

the correlation between clinical severity and itching intensity. The results obtained in our study revealed that the EASI score is not significantly correlated with VAS_{itch}. Furthermore, the EASI score was not significantly correlated with VAS_{itch} in adult AD patients older than 18 years (data not shown).

Itch in AD is associated not only with inflammation of the cutaneous lesions but also with various other factors, such as epidermal barrier abnormality, neural processing of itch, and participation of many biologic mediators in AD development.⁶ Moreover, the threshold of itch varies in different body regions.⁷ Psychological and environmental conditions also affect the onset of itch. Thus, itch in AD may not be correlated with the severity of cutaneous lesion of AD.

VAS_{sleep} showed significant correlation with EASI score and with VAS_{itch} in our study. These results suggest that the quality of sleep in AD patients is not only influenced by the severity of the cutaneous lesions but also by the itching intensity. Therefore, management of both cutaneous lesion and itching intensity is important for better quality of sleep.

The findings of the strong correlation between SCORAD index and itching intensity in the study by Chrostowska-Plak et al¹ and our findings of no significant correlation between the EASI score and the itching intensity could provide useful information for the selection of clinical parameters for determining the severity of itch in clinical investigations. However, our study has a limitation: our patient population comprised a relatively small number of patients, and there were very young patients whose parents had replied to the questionnaire instead of the patients themselves. The lack of VAS assessment of the itching intensity at the time of maximal itching also decreases the significance of our study. Nevertheless, it is worthy of notice that different techniques of management in addition to control of cutaneous lesions are required to relieve the itch in AD patients.

WOO-HAING SHIM, MD*
HYUN-JE PARK, MD*
HOON-SOO KIM, MD*
SU-HAN KIM, MD*
HYUN-CHANG KO, MD*†
MOON-BUM KIM, MD, PhD*‡
DO-WON KIM, MD, PhD‡
BYUNG-SOO KIM, MD, PhD*‡

*Department of Dermatology
School of Medicine

†Medical Research Institute
Pusan National University
Busan, Korea

‡Department of Dermatology
School of Medicine
Kyungpook National University
Daegu, Korea
dockbs@pusan.ac.kr

1. Chrostowska-Plak D, Salomon J, Reich A, Szepietowski JC. Clinical aspects of itch in adult atopic dermatitis patients. *Acta Derm Venereol*. 2009;89:379–383.
2. Hanifin JM. Diagnostic criteria for atopic dermatitis: consider the context. *Arch Dermatol*. 1999;135:1551.
3. Schmitt J, Langan S, Williams HC. What are the best outcome measurements for atopic eczema? a systematic review. *J Allergy Clin Immunol*. 2007;120:1389–1398.
4. Finlay AY. Measurement of disease activity and outcome in atopic dermatitis. *Br J Dermatol*. 1996;135:509–515.
5. Rullo VE, Segato A, Kirsh A, Sole D. Severity scoring of atopic dermatitis: a comparison of two scoring systems. *Allergol Immunopathol (Madr)*. 2008;36:205–211.
6. Yosipovitch G, Papoiu AD. What causes itch in atopic dermatitis? *Curr Allergy Asthma Rep*. 2008;8:306–311.

7. Ozawa M, Tsuchiyama K, Gomi R, Kurosaki F, Kawamoto Y, Aiba S. Neuroselective transcutaneous electrical stimulation reveals neuronal sensitization in atopic dermatitis. *J Am Acad Dermatol*. 2009;60:609–614.

SUCCESSFUL DESENSITIZATION WITH TEMOZOLOMIDE

Temozolomide is an oral alkylating agent used for the treatment of aggressive brain tumors, such as grade IV astrocytoma, glioblastoma multiforme, and melanoma. Allergic reactions to alkylating agents are uncommon. Hypersensitivity reactions to temozolomide have been described,¹ such as urticaria,² hypersensitivity pneumonitis,³ Stevens-Johnson syndrome, and toxic epidermal necrolysis.⁴

We report the case of a 57-year-old woman with a history of allergy to trimethoprim-sulfamethoxazole and gemistocytic astrocytoma (grade 4 according to the Daumas-Duport scheme). The patient was prescribed temozolomide (Temodal), 120 mg/d for 5 days each month for 6 cycles. The first cycle was tolerated well.

The patient was referred to our clinic after the onset of symptoms of pruritus, generalized erythema, and angioedema 10 minutes after taking temozolomide on the third day of the second cycle. Her symptoms were resolved with methylprednisolone 80 mg, and dexchlorpheniramine 2 mg. Baseline serum tryptase and total IgE levels were 3.56 µg/L (reference range, <13.5 µg/L) and 89 IU/L (reference range, <100 IU/L), respectively.

