

# Safety of oral itraconazole in the treatment of seborrheic dermatitis

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**Abstract** *Background* Seborrheic dermatitis (SD) is a chronic, papulosquamous dermatosis and *Malassezia* yeasts are considered as causative factors. The dual antifungal and anti-inflammatory effects of oral itraconazole account for its prolonged therapeutic action in SD.

*Objectives:* To assess the safety of oral itraconazole in the treatment of seborrheic dermatitis.

*Patients and methods* During a period of total 2 years from January, 2008 to December, 2009, 37 patients of SD were treated with oral itraconazole (200 mg/day for 7 days) in first month and consecutive use of 200 mg/day for the first 2 days of the following 11 months. Patients were followed up monthly for clinical side effects and biochemical derangements.

*Results* 16 (43.2%) patients suffered from different side effects of drug i.e. nausea in 16 (76.2%) patients, followed by abdominal pain in 3 (14.3%) and diarrhea in 2 (9.5%). These were self-limiting and did not warrant discontinuation of therapy. Biochemical abnormalities were not seen in any patient.

*Conclusion* The study suggests that oral itraconazole is a safe treatment option of seborrheic dermatitis.

## Key words

Itraconazole, seborrheic dermatitis, safety.

## Introduction

Seborrheic dermatitis (SD), also known as seborrheic eczema, affects 2% to 5% of the population.<sup>1</sup> It is a common chronic superficial papulosquamous dermatosis that is often associated with seborrhea of the scalp and affects the sebaceous follicle-rich areas of the face and trunk. The involved skin is

erythematous and covered with yellow-brown scales and crusts. The disease varies from mild to severe; including psoriasiform patterns and erythroderma.<sup>2</sup> Patients with human immunodeficiency virus (HIV) infection have an increased risk of seborrheic dermatitis.<sup>3</sup> Consequently, it is included in the spectrum of premonitory lesions and should be carefully evaluated in high-risk patients.<sup>3</sup>

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The skin commensal yeasts *Malassezia* are known to cause the disease. Correlation of severity of the disease with the number of yeasts and decrease in the number of *Malassezia* after

treatment seem to support that this may be caused by *Malassezia* yeast.<sup>4</sup>

Oral antifungal itraconazole seems to be the treatment of choice when the seborrheic dermatitis is widely diffuse, resistant to topical preparations, or when it induces psychological problems that could modify the lifestyle of the patient.<sup>5</sup> Its anti-inflammatory effect and antifungal activity against *Malassezia* suggest that oral itraconazole will be the first-line oral treatment option for refractory seborrheic dermatitis in future. Itraconazole is a lipophilic and keratinophilic systemic antifungal agent. Its high lipophilicity means that it persists in the skin and appendages above the therapeutic concentration for some weeks even after the cessation of therapy i.e. reservoir effect which may account for the prolonged therapeutic action of low dose itraconazole in SD.<sup>6</sup> This drug does not have the same potential to cause hepatotoxicity as ketoconazole and may, therefore, be a safer alternative for patients who require an oral treatment.<sup>7</sup> In Bangladesh, itraconazole has recently been used to treat seborrheic dermatitis. Although, there are several studies affirming its efficacy in seborrheic dermatitis, there is no data-based study on the safety profile of this drug in Bangladeshi people. The present study was designed to assess the adverse effect of oral itraconazole, when used for seborrheic dermatitis.

### **Patients and methods**

This was an interventional study, carried out for a period of total two years from January, 2008 to December, 2009. Data were collected from Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh. Patient suffering from seborrheic dermatitis were selected as study

population. During this period, 37 patients of seborrheic dermatitis were enrolled purposively considering exclusion criteria like known hypersensitivity to any ingredients of the itraconazole, pregnancy/ lactation, impaired hepatic functions, impaired renal functions and severe systemic illness. The inclusion criteria of patient selection included both male and female patients of any age, patients willing to take part in the study and expected to be available for the duration of study and comply with the study visits and those who had not received any topical treatment for 2 weeks prior to the study and no systemic antifungal intake during last 4 weeks.

