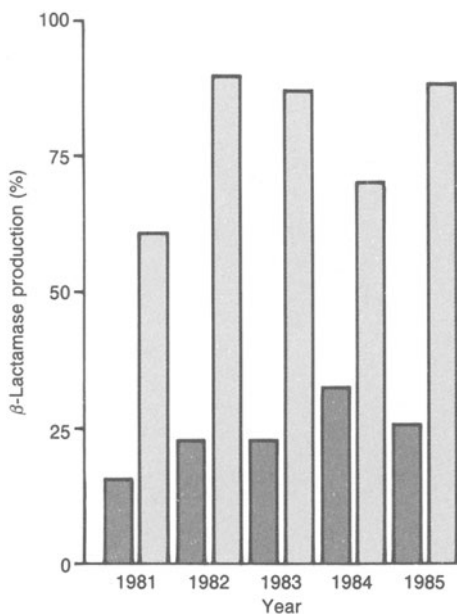


Fig. 1. Sensitivity to β -lactam antibiotics in otitis media. ■ = *Haemophilus influenzae*; □ = *Branhamella catarrhalis* (after Bluestone 1986).

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