

Fluconazole-induced Stevens-Jonson syndrome**Umashanker P. Keshri^{1*}, Naresh Kumar², Rajiv Kumar¹, Manju Gari¹**¹Department of Pharmacology,
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commercial use, distribution, and
reproduction in any medium,
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properly cited.**ABSTRACT**

A 25-year-old girl self-administered tab fluconazole for vulvovaginal candidiasis and developed fever, myalgia and erythematous papular eruptions with itching at both upper and lower lip, mucous membrane of the mouth, vaginal region, which subsequently changed into blister and multiple ulcers. She also had difficulty in swallowing due to painful erosions of the mouth and oropharynx and severe burning pain at vulval and vaginal region. There was bilateral conjunctival hemorrhage. Investigation report revealed leukocytosis and elevated C-reactive protein, which was suggesting the diagnosis of Stevens-Johnson syndrome. She was treated mainly by corticosteroids, antihistamines and antimicrobials and improved. Time taken for resolution of the lesion was 14 days. Rechallenge with the offending drug was not done in the interest of the patient and due to ethical constraints.

Keywords: Fluconazole, Papular eruptions, Stevens-Johnson syndrome**INTRODUCTION**

Fluconazole is used in the treatment of oropharyngeal, esophageal and vaginal candidiasis, cryptococcal meningitis, and coccidioidomycosis. It has activity against histoplasmosis, blastomycosis, sporotrichosis, and tinea infection also.

Side-effects in patients receiving the drug, regardless of dose are nausea, headache, skin rash, vomiting, abdominal pain, and diarrhea. The adverse effect is more common with human immunodeficiency virus patient.¹ Reversible alopecia may occur with prolonged therapy at 400 mg daily dose.² Anorexia also have been reported.³ Neurotoxicity can occur with very high doses above 1200 mg/day.⁴ Rare cases of deaths due to hepatic failure or Stevens-Johnson syndrome (SJS) have been reported.⁵ Acquired immunodeficiency syndrome patient has a higher risk for hepatotoxicity with this drug.⁶

Although anaphylactic reaction and SJS is very rare;⁵ we report a case of 25-year-old girl who developed SJS after receiving single tablet of fluconazole treatment.

CASE REPORT

A 25-year-old girl had pruritus vulva. Tablet fluconazole (onacan 150 mg, single dose, Wallace Pharma) was self-administered on the suggestion of her friend who also had vaginal infection and had responded with this drug. She developed burning sensation in mouth, eyes, vaginal and vulval region and on the face 2-3 hrs after intake of this drug. She took tab cetirizine 10 mg for this problem, but no relief was felt and symptom exaggerated. The patient developed fever, myalgia, and erythematous papular eruptions with itching at both upper and lower lips, mucous membrane of the mouth, vaginal region, and swelling on the face. Subsequently oral and vulval eruption changed into blisters and multiple ulcers.

There was severe burning pain at the mucosal area of mouth and at vaginal region. She had difficulty in swallowing due to painful erosions of the mouth and oropharynx. There was bilateral sub-conjunctival hemorrhage. Bullae continued to appear for about a week (Figures 1 and 2).

Necessary investigation was done. It revealed leukocytosis and elevated C-reactive protein and full-thickness necrosis of the epidermis; suggesting the diagnosis of SJS.

The patient was treated with tablet amoxicillin and clavulinic acid to prevent secondary infections by the clinician of the department of dermatology of a tertiary care center. As supportive treatment tablet prednisolone, tablet ranitidine, tablet cetirizine, and local application of glycerin for a soothing effect and gentian violet as antiseptic were also given. The patient improved in 2 weeks without any further complication.

DISCUSSION

SJS is thought to arise from a disorder of the immune system.⁷ The immune reaction can be triggered by drugs or infections.⁸ Genetic factors are associated with a predisposition to SJS. The cause of SJS is unknown in one-quarter to one-half of cases.

Although SJS can be caused by viral infections and malignancies, the main cause is drugs. A leading cause appears to be the use of antibiotics.⁹ No reliable test exists to establish a link between a particular drug and SJS for an individual case. Determining what drug is the cause is based on the time interval between first dose of the drug and the beginning of the skin reaction.

In this case report, we found that SJS has a temporal relationship with the intake of tab. fluconazole. No other drugs were taken concurrently. We also found that there is no history of intake of fluconazole in the past. A dechallenge

with fluconazole improved the condition. However, rechallenge was not done due to ethical constraints and fatal consequences. Other blistering skin diseases like pemphigus vulgaris and bullous pemphigoid, mucocutaneous diseases like Behcet's syndrome and Reiter's syndrome, vasculitides like systemic lupus erythematosus and polyarteritis nodosa were excluded on clinical grounds.

The appearance of SJS in this patient who had taken oral fluconazole could not be explained by any other concurrent diseases or drug or chemical intake. This adverse reaction is not dose-related and can be labeled as Type B class of adverse effect. It can be considered as probable/likely adverse drug reaction as per causality assessment of suspected adverse drug reactions.¹⁰ The estimated incidence of the SJS ranges between 1.2 and 6/million populations/year, but the mortality rate is 15%.¹¹ There are reports of fluconazole-induced SJS;⁵ but, it is often overlooked in its adverse effect profile. Thus, the idea of this written statement is to create awareness about the rare, but potentially fatal drug reaction like SJS with fluconazole, which is commonly used for systemic fungal infection.

We found in this case report that the decision of the use of this drug was taken by the patient herself without an opinion of an expert doctor. One of the causes of this is direct advertising of the drug to the consumer by the pharmaceutical industry, which enhances the chances of serious adverse drug reaction. It promotes inappropriate use of drugs.¹²

CONCLUSION

Although fluconazole is the first-line treatment option in several cases of invasive candidiasis there is a need of careful prescribing and monitoring of the use of the drug by the medical professional due to occasional report of severe and life-threatening reaction like SJS. Chances of serious adverse effect are also increases when these drugs are prescribed by an untrained person and when self-application is applied.



Figure1: Multiple ulcers on the upper and lower lip of the patient.



Figure 2: Subconjunctival hemorrhage.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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doi: 10.5455/2319-2003.ijbcp20140629

Cite this article as: Keshri UP, Kumar N, Kumar R, Gari M. Fluconazole-induced Stevens-Jonson syndrome. *Int J Basic Clin Pharmacol* 2014;3:566-8.