


Cure of Metronidazole- and Tinidazole-Resistant Trichomoniasis with Use of High-Dose Oral and Intravaginal Tinidazole

Trichomonas vaginalis organisms infect an estimated 3 million American women every year [1]. When the recommended treatment with metronidazole [2] is unsuccessful because of resistance or side effects, the options available to the clinician are limited [3].

We describe a patient with proven metronidazole- and tinidazole-resistant trichomoniasis whose condition failed to respond to therapy with high-dose oral and vaginal metronidazole as well as intravaginal furazolidone and nonoxynol-9 but responded to simultaneous administration of oral and intravaginal tinidazole.

A 33-year-old woman with no significant medical history was referred in October 1995 for evaluation of trichomoniasis that had failed to respond to repeated courses of metronidazole since December 1991. She had been sexually inactive since 1992.

Physical examination showed an obese, 330-lb woman in no distress. Significant findings included erythematous vulvar mucosa, introital tenderness, and a purulent vaginal discharge. A wet mount preparation revealed many motile trichomonads. In addition, the organisms were grown in modified Diamonds media (Remel Microbiology Products, Lenexa, KS). Results of susceptibility testing at the Centers for Disease Control and Prevention (CDC) indicated resistance to metronidazole and tinidazole (Table 1).

Administration of a combination of oral (2.5 g/d) and intravaginal (0.5 g at bedtime) metronidazole for 20 days with oral prochlorperazine caused vomiting and failed to eradicate the infection.

Treatment with oral furazolidone, 300–400 mg q.i.d. for 7 days, was initiated. The patient developed nausea and brown-colored urine but was able to complete the treatment course, which resulted in minimal symptomatic improvement. Wet mount preparations and cultures of vaginal secretions continued to be positive for trichomonads. Subsequently, she received a vaginal preparation containing 100 mg of furazolidone in 5 g of 3% nonoxynol-9 one to three times daily for 7 days. She noted clinical improvement that persisted for >1 month after treatment. Her symptoms eventually returned, and trichomonads were again noted in her vaginal secretions. There was no interim sexual activity.

Table 1. Minimum lethal concentrations of metronidazole, tinidazole, and furazolidone for Trichomonas vaginalis.

<table>
<thead>
<tr>
<th>Date</th>
<th>Aerobic/anaerobic</th>
<th>Aerobic/anaerobic</th>
<th>Aerobic/anaerobic</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/23/96</td>
<td>400/12.5</td>
<td>200/25</td>
<td>ND</td>
</tr>
<tr>
<td>12/15/96</td>
<td>&gt;400/6.3</td>
<td>400/12.5</td>
<td>0.4/3.1</td>
</tr>
<tr>
<td>08/30/96</td>
<td>&gt;400/12.5</td>
<td>400/12.5</td>
<td>0.4/0.4</td>
</tr>
<tr>
<td>04/02/97</td>
<td>&gt;400/25</td>
<td>100/25</td>
<td>0.8/1.6</td>
</tr>
</tbody>
</table>

NOTE. Values are presented as mg/L. ND = not done.

* Multiple determinations were done on each date. The highest minimum lethal concentration for each date is listed.

Tinidazole therapy was initiated (500 mg orally q.i.d. in addition to 500 mg intravaginally b.i.d.) and was continued for a total of 14 days. All of her symptoms resolved. Cultures of vaginal secretions and urinary sediments in modified Diamonds media, 21 and 60 days after completion of treatment, were negative for T. vaginalis. Tinidazole was well tolerated by the patient, causing only mild nausea. She remains symptom free 5 months later.

This case illustrates resistance in T. vaginalis organisms. Among cases of trichomoniasis that fail to respond to treatment, clinicians tend to attribute the treatment failure to poor compliance or to reinfection. As is true for any antimicrobial treatment, resistant strains should be considered in cases of persistent infection. Estimates of the prevalence of infection due to metronidazole-resistant T. vaginalis range from marginal (one in 50–75 cases) to high (one in 2,000–3,000 cases) [3]. The case we have described demonstrates that high doses of tinidazole may be an option for patients who have infections due to resistant T. vaginalis, even in instances of intravaginal resistance to the agent. High doses tinidazole therapy was well tolerated in this case. There were fewer side effects than associated with metronidazole therapy. The organisms were susceptible to furazolidone. However, oral treatment with furazolidone was ineffective, whereas a vaginal preparation containing furazolidone in nonoxynol-9 was associated with impressive, albeit short-lived, symptomatic improvement.

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Severe reactions to vancomycin are rare. Fever and rashes (ranging in activity is bactericidal against all but enterococci. In combination, it is limited. There is no apparent synergy with aminoglycosides.

Additionally mild (flushing, pruritus, and hypotension) and preventable. icillin-resistant staphylococci, streptococci, and enterococci; its ac-

prosthetic valve. The patient remains well after 12 months. This investigational streptogramin is active against a spectrum of infections in humans; however, data regarding this are lim-

Despite symptoms including myalgias, arthralgias, and fatigue, the patient completed a 6-week course. Cultures of blood obtained prior to completion of therapy were sterile. An echocardiogram obtained 12 weeks after the cessation of therapy showed a normal prosthetic valve that is not influenced by most forms of bacterial resistance [6].

One week after discharge, the patient developed fever (temperature, to 102°F). Findings on physical examination were unremarkable. Blood cultures were negative. The fever continued, and a maculopapular rash developed despite discontinuation of rifampin therapy. A repeated TEE showed normal prosthetic function. Vancomycin therapy was discontinued. The patient was rechallenged with vancomycin, rifampin, and gentamicin. We describe a patient who had a severe allergic response to vancomycin during therapy for PVE due to methicillin-resistant Staphylococcus epidermidis (MRSE).

