Dirithromycin: a new macrolide
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Authors' objectives
To assess the clinical microbiology and therapeutic use of dirithromycin, emphasising comparative data between dirithromycin, and the standard macrolide erythromycin, as well as clarithromycin and azithromycin.

Searching
MEDLINE was searched from 1966 to 1996, and an extensive review of journals was undertaken.

Study selection
Study designs of evaluations included in the review
Controlled single- or double-blind studies were included.

Specific interventions included in the review
Dirithromycin, erythromycin, clarithromycin, azithromycin and penicillin V potassium.

Participants included in the review
Patients eligible for evaluation, as defined by medication compliance and the positive culture of an erythromycin-sensitive isolate prior to therapy, were evaluated. The mean age ranged from 12 to 63 years.

Outcomes assessed in the review
Clinical response (cure or improvement), bacterial eradication and adverse effects for: chronic bronchitis, acute bronchitis, community-acquired pneumonia, streptococcal pharyngitis, and skin or soft tissue infections.

How were decisions on the relevance of primary studies made?
All trials that met the study design inclusion criteria, and expressed upper and lower respiratory tract infections, or skin and soft tissue infections were assessed.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
For each of the major outcomes, data were expressed as either early response (3 to 5 days after therapy) or late response (2 to 4 weeks after discontinuation of therapy). Data were extracted in an intention to treat format where possible.

Methods of synthesis
How were the studies combined?
The studies were combined by a narrative review.

How were differences between studies investigated?
No formal statistical analysis was performed, but differences between the studies were discussed narratively.

Results of the review
Chronic bronchitis: 4 studies of dirithromycin versus erythromycin, 521 and 518 participants, respectively; 1 study of dirithromycin versus clarithromycin, 95 and 96 participants, respectively.
Acute bronchitis: 1 study of dirithromycin versus erythromycin, 72 and 63 participants, respectively.

Community-acquired pneumonia: 2 studies of dirithromycin versus erythromycin, 217 and 201 participants, respectively.

Streptococcal pharyngitis: 3 studies of dirithromycin versus erythromycin, 317 and 383 participants, respectively; 1 study of dirithromycin versus penicillin V potassium, 121 and 136 participants, respectively.

Skin or soft tissue infections: 3 studies of dirithromycin versus erythromycin, 560 and 530 participants, respectively.

Clinical effectiveness and bacterial eradication by dirithromycin was not significantly different from erythromycin, clarithromycin and penicillin V potassium for chronic bronchitis, acute bronchitis, community-acquired pneumonia, streptococcal pharyngitis, and skin or soft tissue infections in the closely matched study groups.

Dirithromycin is reported to have the same proportion of adverse effects as those reported for erythromycin, clarithromycin and penicillin V potassium.

No significant drug interactions of dirithromycin with theophylline, terfenadine, cyclosporine, or oral contraceptives have been reported. Contraindications are: hypersensitivity to macrolide antibiotics. Precautions are: medications that are known to interact with other macrolide antibiotics; pregnancy (category C agent).

Recommended dosage:

500 mg/day for 7 days in the treatment of acute bronchitis, acute exacerbation of chronic bronchitis, and skin and soft tissue infections; shorter regimes of 5 days may be equally effective. Community-acquired pneumonia, streptococcal pharyngitis, and tonsillitis require a similar dosage (500 mg/day) but given for an extended time period, i.e. 10 to 14 days.

Cost information

Estimated cost for a full course of therapy in the USA:

Agent: erythromycin Regimen: 250 mg, four times daily, for 7 to 14 days Average wholesale price (AWP)/Regimen ($) : 7.56 to 15.12

Agent: dirithromycin Regimen: 500 mg/day for 7 to 14 days AWP/Regimen ($) : 56.32 to 52.64

Agent: azithromycin Regimen: 500 mg on day 1 Regimen: 250 mg on days 2 to 5 AWP/Regimen ($) : 36.24

Agent: clarithromycin Regimen: 250 mg, twice daily, for 7 to 14 days AWP/Regimen ($) : 41.58 to 83.16

Authors’ conclusions

The pharmacokinetic profile of dirithromycin allows once-daily dosing with higher and maintained tissue concentrations than achievable with erythromycin. Dosing adjustments are not needed in the elderly, or in patients with renal or mild hepatic impairment. Clinical efficacy, spectrum of activity, adverse effect profile, and bacterial eradication rate of dirithromycin are similar to those of erythromycin. However, there is no evidence that dirithromycin offers a clinical advantage over clarithromycin or azithromycin.

CRD commentary

A good overview of the activity and effectiveness of dirithromycin, which would provide sufficient depth for those wishing to develop further research into this antibiotic. However, the broad scope of the article may not provide the detailed information necessary for the formulation of clinical policy.

The review also includes other features of the antibiotic including: microbiological activity and pharmacokinetics.
(absorption, distribution, metabolism).

The reviewers chose not to perform a meta-analysis to compare the clinical effectiveness of dirithromycin with erythromycin, and this is probably wise with the omission of a validity assessment.

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