A New Rush Schedule for Cotrimoxazole Desensitization: A Report of 2 Cases

Rial Prado MJ¹, Rico Díaz MA², Cosgaya Ceballos A¹, Cuesta Herranz J³
¹Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain
²Complejo Hospitalario Universitario A Coruña, A Coruña, Spain

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Trimethoprim-sulfamethoxazole (cotrimoxazole) is an effective drug for the treatment of infectious diseases caused by gram-positive bacteria, gram-negative bacteria, and protozoa that reduces the risk of opportunistic infection by *Pneumocystis jiroveci* [1]. Sulfonamides are the most common culprits of adverse reactions to cotrimoxazole [2]. The prevalence of adverse reactions to cotrimoxazole ranges from 20% to 100% in certain populations, such as HIV-infected patients, while in healthy individuals the prevalence is normally between 5% and 8% [3]. The 2 possible therapeutic approaches following confirmed diagnosis of adverse reactions to cotrimoxazole are withdrawal of the drug and desensitization. We report 2 cases in which a new rush desensitization schedule for cotrimoxazole was used. A maintenance dose was achieved in 135 minutes, thus enabling a regimen that could be administered on alternate days.

The first case involved a 67-year-old white woman with stage IIIA follicular lymphoma. Approximately 4 months before presenting at our department, she was prescribed cotrimoxazole on alternate days as prophylactic treatment for *P jiroveci* infection. A few days after beginning treatment, she presented generalized itchy rash, mainly on her legs, which resolved with antihistamines and withdrawal of cotrimoxazole. For this reason, the patient was referred to our allergy department, where skin prick tests were performed with trimethoprim at 32 mg/mL and sulfamethoxazole at 200 mg/mL (Almofarma SL) and intradermal tests at 0.001 mg/mL of trimethoprim and 20 mg/mL of sulfamethoxazole, as previously reported [3]. The results were negative. An oral challenge test elicited a generalized exanthematous rash 30 minutes after a dose of 200/40 mg of trimethoprim/sulfamethoxazole. Desensitization to cotrimoxazole was indicated, as this was the only oral antimicrobial available for prophylaxis of *P jiroveci*.

Desensitization was performed using a new rush intravenous desensitization protocol based on the protocol of Gluckstein and Ruskin [4] (Table), with good tolerance. The procedure was performed at the hospital, with a physician and nurse in attendance and emergency medication readily available. Written informed consent (both for the challenge test and desensitization procedure) was given by
Desensitization protocols have been developed to safely reintroduce critical drugs in patients with prior reactions to these drugs. The mechanisms of desensitization are still unknown [5]. Several protocols for desensitization to cotrimoxazole have been described. These can last from a single day to several days, the shortest being from 90 minutes to 6 hours [6]. Most of the protocols described involve oral administration and are normally used in adults, although protocols have also been described in children [7,8]. Pyle et al [6] reported the safety and efficacy of outpatient administration of cotrimoxazole in immunocompetent persons with a history of adverse reaction to sulfonamides. Our protocol is one of the fastest published to date, and is original in that it is intravenous, which has the advantage of more accurate dosing. Additionally, protocols such as ours may be suspended in the case of adverse effects, although very rapid administration can cause undesirable effects. We administer the dose corresponding to each of the first 3 steps in a milliliter bolus. The last 2 doses are given slowly in a volume of 100 mL.

Table. Intravenous Desensitization Protocol

<table>
<thead>
<tr>
<th>Steps</th>
<th>Rate</th>
<th>Time, min</th>
<th>Cumulative Time, min</th>
<th>Volume Administered, mL</th>
<th>Dose Administered, mg*</th>
<th>Cumulative Dose, mg</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bolus</td>
<td>15</td>
<td>15</td>
<td>1 mL</td>
<td>0.02/0.004</td>
<td>0.02/0.004</td>
<td>0.02/0.004 mg/mL</td>
</tr>
<tr>
<td>2</td>
<td>Bolus</td>
<td>15</td>
<td>30</td>
<td>1 mL</td>
<td>0.2/0.04</td>
<td>0.22/0.044</td>
<td>0.2 mg/mL</td>
</tr>
<tr>
<td>3</td>
<td>Bolus</td>
<td>15</td>
<td>45</td>
<td>1 mL</td>
<td>2/0.4</td>
<td>2.22/0.444</td>
<td>2/0.4 mg/mL</td>
</tr>
<tr>
<td>4</td>
<td>40 mL/h</td>
<td>15</td>
<td>60</td>
<td>10 mL</td>
<td>20/4</td>
<td>22.22/4.444</td>
<td>2/0.4 mg/mL</td>
</tr>
<tr>
<td>5</td>
<td>200 mL/h</td>
<td>30</td>
<td>90</td>
<td>100 mL</td>
<td>200/40</td>
<td>222.22/44.444</td>
<td>2/0.4 mg/mL</td>
</tr>
<tr>
<td>6</td>
<td>133 mL/h</td>
<td>45</td>
<td>135</td>
<td>100 mL</td>
<td>800/160</td>
<td>1022.22/204.444</td>
<td>8/1.6 mg/mL</td>
</tr>
</tbody>
</table>

