Is intravaginal Boric acid an alternative therapeutic option for vaginal trichomoniasis?

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Background

- Current national guidance recommends treating *Trichomonas vaginalis* (TV) infection with nitro-imidazole therapy (Metronidazole or Tinidazole).
- Nitro-imidazoles are associated with gastrointestinal intolerance which limits their use in some patients. In addition, 4-10% of clinical isolates of TV exhibit metronidazole resistance in vitro.
- The high prevalence of TV in certain populations, high rate of metronidazole resistance and limited tolerability to nitroimidazoles when treating TV, suggest that alternative treatment regimens are required.
- The use of intravaginal therapy for TV offers potential advantages over systemic therapy. Reducing the use of systemic antibiotics limits the development of antimicrobial resistance within the community, and local intravaginal therapy is less likely to cause systemic adverse effects.

Aim

Our aim was to review the evidence for the safety and efficacy of intravaginal Boric acid (BA) for the treatment of TV.

Methods

- We performed a systematic review, in accordance with Centre for Reviews and Dissemination methodology, of the evidence for the efficacy of BA as a topical treatment for TV.
- A systematic review was performed on 2/6/16. A keyword search was performed using MEDLINE and EMBASE without additional limits (BORIC ACID combined using AND with TRICHOMONADS, TRICHOMONIASIS, TRICHOMONAS VAGINALIS, CANDIDA, BACTERIAL VAGINOSIS, VAGINAL INFECTIONS, SEXUALLY TRANSMITTED INFECTIONS, CANDIDIASIS or VAGINAL SUPPOSITORIES).

Results

- 170 papers were identified and, after removal of 6 duplicates and review of the article reference lists, 12 studies were included (Fig. 1).^[1-12]
- BA intravaginal pessaries have been used safely for the treatment of vulvovaginal conditions, including candidiasis and bacterial vaginosis.^[1-7]
- BA's exact mechanism of action against TV remains unclear. Its activity may be mediated by vaginal acidification resulting in cell wall penetration and disruption of the cell membrane;^[8-9] however studies evaluating its minimum inhibitory concentration indicate that it works at a pH similar to that of the untreated vaginal tract indicating that it possesses additional antimicrobial activity beyond that due to acidification.^[8-10]
- Reported adverse effects were mild and occurred rarely with topical BA but included a vaginal burning sensation (< 10% of cases), watery discharge during treatment and vaginal erythema.^[2] Longterm safety is unknown because of a lack of data, but the risk of systemic toxicity due to vaginal administration has been shown to be minimal in doses of one to two 600mg BA capsules daily for up to 2 weeks.^[10]
- No randomised controlled trials or case series assessing the efficacy of BA for treating TV were found. No studies assessed the efficacy of BA in uncomplicated TV infection.
- 3 case reports provided in vivo evidence that intravaginal boric acid can safely and effectively treat TV.^[11-12] These reported cases were in the setting of resistant TV or severe metronidazole allergy with combination treatment given over a period of 4 weeks to 5 months using doses of BA ranging from 600mg once a day to 600mg twice a day.

- In vitro, low concentrations (0.2%) of BA reduced the growth rate of TV, whereas higher concentrations ($\geq 0.4\%$) were lethal to both laboratory TV strains and clinical isolates, providing evidence that the inhibitory effect of BA on TV may be dose-dependent.^[9]
- There was limited data on the solubility and distribution of BA administered intravaginally; it is therefore difficult to correlate in vitro and in vivo concentrations.

Figure 1: PRISMA Flow Diagram

Conclusion

- **BA is well-tolerated and has in vitro and in vivo activity against TV. There is limited evidence on the appropriate dosing schedule. There is need for further evaluation in a clinical trial.**
- **If shown to be safe and effective, intravaginal BA would provide an alternative treatment without systemic side effects, and reduce community exposure to antibiotics supporting the UK Antimicrobial Resistance Strategy and meeting a research priority area for the NIHR.**

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