Bladder irrigation with amphotericin B and fungal urinary tract infection: systematic review with meta-analysis

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CRD summary
The review attempted to establish the best place in therapy for amphotericin B bladder irrigation in the treatment of asymptomatic candiduria (Candida fungi present in the urine), and concluded that it appeared to be as effective as fluconazole. Due to uncertainties about quality of included studies and variability among studies, the authors' conclusions are unlikely to be reliable.

Authors' objectives
To determine the best place in therapy for amphotericin B bladder irrigation in the treatment of asymptomatic candiduria.

Searching
MEDLINE, EMBASE, Web of Science and LILACS were searched from January 1960 to June 2007; the Cochrane Library database was searched up to 2007. Search terms were reported. Bibliographies of retrieved articles were also scanned for additional studies. There were no language restrictions.

Study selection
Studies evaluating the use of amphotericin B bladder irrigation for treatment of asymptomatic candiduria were eligible for inclusion. The outcome of interest was candiduria clearance, which was determined qualitatively or quantitatively by the presence of *Candida* species in at least two urine samples. To be eligible, studies could be comparative (amphotericin B bladder irrigation with another treatment), single-armed, or dose-finding comparing different dosing regimes of amphotericin B bladder irrigation.

All the included studies were prospective in design. Included patients were hospitalised adults with urine cultures showing the presence of *Candida albicans* and *Candida* species; in some cases, the species identification was "unknown". Where relevant, fluconazole was the comparator drug. The dose of amphotericin B bladder irrigation varied, depending on continuous (10 to 50mg/L) or intermittent (1mg/200mL to 30mg/100mL) treatment.

The authors did not state how the papers were selected for the review.

Assessment of study quality
Validity was assessed but no particular scale was used. The level of blinding, randomisation, control groups and study design were considered.

The authors did not state how many reviewers performed the validity assessment.

Data extraction
Data on candiduria clearance and treatment failure were extracted to calculate odds ratios (OR) with corresponding 95% confidence intervals (CI).

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Meta-analysis was used to calculate pooled odds ratios with corresponding 95% confidence intervals for persistence of candiduria (candiduria clearance). Pooled outcomes were reported separately for comparisons of: amphotericin B bladder irrigation (continuous or intermittent) versus fluconazole at 24 hours and five days after treatment; continuous
amphotericin B bladder irrigation versus intermittent amphotericin B bladder irrigation at 24 hours and five days after treatment; and continuous amphotericin B bladder irrigation for five days or more versus treatment of less than five days.

Results of the review
Nine studies were included in the review (n=377 patients; range 10 to 88). All studies were open-label; five were reported as randomised controlled trials. Included studies varied in duration of follow-up (at discharge or between seven to 30 days).

Amphotericin B bladder irrigation (continuous or intermittent) versus fluconazole: Amphotericin B bladder irrigation was associated with lower rates of candiduria persistence 24 hours after treatment, but this result did not achieve statistical significance (OR 0.57, 95% CI 0.32 to 1.00). There were no differences in candiduria persistence between the treatment groups five days after treatment.

Continuous versus intermittent amphotericin B bladder irrigation treatment: Continuous bladder irrigation with amphotericin B was superior to intermittent treatment at seven days after treatment (OR 0.52, 95% CI 0.29 to 0.94), but at 24 hours after the end of treatment. Continuous amphotericin B bladder irrigation for five days or more had lower candiduria persistent rates than intermittent treatment, but did not achieve statistical significance.

Authors' conclusions
The authors concluded that, although definitive conclusions could not be drawn, amphotericin B bladder irrigation treatment appeared to be as effective as fluconazole and should only be used for systemic candiduria.

CRD commentary
The review addressed a clear question with respect to participants, intervention and outcome. Inclusion criteria regarding study design was not explicitly stated. Relevant databases were searched for studies in any language and efforts were made to retrieve additional articles by searching references lists. The search was somewhat limited as there were no attempts to retrieve unpublished studies, increasing the possibility of publication bias.

The quality assessment suggested that the included studies may have been of poor quality, all of which were open-label studies with small number of patients. Statistical heterogeneity was not assessed, but the authors considered clinical heterogeneity which was found to be present. Given the heterogeneity of the data and a lack of description of statistical methods, combining the studies in a meta-analysis may not have been appropriate.

The inclusion of small studies with questionable quality and the variability among studies raises uncertainties about the reliability of the results, so the authors' conclusions may have been optimistic and are unlikely to be reliable.

Implications of the review for practice and research
Practice: The authors tentatively suggested that amphotericin B bladder irrigation can be used in patients with asymptomatic candiduria showing risk of dissemination and that the best method involves continuous treatment for more than five days.

Research: The authors did not state any implications for further research.

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