Azithromycin versus doxycycline for genital chlamydial infections: a meta-analysis of randomized clinical trials

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Authors' objectives
To evaluate the efficacy and tolerance of azithromycin versus doxycycline for genital chlamydial infection.

Searching
Studies published in English were retrieved from the following databases: MEDLINE and Pre-MEDLINE (from 1975 to August 2001), HealthSTAR (from 1975 to August 2001), EBM Reviews: Best Evidence (from September 1991 to January/February 2001), EBM Reviews: Cochrane Database of Systematic Reviews (second quarter of 2001), and EBM Reviews: DARE (second quarter of 2001). The medical subject headings 'CT' and 'doxycycline' or 'CT' and 'azithromycin' were used as search terms. Bibliographies of computer-identified articles were manually searched for additional trials for inclusion.

Study selection
Study designs of evaluations included in the review
Randomised trials were eligible.

Specific interventions included in the review
Regimens of either oral doxycycline (100 mg twice daily for 7 days) or oral azithromycin (1 g once) were eligible.

Participants included in the review
Male and non-pregnant females aged greater than 15 years, who were being treated for Chlamydia trachomatis (CT) cervicitis (females) and urethritis (males), were eligible.

Outcomes assessed in the review
The studies had to assess microbial cure at follow-up. Microbial cure was defined as CT negativity in the biological assay. Adverse events were separated by type (see 'Data extraction' field).

How were decisions on the relevance of primary studies made?
Both authors independently evaluated all trials comparing doxycycline with azithromycin.

Assessment of study quality
No formal assessment of validity was undertaken.

Data extraction
The authors state that the data were extracted from selected studies. The data extracted included: diagnostic assay, follow-up time, study design, sponsorship, patient's characteristics, adverse events, attrition rates and outcomes. Adverse events were separated by type, (gastrointestinal, neurological dermatological and other). When the occurrence of adverse events among patients with chlamydia infection was not distinguished from that of patients with non-gonococcal urethritis, results from patients with nongonococcal urethritis were used as proxies for those with CT infection. Attrition rates based on the last available follow-up were calculated by intention-to-treat analysis. The efficacy difference (ED), i.e. the difference in cure rates between azithromycin and doxycycline, of treatment success was computed. The risk difference (RD) of adverse events was also calculated.

Methods of synthesis
How were the studies combined?
To pool dichotomous outcomes, an overall weighted average of the ED from each trial was calculated by assigning each a weight derived from the standard error of the ED. Thus, the contribution of each trial to the pooled estimate of the ED was directly proportional to the amount of information provided. A similar approach was taken for computing the RD. Each pooled RD and ED was tested for statistical significance and the 95% confidence intervals (CIs) were calculated.

How were differences between studies investigated?
The authors state that they used a chi-squared test of homogeneity to test the assumption of uniform RD and ED. A stratified meta-analysis was used to assess possible bias in the results. Begg's and Egger's tests were used to test for publication bias. A P-value of 0.10 was used as the criterion for determining statistical significance of the tests for publication bias.

Results of the review
Twelve trials involving 726 males and 817 females were included.

From the twelve included trials, some 1,543 patients were evaluated for microbial cure and 2,171 for adverse events. The cure rates were 97% for azithromycin and 98% for doxycycline. Adverse events occurred in 25 and 23% of the patients treated with azithromycin and azithromycin, respectively. Following data pooling the ED and RD were computed. The ED for microbial cure (0.01, 95% CI: -0.01, 0.02) and the RD for adverse events (0.01, 95% CI: -0.02, 0.04) between the two drugs were not statistically significant.

Authors' conclusions
Azithromycin and doxycycline are equally efficacious in achieving microbial cure and have similar tolerability. Further head-to-head trials comparing these antibiotics are unnecessary.

CRD commentary
Only a brief description of the methods used to conduct the review was given. The search only included English language papers; therefore, there is always the possibility that some important papers may have been missed. There was no formal assessment of the validity of the included randomised controlled trials. The study details were well presented and the authors discussed the results in a balanced manner.

Implications of the review for practice and research
Practice: Both azithromycin and doxycycline are equally efficacious in achieving microbial cure and are similarly tolerated by patients.

Research: The authors state that there is no need for further head-to-head trials of these two antibiotics.

Bibliographic details

PubMedID
12218839

Indexing Status
Subject indexing assigned by NLM

MeSH
Anti-Bacterial Agents /adverse effects /therapeutic use; Azithromycin /adverse effects /therapeutic use; Chlamydia
Infections /drug therapy /microbiology; Chlamydia trachomatis; Doxycycline /adverse effects /therapeutic use; Female; Humans; Male; Randomized Controlled Trials as Topic; Treatment Outcome; Urethritis /drug therapy /microbiology; Uterine Cervicitis /drug therapy /microbiology

**AccessionNumber**
12002002117

**Date bibliographic record published**
30/09/2003

**Date abstract record published**
30/09/2003

**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.