

Recalcitrant *Trichomonas Vaginalis* Infections Successfully Treated With Vaginal Acidification

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Abstract

Background: Recalcitrant vaginal trichomoniasis is extremely distressing for patients and frustrating for physicians because there are no current guidelines for treatment. Numerous studies have shown that an increase in vaginal pH creates a better environment for the growth of *Trichomonas vaginalis*. We describe two patients with recalcitrant trichomoniasis who were successfully treated using vaginal acidification.

Cases: The first patient with trichomoniasis had a severe reaction to metronidazole, but the infection subsequently resolved after treatment with a combination of boric acid and clotrimazole. The second patient with resistant trichomoniasis had been treated unsuccessfully with multiple courses of metronidazole but was treated successfully with vaginal acidification using boric acid.

Conclusion: A process of vaginal acidification resulted in resolution of recalcitrant *Trichomonas vaginalis* in two patients.

Résumé

Contexte : La trichomonase vaginale récalcitrante est extrêmement troublante pour les patientes et frustrante pour les médecins, puisque aucune directive clinique actuelle ne s'est penchée sur sa prise en charge. De nombreuses études ont indiqué qu'une hausse du pH vaginal crée un meilleur environnement pour la prolifération de *Trichomonas vaginalis*. Nous décrivons le cas de deux patientes présentant une trichomonase récalcitrante qui ont été traitées avec succès au moyen d'une acidification vaginale.

Cas : Bien que la première patiente présentant une trichomonase ait connu une grave réaction au métronidazole, l'infection a subséquemment été résolue par la mise en œuvre d'un traitement faisant appel à une combinaison d'acide borique et de clotrimazole. La deuxième patiente présentant une trichomonase résistante avait été traitée, sans succès, au moyen de multiples traitements au métronidazole; toutefois, la mise en œuvre d'une acidification vaginale au moyen d'acide borique a mené à la résolution de l'infection.

Conclusion : La mise en œuvre d'un processus d'acidification vaginale a entraîné la résolution d'une infection récalcitrante à *Trichomonas vaginalis* chez deux patientes.

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INTRODUCTION

Trichomoniasis is a sexually transmitted infection caused by the parasitic protozoan *Trichomonas vaginalis*. The World Health Organization estimates that 180 million new cases of trichomoniasis occur each year.¹ This is more than the incidence rates of gonorrhea, chlamydia, and syphilis combined. Trichomoniasis accounts for 4% to 35% of vaginitis diagnosed in symptomatic women in a primary care setting in the United States.² The symptoms of trichomoniasis in women range from none at all to a severe acute inflammatory state. Classic signs and symptoms include a purulent, malodorous vaginal discharge with associated pruritus, burning, dysuria and dyspareunia. Physical examination in affected women shows vaginitis and vulvitis, with a frothy, yellow-green mucopurulent discharge. Colpitis macularis ("strawberry cervix") may be seen colposcopically.³ Trichomoniasis is a risk factor for post-hysterectomy cellulitis, tubal infertility, cervical neoplasia, premature rupture of membranes, and preterm labour.⁴⁻⁷ It has also been associated with an increased risk of HIV transmission (likely due to genital inflammation),⁸ and appropriate treatment is therefore imperative.

Currently, the mainstay of treatment for infection with *Trichomonas vaginalis* is oral metronidazole. Metronidazole is a 5-nitroimidazole derived from the *Streptomyces* antibiotic azomycin. It was developed in 1959 and approved for the treatment of trichomoniasis in the early 1960s. Metronidazole was the first drug to have a cure rate in trichomoniasis that approached 100% with systemic treatment.⁹ At present, metronidazole is prescribed either as a single 2 g oral dose or as a seven-day course of 500 mg twice daily for the treatment of trichomoniasis. A strain of metronidazole-resistant *Trichomonas vaginalis* was first isolated in 1978,¹⁰ although there were prior reports of treatment failures.¹¹ Data published by the Centers for Disease Control (CDC) indicate that 5% of trichomoniasis showed some resistance to metronidazole, although 80% of cases

responded to an increase in dose or duration.¹² The current CDC guidelines for the treatment of refractory cases recommend the use of tinidazole (in a single 2 g oral dose) or an increased dose of metronidazole (2 g daily for 5 days).¹³ Most cases of refractory trichomoniasis are treated with metronidazole given in increased doses, increased duration of treatment, or multiple courses of treatment. Resistance appears to be relative, so an increased dose of metronidazole can overcome resistance but will also lead to an increase in the occurrence of side effects. Concurrent use of alcohol must be avoided, because reactions similar to those occurring with disulfiram can occur at any metronidazole dose level. Nuisance adverse effects are mostly gastrointestinal symptoms; however, because high dose metronidazole has been associated with irreversible peripheral neurotoxicity, this therapy is not without significant complications.