*After the last dose is administered, the patient is kept under observation for 2 hours

the patient following an explanation of the risks involved. As the recommended regimen for long-term prophylaxis of pneumocystis is administration of the drug every 48 hours, a challenge with cotrimoxazole was performed at 48 hours after desensitization, with no adverse reaction. Cotrimoxazole at was prescribed at 800/160 mg every 48 hours uninterruptedly for the next 6 months to maintain the tolerance acquired.

The second case involved a 26-year-old white woman who had undergone lung transplantation owing to cystic fibrosis. She had experienced generalized urticaria within 72 hours of beginning treatment with trimethoprim-sulfamethoxazole, which was prescribed as in the previous case for prophylaxis of *P jiroveci*. The results of skin prick testing were negative. We decided to perform an oral challenge test, which induced hives after 40 minutes of administration at a dose of 100/20 mg. Once a diagnosis of adverse reaction to cotrimoxazole was established, we decided to perform desensitization with the protocol described in the previous case (Table). The patient tolerated the protocol well. After 48 hours of desensitization, provocations in the allergy clinic caused no adverse reactions. Once it was established that the patient tolerated the doses well, we indicated that she should continue home administration of cotrimoxazole at a dose of 800/160 mg every 48 hours. She experienced no adverse reactions over the full 6-month period indicated for posttransplant pulmonary prophylaxis.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

Latex Allergy and Occupational Exposure: The Patient's Perspective

Baiardini I1, Di Leo E2, Molinengo G3, Braido F4, Canonica GW1,5, Nettis E6

1 Department of Biomedical Sciences, Humanitas University, Milan, Italy
2 Section of Allergy and Clinical Immunology, Unit of Internal Medicine “F. Miulli” Hospital, Acquaviva delle Fonti, Bari, Italy
3 Department of Psychology, University of Turin, Turin, Italy
4 Department of Internal Medicine, IRCCS San Martino di Genova University Hospital, Genoa, Italy
5 Personalized Medicine, Asthma and Allergy Clinic, Humanitas Research Hospital, Milano, Italy
6 Department of Biomedical Sciences and Human Oncology Unit of Internal Medicine “G. Baccelli” 8, “Aldo Moro” University of Bari Medical School, Policlinico, Bari, Italy

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Natural rubber latex (NRL) allergy affects 0.3% to 1% of the general population [1], and its prevalence is higher among health care workers (range, 2.8%-17%) [2,3].

In sensitized patients, exposure to NRL proteins can provoke a type I IgE-mediated hypersensitivity reaction involving various organs and systems and a type IV reaction responsible for contact dermatitis [2,3]. Clinical manifestations, which occur within a few minutes after contact with NRL proteins, include urticaria, angioedema, conjunctivitis, allergic rhinitis, asthma, and anaphylaxis [4].

Unlike other allergic diseases, where patient-reported outcomes (PROs) are increasingly investigated, few data are available on the impact of latex allergy on the patient's experience.

Nienhaus et al [5] explored the effect of specific interventions for patients with occupational allergy and found that, when contact with NRL is avoided, health-related quality of life (HRQOL) and work activity improve.

Similar results were found by Power et al [6], who detected an improvement in HRQOL in 39 health care workers with latex allergy after avoidance of latex exposure.

Lewis-Jones et al [7,8] developed a specific HRQOL questionnaire for latex allergy and showed that this condition has a profound effect on both patients and caregivers. The tool was also validated in Spanish, although it has not yet been used to explore HRQOL in these patients [1].

The aim of our study was to add to current knowledge about patients' experience of latex allergy resulting from occupational exposure. In particular, we were interested in testing the following:

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Manuel Jorge Rial Prado
Allergy Department
Hospital Universitario Fundación Jiménez Díaz
Avenida de los Reyes Católicos, 2
28040, Madrid, Spain
E-mail: manuel.rial@quironsalud.es