Clarithromycin for children

**CLARITHROMYCIN AND AZITHROMYCIN ARE THE FIRST TWO** semisynthetic macrolides to be licensed in Canada. Recently, a liquid suspension of clarithromycin has been licensed for use in children.

Clarithromycin and azithromycin have several advantages over erythromycin, including
- longer half-life, allowing once- or twice-daily dosing;
- greater bioavailability after oral doses;
- lower incidence of the side effects abdominal pain, nausea and vomiting;
- wider spectrum of antimicrobial activity.

**PHARMACOLOGY**

Clarithromycin is well absorbed and the extent of adsorption is not significantly altered when administered with food (1). Absorption of the liquid suspension in children appears comparable with that in adults receiving capsules. Clarithromycin is concentrated in cells and tissues providing levels greater than serum levels in the middle ear fluid and in lung tissue (2). Approximately a third of the drug is excreted by the kidney and the rest is metabolized in the liver. Its major metabolite, 14-hydroxy clarithromycin, also has antimicrobial activity, being about half as active as clarithromycin, except for *Haemophilus influenzae*, against which it is more active (3). Its long half-life permits a twice-daily dosing schedule. The recommended dose for most indications is 7.5 mg/kg bid.

**ANTIMICROBIAL ACTIVITY**

Clarithromycin has good activity against: group A streptococcus, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, *Mycoplasma pneumoniae*, *Bordetella pertussis*, *Legionella pneumophila*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Helicobacter pylori* and *Propionibacterium acnes*.

It has good activity, but with more variable minimum inhibitory concentrations, against: *H influenzae*, methicillin-susceptible *Staphylococcus aureus*, campylobacter, some atypical mycobacteria including *Mycobacterium avium complex (MAC)* and *Mycobacterium leprae*.

It is not very active against methicillin-resistant *S aureus*, coagulase-negative staphylococci and enterococci.

*S pneumoniae* resistant to clarithromycin have already been reported (4).

**CLINICAL TRIALS IN CHILDREN**

Clinical trials in Europe and North America have shown that clarithromycin is similar in efficacy to other oral antibiotics, such as amoxicillin-clavulanate, cefaclor and amoxicillin, for treatment of acute otitis media in children six months to 12 years of age (5-9). Duration of therapy was seven to 10 days in the North American trials and five days in the European trials. In all trials clarithromycin and the alternative antibiotic achieved similar rates of symptomatic and bacterial cure.

Clarithromycin capsules or suspension are as effective as penicillin V for treatment of streptococcal pharyngitis (10). The eradication rate of group A streptococcus was slightly better with clarithromycin than with penicillin V.

Evidence from clinical trials on the efficacy of clarithromycin in the treatment of lower respiratory tract infections in children is not yet available.

**ADVERSE EFFECTS**

In children, adverse effects of clarithromycin have been infrequent (in comparative trials, rates were similar to those with amoxicillin) (11). The most common adverse effects are gastrointestinal, but they are less frequent with clarithromycin than with erythromycin or amoxicillin-clavulanate.

**USES OF CLARITHROMYCIN IN CHILDREN**

The spectrum of antimicrobial activity combined with a relatively low rate of adverse events and the convenience of twice-daily dosing will make clarithromycin an attractive option in the treatment of respiratory tract infections in children.

- For otitis media, clarithromycin offers no advantage over the less expensive first-line agents such as amoxicillin, pivampicillin and trimethoprim-sulfamethoxazole. It should be considered as a second-line agent for otitis media with similar
efficacy, adverse event rate and dosing schedule to several other second-line agents.

• For pharyngitis, clarithromycin offers little advantage to standard therapy.

• For pneumonia, although there are no clinical trials to show efficacy of clarithromycin in the treatment of children with pneumonia, it is reasonable to assume that for pediatric respiratory pathogens the response to clarithromycin would be comparable with that to erythromycin. The lower incidence of gastrointestinal symptoms and twice-daily dosing are clearly advantages of clarithromycin over erythromycin.

• For skin and soft tissue infection, topical agents or less expensive oral agents would usually be the first choice. However, clarithromycin may be useful for treatment of moderate to severe infections, particularly in the penicillin-allergic patient.

• For atypical mycobacterial infections, clarithromycin is likely to become a first-line agent. In children with AIDS and MAC infection, clarithromycin was well-tolerated but decreased susceptibility to clarithromycin occurred rapidly on therapy (12). Therefore, as with other agents for mycobacteria, clarithromycin for MAC will be useful as one of a combination of agents used for treatment and prophylaxis.

• For adult contacts of children with pertussis, clarithromycin offers a good alternative to erythromycin and may improve compliance because it may be better tolerated than erythromycin.

As with all new antibiotics, we can expect resistance to emerge. And resistance of *S pneumoniae* has already been reported. Therefore, judicial use of clarithromycin is essential to ensure that it remains an effective weapon against infections for which it would be the agent of choice.

REFERENCES

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