Several alternatives to the standard dosing of metronidazole have been reported. A combination of oral and vaginal courses of treatment or an increase in dose and duration have been shown to be effective.^{14,15} Tinidazole, another nitro-imidazole, has been shown to achieve cure in cases of metronidazole failure; one study reported cure rates as high as 92% (in a special access program, as tinidazole was not commercially available).^{15,16} Topical treatments have also been studied, both in combination with oral metronidazole and alone, but they have shown much lower efficacy. Paromycin cream was the first to be used with any success, but it was associated with side-effects ranging from mild to severe, including vaginal and vulvar ulceration.^{17,18} Normal saline douching and pessaries containing acetarsol, clotrimazole, and providine-iodine have all been used in cases of recalcitrant trichomoniasis with differing results.^{11,19–26} A recent study cited a cure rate of 90% when combining clotrimazole pessaries with oral tinidazole in cases of metronidazole-resistant *Trichomonas vaginalis*.²⁷ A combination of metronidazole with nonoxynol-9 intravaginal spermicide resulted in a cure rate of 90%, while nonoxynol-9 alone resulted in cure rates of 17.6% to 40%.^{28,29} Zinc sulphate douching has also been used in combination with metronidazole; one study found that lower doses of metronidazole were required in patients who also douched with zinc sulphate.³⁰

Numerous studies have shown that an increase in pH creates a better environment for the growth of *Trichomonas vaginalis*, but to date there have been no case reports on the use of vaginal acidification for the treatment of trichomoniasis.^{31–33} We describe here two patients with recalcitrant trichomoniasis who were successfully treated using vaginal acidification.

CASE ONE

A 58-year-old woman with symptomatic vaginitis was shown to have a diamond media culture-positive *Trichomonas vaginalis* infection. She and her partner were both treated with a single 2 g oral dose of metronidazole. Her infection persisted. She was prescribed a second course of metronidazole, but she developed severe urticaria and acute respiratory suppression. She received resuscitative therapy, and the metronidazole was discontinued. It was concluded that she had developed an allergy to metronidazole, and various other therapies were then instituted; these included saline douches, iodine (Betadine) douches, and vaginal clotrimazole, both with and without vaginal conjugated equine estrogen cream.^{11,19,23–26} The infection persisted despite these treatments. The patient was then treated with paromycin topical cream, but she developed severe vestibular sloughing, and this treatment was discontinued.^{17,18}

The patient was referred to the colposcopy unit. She was no longer sexually active, and she remained severely symptomatic with wet preparation and cultures positive for *Trichomonas vaginalis*. Treatment was begun using vaginal conjugated equine estrogen cream 1g nightly alternating with vaginal clotrimazole cream. The patient was re-evaluated two weeks later, and *Trichomonas vaginalis* was found to be still present. A 4% acetic acid vaginal douche/debridement was applied, and a routine began of using vaginal clotrimazole alternating nightly with vaginal boric acid 600 mg in gelatin capsules to acidify the vagina. After six weeks, this regimen was stopped, and the vaginal symptoms with culture positive *Trichomonas vaginalis* returned within two weeks. The patient had not been sexually active during this time.

The previous routine using boric acid alternating with clotrimazole was reintroduced and continued for a further five months. The patient has remained asymptomatic and culture negative for more than five years.

CASE TWO

A 40-year-old gravida 2, para 2 woman with symptomatic vaginitis was found to have a diamond media culture-positive and wet preparation positive *Trichomonas vaginalis* infection. She was not sexually active. She was treated initially with a single 2 g dose of oral metronidazole, but the infection persisted. She was then treated with metronidazole 250 mg three times daily for seven days, 2 g daily for five days, and 2 g daily for seven days, but all of these regimens failed to clear the infection.

The patient was referred to the colposcopy unit. She remained severely symptomatic, with wet preparation and cultures positive for *Trichomonas vaginalis*. A 4% acetic acid

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