To confirm a hypersensitivity reaction to temozolomide, we performed an oral provocation challenge with 120 mg of temozolomide; 60 minutes after the challenge, the patient developed pruritus in the hands, facial angioedema, dyspnea, hypotension (blood pressure, 74/45 mm Hg), and vomiting, which were resolved 30 minutes after administration of adrenaline 0.6 mg, methylprednisolone 60 mg, and dexchlorpheniramine 5 mg.

Skin testing was not performed because the procedure has not been validated for temozolomide and because of our lack of knowledge on its potential skin toxicity. Two hours after the reaction, serum tryptase and total IgE levels were 4.28 µg/L (reference range, <13.5 µg/L) and 81 IU/L (reference range, <100 IU/L), respectively.

No alternative treatment for this patient existed, leading us to perform a desensitization protocol with temozolomide according to other publications regarding desensitization with other chemotherapy agents.¹

On the first day of each cycle, the patient was admitted to our hospital and was given cetirizine 10 mg, lorazepam 0.5 mg, and ranitidine 150 mg, 30 minutes before the initiation of the protocol. Our protocol was as follows: 0.025 mg, 0.05 mg, 0.1 mg, 0.5 mg, 1 mg, 2 mg, 5 mg, 10 mg, 20 mg, 30 mg, 60 mg, and 110 mg at an interval of 30 minutes between doses. The maximum dose was set at 238.6 mg according to the recommendation of an oncologist.

Sixty minutes after the last dose, the patient developed erythema and pruritus in the palms, which resolved in 20 minutes with methylprednisolone 40 mg, and dexchlorpheniramine 5 mg. On the second day she was given 120 mg and 120 mg at an interval of 30 minutes; having tolerated this well, she was discharged. Once at home, the patient demonstrated tolerance to 240 mg/d for the rest of the cycle.

In light of this response, for the next 5 desensitization cycles the patient was also given prednisone, 30 mg, 30 minutes before initiation. In addition, we included one more step to the protocol: 0.025 mg, 0.05 mg, 0.1 mg, 0.5 mg, 1 mg, 2 mg, 5 mg, 10 mg, 20 mg, 30 mg, 50 mg,

Disclosures: Authors have nothing to disclose.

© 2011 American College of Allergy, Asthma & Immunology.

Published by Elsevier Inc. All rights reserved.

doi:10.1016/j.anai.2011.02.009

60 mg, and 60 mg. Sixty minutes after the last dose, she developed erythema and pruritus in the palms, although these symptoms were milder, with complete resolution in 10 minutes with methylprednisolone 40 mg, and dexchlorpheniramine 5 mg. On the second day she was given 120 mg and 120 mg at an interval of 30 minutes, which she tolerated well, followed by 240 mg/d for the rest of the cycle.

We present a case of an anaphylactic reaction to temozolomide presumably due to an IgE-mediated reaction or pseudoallergy. To the best of our knowledge, ours is the first case of successful desensitization with temozolomide to be presented. The second protocol described seems safer. The patient was able to complete her chemotherapy treatment successfully.

RUIZ-GARCIA, MÓNICA, MD*

MANUEL DE LAS HERAS GOZALO, MD*

ELENA HERNANDEZ GARCIA DE LA BARRERA, MD*

JOAQUIN SASTRE DOMINGUEZ, MD, PhD*

*Fundación Jimenez Diaz

Madrid, Spain

monicaruizgarcia@hotmail.com, mruizga@fjd.es

1. Castells MC, Tennant NM, Sloane DE, et al. Hypersensitivity reactions to chemotherapy: outcomes and safety of rapid desensitization in 413 cases. *J Allergy Clin Immunol*. 2008;122:574–580.
2. Pothiwala S, Hsu MY, Yang C, et al. Urticarial hypersensitivity reaction caused by temozolomide. *J Drugs Dermatol*. 2010;9:1142–1144.
3. Guilleminault L, Carré P, Diot P. Hypersensitivity pneumonitis associated with temozolomide. *Eur Respir J*. 2009;34:526.
4. Sarma N. Stevens-Johnson syndrome and toxic epidermal necrolysis overlap due to oral temozolomide and cranial radiotherapy. *Am J Clin Dermatol*. 2009;10:264–267.

A NOVEL METHOD OF DESENSITIZATION FOR FLUCONAZOLE HYPERSENSITIVITY IN A PATIENT WITH AIDS

Fungal infections are common in human immunodeficiency virus (HIV)-infected patients and range from skin infections to oral or esophageal candidiasis to cryptococcal meningitis. Fluconazole is one of the mainstay therapies for such infections. Adverse effects of fluconazole include nausea, headache, rash, hepatitis, and anaphylaxis.¹⁻⁴ Fluconazole hypersensitivity has been described, and if acceptable alternative therapy is not available, desensitization may be required. Published desensitization protocols have ranged from 3 to 4 hours in non-HIV-infected patients and from 7 to 15 days in HIV-infected patients.^{1,5,6} We describe a case of successful desensitization to fluconazole in 2 days in an HIV-infected patient with cryptococcal meningitis.

