Itraconazole vs fluconazole for the treatment of uncomplicated acute vaginal and vulvovaginal candidiasis in nonpregnant women: a metaanalysis of randomized controlled trials

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CRD summary
This review assessed the effectiveness and safety of oral itraconazole and fluconazole for uncomplicated acute vaginal and vulvovaginal candidiasis in non pregnant women, concluding that both regimens had similar effectiveness and safety. The reliability of the conclusion was uncertain given the poor quality of the included studies.

Authors’ objectives
To assess the effectiveness and safety of oral itraconazole and fluconazole for uncomplicated acute vaginal and vulvovaginal candidiasis in non pregnant women.

Searching
PubMed, Scopus, Web of Science and The Cochrane Library were searched (no dates given); search terms were reported. The search was restricted to English language papers.

Study selection
Randomised controlled trials (RCTs) comparing itraconazole and fluconazole oral for the treatment of acute uncomplicated vaginal and vulvovaginal candidiasis in non pregnant women were eligible for inclusion. Excluded were those studies where vaginal/vulvovaginal candidiasis was not confirmed mycologically, where clinical cure data were not presented and where pregnant women were included. The included studies assessed oral fluconazole 150 mg/day as a single dose and oral itraconazole at varying regimens: 200 mg two times a day for seven days (one study); 200 mg two times on one day (three studies); and 200 mg a day for three days (two studies). Where stated, the mean age varied across studies from 25 to 34 years (range 16 to 62 years). The primary outcomes were clinical cure and mycologic cure. Further outcomes included adverse events and recurrence of symptoms.

Two reviewers independently selected the studies.

Assessment of study quality
Two reviewers independently assessed the studies for quality using the Jadad scale, with the addition of a criterion relating to allocation concealment. Each study was allocated a score ranging from 0 (lowest) to 6 (highest). It was not reported how disagreements were resolved.

Data extraction
Data were independently extracted by two reviewers, who were blinded to study details. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for all outcomes.

Methods of synthesis
Studies were pooled in a meta-analysis using both fixed- and random-effects models for each outcome. A random-effects model was used where statically significant heterogeneity was observed. Heterogeneity was assessed using the \( \chi^2 \) and \( I^2 \) tests, with \( p<0.10 \) defined as statistically significant. Publication bias was assessed using a funnel plot and with Egger's test, with \( p<0.05 \) defined as statistically significant.

Results of the review
Six RCTs (n=1,092) were included. The included trials were of low quality, with none meeting more than three of the six quality criteria.

There was no significant difference between treatments for: either clinical cure or mycologic cure at first or second visit; or between adverse events from the nervous system or the digestive system; or with respect to withdrawal of
patients because of severe adverse events. A difference was detected in favour of fluconazole for the combined clinical and microbiologic cure (n=491) based on data from three RCTs (OR 0.5, 95% CI: 0.32, 0.79). There was no evidence of significant publication bias.

Intention to treat patients (n=186) had no adverse events from skin tissues noted for either treatment. The proportion of patients with adverse events in subcutaneous tissues was two per cent for fluconazole and 12 per cent for itraconazole. Recurrence of symptoms (n=376) was noted in nine per cent of fluconazole patients and 13 per cent of itraconazole patients.

**Authors' conclusions**
Itraconazole and fluconazole had similar effectiveness and safety in non pregnant women with acute uncomplicated vaginal and vulvovaginal candidiasis.

**CRD commentary**
The review addressed a clear question with defined inclusion criteria. The literature search was restricted to publications in the English language, so there was a risk of language bias. There was no specific search for unpublished studies, nor for studies outside of the databases, so publication bias may have been present (although this was not found to be the case). Search dates were not reported, so it was unclear over what period the authors searched for studies. Steps were taken to reduce the risk of reviewer error and bias in the study selection, data extraction and validity assessment. Only RCTs were included. An assessment of the methodological quality of the included studies was undertaken, with the result that all were found to be of poor quality. Suitable methods were used for the meta-analysis and heterogeneity was assessed (none was reported). The review was generally well conducted and clearly reported with the authors' conclusions reflective of the evidence included in the review. However, given the poor quality of the included studies the conclusions should be regarded with caution.

**Implications of the review for practice and research**
The authors did not state any implications for practice or further research.

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