

Successful Metronidazole Desensitization Using Modified Oral Protocol

Shijun Cindy Xi,
Lori P Banka,
Salima Thobani,
Marilyn Li,
Kenny YC Kwong and
Lyne Scott

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Short Communication

Trichomoniasis is the most prevalent nonviral sexually transmitted infection in the United States and affects over 11% of women over the age of 40 [1]. Metronidazole and tinidazole are the only medications that are recommended by the Centers for Disease Control for the treatment of trichomoniasis¹. Alternative therapies are not standardized and limited in efficacy [2]. Case reports suggest that there is cross-reactivity between metronidazole and tinidazole [3]. The body of literature describing metronidazole hypersensitivity is scarce and to date, the incidence is unknown. Skin-prick testing to metronidazole is not validated. Three metronidazole desensitization protocols have been described, including one intravenous³ and two oral protocols [4,5]. In 2008, the Centers for Disease Control and Prevention published a study documenting a total of 127 patients with suspected metronidazole hypersensitivity, among whom 15 patients underwent metronidazole desensitization². Among those 15 patients, 7 patients underwent a 14-dose intravenous protocol³ and 8 patients underwent an 8-dose oral protocol⁵. All 15 patients achieved infection cure. More recently, a 12-dose modified oral desensitization protocol was described by Gendelman and colleagues in 2014.

We present the case of a 48 year old African-American female with diagnosis of vaginal trichomoniasis who had been untreated for 9 months due to a history of metronidazole hypersensitivity. She had received oral metronidazole (8 tablets, presumably a total of 2 gm) approximately 30 years ago for treatment of vaginal trichomoniasis. Within 1-2 hrs, she developed hives, "distended veins," and shortness of breath. She called paramedics and was treated in the emergency department for presumed anaphylaxis. Since then, she has avoided the drug. She was referred for Allergy/Immunology evaluation of metronidazole sensitivity. At her initial evaluation, her past medical history was significant for hypertension, depression, tobacco exposure and a diagnosis of "bronchitis." She described dyspnea and wheeze with exertion and occasional albuterol use. The patient had no previous respiratory-related emergency department visits or hospitalizations.

The patient was admitted to the intensive care unit for oral metronidazole desensitization. She was pretreated with

Division of Allergy and Immunology,
Los Angeles County and University of
Southern California Medical Center, USA

Corresponding author: Shijun Cindy Xi

✉ xicindy@gmail.com

Division of Allergy and Immunology, Los
Angeles County and University of Southern
California Medical Center, USA.

Tel: 6178529714

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prednisone 40 mg oral daily 2 days prior to and on the day of desensitization. Antihistamines were discontinued one week prior to admission. Vital signs, cardiac and pulmonary examination were within normal limits. FEV1 was 80% of predicted. Skin prick test was performed to metronidazole 2 mg/mL, glycerin control and histamine control. Glycerin control and metronidazole were negative and histamine was positive. Following skin prick testing, she received pretreatment with oral diphenhydramine 50 mg. She then underwent an oral, 12-dose modified protocol (**Table 1**) as described by Gendelman et al. Doses were given at 30-minute intervals and vital signs were checked every 30 minutes. She tolerated the protocol without any reactions, was observed for 4 hrs after completion of the protocol, and was discharged home the same day.

In determining the optimal management strategy for this patient, we weighed a number of "low-risk" as well as "high-risk" factors. The patient's reaction to metronidazole was remote, so theoretically, IgE specific to metronidazole should have waned over time. However, her reaction was severe and she had a history consistent with chronic pulmonary disease that would make her at risk for a more severe reaction. Given the paucity of literature

Table 1 Modified oral desensitization protocol (Gendelmen et al.).

Dose 1	0.0025 mg
Dose 2	0.025 mg
Dose 3	0.25 mg
Dose 4	2.5 mg
Dose 5	5 mg
Dose 6	10 mg
Dose 7	25 mg
Dose 8	50 mg
Dose 9	100 mg
Dose 10	250 mg
Dose 11	500 mg
Dose 12	1000 mg

on metronidazole hypersensitivity and lack of predictability of skin prick testing; we proceeded cautiously by performing the modified oral desensitization protocol in a monitored setting. We hope that as the body of literature grows on metronidazole hypersensitivity (and drug hypersensitivity in general), we may develop standardized testing to help guide management. In the meantime, we provide another example of successful treatment with the modified oral metronidazole desensitization protocol.

References

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- 4 Gendelman SR, Pien LC, Gutta RC, Abouhassan SR (2014) Modified oral metronidazole desensitization protocol. *Allergy Rhinol* 5: e66-e69.
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