The patient is a 29-year-old, Hispanic woman with HIV/AIDS diagnosed 14 years ago (recent CD4 cell count of 14/mm³, viral load of 130,000, and highly active antiretroviral therapy with intermittent compliance), chronic active hepatitis B virus, and *Mycobacterium avium*-intracellulare. She presented with a headache for 1.5 weeks and was found to have a positive serum cryptococcal antigen (1:1,024). Laboratory studies revealed a normal basic metabolic profile, an aspartate aminotransferase level of 54 IU/L (reference range, 7–40 IU/L), an alanine aminotransferase level of 56 IU/L (reference range, 7–40 IU/L), and an alkaline phosphatase level of 252 IU/L (reference range, 70–230 IU/L). Blood cell count revealed leukopenia (leukocyte count of 3,000/mm³ with 6.6% eosinophils, absolute eosinophil count of 200/mm³) and anemia (hemoglobin level of 8.4

g/dL). Outpatient medications included tenofovir/emtricitabine, ritonavir, darunavir, azithromycin, ethambutol, and atovaquone. The patient reported previous allergies from fluconazole (rash), trimethoprim-sulfamethoxazole (itch), dapsone (rash), and shellfish (rash).

This patient was initially prescribed flucytosine and amphotericin and received subsequent lumbar punctures to decrease intracranial pressure. On day 9 of therapy, the patient experienced a neck rash and a low-grade fever (temperature of 100.3°C); flucytosine and amphotericin therapy was discontinued and her rash improved. Five days later, the patient was prescribed oral fluconazole (400 mg/d), and within 10 minutes of the first dose, the patient became febrile (temperature of 100.3°C) and developed a pruritic, maculopapular rash on her face, neck, upper chest, and back with no mucosal involvement. The patient had a similar rash 1 year before admission when treated with fluconazole for oral candidiasis. At that time, the rash had appeared within 3 minutes of the first dose and then improved within the course of 1 day; fluconazole therapy was not restarted after the first dose and subsequent development of symptoms. Our differential diagnosis in light of the symptoms after fluconazole administration included the following: immediate-type hypersensitivity, cytotoxic (ie, type II) hypersensitivity, immune complex-mediated (ie, type III) hypersensitivity, hypersensitivity caused by the other medications used by this patient, and drug fever. Because the patient similarly reacted within minutes of the most recent dose of fluconazole, we presumed immediate-type hypersensitivity with this recent dose. Of note, a previously reported HIV-infected patient was successfully desensitized with fluconazole after also experiencing fever and rash following medication administration.⁶ Skin prick testing was not performed in our patient because of the recent antihistamines received by the patient after the rash induced by fluconazole and because of the lack of available standardized fluconazole skin testing methods. Given the necessity for maintenance therapy for cryptococcal meningitis with fluconazole, the patient was advised of the risks of desensitization and agreed to the procedure.

The patient underwent oral fluconazole desensitization starting with 200 µg of fluconazole. A 2-mg/mL fluconazole solution was made by dissolving 200 mg of fluconazole in 100 mL of sterile water, and the starting dose was 2 drops of the solution (200 µg). The starting dose was gradually increased every 6 hours (Table 1) until a dose of 200 mg was reached. The interval of 6 hours is shorter than in available protocols regarding HIV patients. This case represents the most rapid oral fluconazole desensitization regimen that

Table 1. Oral Fluconazole Desensitization Protocol^a

Hour	Concentration, mg/mL	Volume administered	Dose administered
0	2	100 µL	200 µg
6	2	1 mL	2 mg
12	2	2 mL	4 mg
18	2	4 mL	8 mg
24	2	8 mL	16 mg
30	2	15 mL	30 mg
36	2	30 mL	60 mg
42	2	60 mL	120 mg
48	NA	NA	200 mg (tablet)
60	NA	NA	200 mg (tablet)

Abbreviation: NA, not applicable.

^a Premedication with diphenhydramine, 25 mg, and famotidine, 20 mg, 30 minutes before the first dose. Continue the diphenhydramine, 25 mg, 3 times daily and famotidine, 20 mg, twice daily during the entire desensitization.

Disclosures: Authors have nothing to disclose.

© 2011 American College of Allergy, Asthma & Immunology.

Published by Elsevier Inc. All rights reserved.

doi:10.1016/j.anai.2011.02.020