A 44-year-old male with a history of St. Jude mitral-valve replacement 6 months earlier presented with cough, fever, and dyspnea. Physical examination revealed only a systolic murmur. A transesophageal echocardiogram (TEE) revealed a mitral annular abscess, multiple vegetations, and instability of the prosthetic valve (Figure 1). Three sets of blood cultures yielded MRSE (bioMérieux Vitek, Hazelwood, MO). The patient underwent mitral-valve replacement with reconstruction of the mitral annulus. After an uncomplicated postoperative course, he was discharged with continued vancomycin, rifampin, and gentamicin therapy.

One week after discharge, the patient developed fever (temperature, to 102°F). Findings on physical examination were unremarkable. Blood cultures were negative. The fever continued, and a maculopapular rash developed despite discontinuation of rifampin therapy. A repeated TEE showed normal prosthetic function. Vancomycin therapy was discontinued. The patient was rechallenged with vancomycin with premedication; this was followed by fever, pruritus, tongue swelling, and worsening rash with conjunctival involvement. Findings on histopathologic evaluation of a skin biopsy specimen were consistent with drug eruption. Therapy with RP 59500 (quinapristin/dalfopristin; Synercid; Rhône-Poulenc Rorer, Collegeville, PA) was initiated at a dose of 7.5 mg/kg q8h. Despite symptoms including myalgias, arthralgias, and fatigue, the patient completed a 6-week course. Cultures of blood obtained after completion of therapy were sterile. An echocardiogram obtained 12 weeks after the cessation of therapy showed a normal prosthetic valve. The patient remains well after 12 months.

Adverse reactions to vancomycin therapy are common but usually mild (flushing, pruritus, and hypotension) and preventable. Severe reactions to vancomycin are rare. Fever and rashes (ranging from a pruritic maculopapular rash to toxic epidermal necrolysis) have been reported [1]. Therapeutic options for these patients are limited.

Teicoplanin, an investigational glycopeptide (not approved by the U.S. Food and Drug Administration) with activity against gram-positive bacteria [2] has been effective for treatment of streptococcal and staphylococcal endocarditis [3]. Cross-reactivity may occur in those patients with vancomycin hypersensitivity who are treated with teicoplanin [4]. In addition, teicoplanin, which could be obtained previously for compassionate use in the United States, has not been available since 1995.

RP 59500 is a combination of two semisynthetic derivatives of pristinamycin: quinapristin and dalfopristin [5]. In combination, quinapristin/dalfopristin, exerts a synergistic antibacterial effect that is not influenced by most forms of bacterial resistance [6]. This investigational streptogramin is active against a spectrum of gram-positive bacteria, including methicillin-susceptible and methicillin-resistant staphylococci, streptococci, and enterococci; its activity is bactericidal against all but enterococci. The mechanism of action involves binding to the 50s bacterial ribosome, resulting in a stable complex that irreversibly inhibits bacterial protein synthesis. There is no apparent synergy with aminoglycosides.

RP 59500 has been effective in animal models for the treatment of endocarditis, showing homogenous distribution throughout experimental vegetations [7]. In a rabbit fibrin clot model, RP 59500 exhibited penetration and sterilization of the clot [8]. These data suggest that RP 59500 should be efficacious therapy for life-threatening infections in humans; however, data regarding this are limited. Furlong and Rakowski [9] recently reported a case of PVE due to vancomycin-resistant Enterococcus faecium treated with

References


Staphylococcus epidermidis Endocarditis Treated with RP 59500 (Quinapristin/Dalfopristin)

Staphylococcus epidermidis is a common cause of prosthetic valve endocarditis (PVE). Treatment for this condition consists of combination antibiotic therapy including vancomycin, rifampin, and gentamicin. We describe a patient who had a severe allergic reaction to vancomycin during therapy for PVE due to methicillin-resistant Staphylococcus epidermidis (MRSE).

A 44-year-old male with a history of St. Jude mitral-valve replacement 6 months earlier presented with cough, fever, and dyspnea. Physical examination revealed only a systolic murmur. A transesophageal echocardiogram (TEE) revealed a mitral annular abscess, multiple vegetations, and instability of the prosthetic valve (Figure 1). Three sets of blood cultures yielded MRSE (bioMérieux Vitek, Hazelwood, MO). The patient underwent mitral-valve replacement with reconstruction of the mitral annulus. After an uncomplicated postoperative course, he was discharged with continued vancomycin, rifampin, and gentamicin therapy.

One week after discharge, the patient developed fever (temperature, to 102°F). Findings on physical examination were unremarkable. Blood cultures were negative. The fever continued, and a maculopapular rash developed despite discontinuation of rifampin therapy. A repeated TEE showed normal prosthetic function. Vancomycin therapy was discontinued. The patient was rechallenged with vancomycin with premedication; this was followed by fever, pruritus, tongue swelling, and worsening rash with conjunctival involvement. Findings on histopathologic evaluation of a skin biopsy specimen were consistent with drug eruption. Therapy with RP 59500 (quinapristin/dalfopristin; Synercid; Rhône-Poulenc Rorer, Collegeville, PA) was initiated at a dose of 7.5 mg/kg q8h. Despite symptoms including myalgias, arthralgias, and fatigue, the patient completed a 6-week course. Cultures of blood obtained after completion of therapy were sterile. An echocardiogram obtained 12 weeks after the cessation of therapy showed a normal prosthetic valve. The patient remains well after 12 months.

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Figure 1. Large mitral annular abscess, with multiple moderate-to-large sized vegetations attached to an unstable prosthetic valve with partial suture dehiscence in a patient with Staphylococcus epidermidis endocarditis. LA = left atrium; LV = left ventricle; MV = mitral valve; V = vegetation; and A = annular abscess.

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