After clinical diagnosis of seborrheic dermatitis, verbal and written consent was taken from the selected patient. Then they were treated with oral itraconazole (200 mg/day for 7 days) in first month and consecutive usage of 200 mg/day for the first 2 days of the following 11 months. Patients were followed up monthly till 14<sup>th</sup> month. On each visit they were clinically evaluated. Skin involvement before and after therapy was assessed by a clinical score based on the involvement of different grades of erythema, papular eruption and desquamation, 0=normal, 1=mild, 2=moderate and 3=severe for all.

For safety profile, patients were enquired and examined on each visit for any side effect related to itraconazole. For hematological and biochemical derangements, patients blood samples were analyzed at baseline and then monthly for three months and three-monthly for rest of the study for complete blood counts and liver function tests.

Data were analyzed by software SPSS (Statistical Package for Social Science) version 11.

**Table 1** Relationship between side effects and clinical signs of seborrheic dermatitis erythema, papular eruption and desquamation before and after treatment with itraconazole.

	<i>Before treatment</i>				<i>After treatment</i>			
	Nil	Mild	Moderate	Severe	Nil	Mild	Moderate	Severe
<i>Erythema</i>								
No side-effect	0	2	11	3	2	3	11	0
Having side effect	0	0	8	13	8	13	0	0
Total	0	2	19	16	10	16	11	0
<i>Papular eruption</i>								
No side-effect	0	4	7	5	2	3	7	4
Having side effect	0	3	13	5	5	16	0	0
Total	0	7	20	10	7	19	7	4
<i>Desquamation</i>								
No side-effect	0	0	9	7	2	3	4	7
Having side effect	0	0	14	7	7	14	0	0
Total	0	0	23	14	9	17	4	7

## Results

Amongst 37 patients, there were 32 males and 5 females and their age ranged from 20 years to 50 years. 21 (56.8%) had no side effects and 16 (43.2%) suffered from different gastrointestinal side effects of drug. Majority of patients suffered from nausea 16 (76.2%), followed by abdominal pain 3 (14.3%) and diarrhea 2 (9.5%). These symptoms were noticed during the first week of therapy. These were of milder severity and did not necessitate discontinuation of therapy and resolved themselves without any intervention. Hematological or biochemical derangements were not seen in any case.

**Table 1** compares the severity of erythema, papular eruption and desquamation between those having side effects and those showing no side effects. The drug was effective in both groups.

## Discussion

Our study showed mild gastrointestinal side effects in 16 (43.2%) of patients after itraconazole use in seborrheic dermatitis. These were nausea 16 (76.2%), followed by abdominal pain 3 (14.3%) and diarrhea 2 (9.5%). However,

these side effects were self-limiting and did not warrant discontinuation of therapy. Our results differ from those by Kose *et al.*<sup>5</sup>, Baysal *et al.*<sup>6</sup> and Shemer *et al.*<sup>7</sup>, who did not find any side effect from using oral itraconazole in the treatment of seborrheic dermatitis.

Kose *et al.*<sup>5</sup> treated 29 patients with itraconazole 200mg/day for one and then 200mg for first two days of every for two months. They did not report any side effect attributable to itraconazole. Similarly, Baysal *et al.*<sup>6</sup> treated 32 patients of SD with itraconazole in a similar protocol; however, they did not report any drug-related side effect in their study population. Shemer *et al.*<sup>7</sup> used itraconazole 200 mg/day for 7 consecutive days for facial seborrheic dermatitis. Later, patients were given a single dose of 200 mg itraconazole every 2 weeks for 18 weeks. They also did not report any clinical or biochemical adverse effect.

Although mild side effects were frequent in our study population, however, therapy could be continued since it was to be used in discontinuous manner just two days a month. So we recommend that itraconazole can be used to treat patients with moderate to severe seborrheic dermatitis not responding to topical therapies.

## Conclusion

The study suggests that oral itraconazole has excellent safety profile for treatment option of seborrheic dermatitis.

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