

Original Article

A Study on Efficacy of Oral Itraconazole in the Treatment of Seborrheic Dermatitis

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Abstract:

Seborrheic dermatitis is a common chronic disease. Malassezia yeasts have been implicated in the pathogenesis of this disease. Antifungal agents are known to be effective in the treatment of Malassezia yeast infections. This study was done to evaluate the efficacy of itraconazole in the treatment of seborrheic dermatitis. Sixty patients with Seborrheic dermatitis were evaluated in an open non-comparative study. Patients were treated with itraconazole capsule 100 mg twice a day for a week; then after a 3-week interval 100 mg capsule was given twice a day for 2 days of following months for two consecutive months. Four clinical parameters (Itching, burning erythema, scaling, and seborrhea) were assessed using a 0 to 3-point (0= absent, 1 = mild, 2 = moderate, 3 = severe) score. Mycological evaluation determined the presence of Malassezia spores in the scales using a direct smear. At the end of the initial treatment significant improvement was reported in four clinical parameters: Itching, burning erythema, scaling, and seborrhea. Maintenance therapy led to further improvement slightly. Burning sensation mildly improved during the treatment. The quantity of Malassezia spores present in the direct smear decreased throughout the treatment period. Blood test abnormalities were not found during the treatment. So initial treatment with itraconazole is beneficial in patients with seborrheic dermatitis.

Key words: Seborrheic dermatitis, Malassezia yeasts, Itraconazole.

Introduction:

Seborrheic dermatitis (SD) is a chronic common skin disease, affecting 1-3% of the adult population which is a common chronic erythematous scaly eruption usually seen in areas rich in sebaceous glands¹. The presence of a generous amount of epidermal lipids and colonization by Malassezia species are two main factors in pathogenesis. Clinical features show varied morphology such as erythematous reddish yellow, poorly circumscribed patches with fine scale, which are mildly pruritic. Common sites are scalp (dandruff), eye

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brows, perinasal areas, ears, retro auricular areas, neck, and anterior and posterior trunk (annular or petaloid forms are seen)². There are several topical and systemic therapies for its management. Itraconazole is a highly keratinophilic and lipophilic triazole, secreted in sebum which is a major route by which the drug reaches the stratum corneum³. Several topical agents such as zinc pyrithione, selenium sulfide, antifungal agents and steroids are usually used in the treatment of mild disease. These topical agents give temporary and partial relief but are less effective in more severe cases. Systemic antifungal agents including itraconazole, which are known to be effective in the treatment of Malassezia species infection, were suggested as one of the therapeutic modalities in cases of moderate to severe seborrheic dermatitis⁴.

Materials and Methods:

This clinical trial was conducted in the Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka from January 2013 to June 2013. The researcher took 60 cases attending in Dermatology and venereology department of BSMMU, during the study period those fulfilled the inclusion criteria. This study included patients with seborrheic dermatitis of age between 18 and 60 years, both males and females, and who gave informed consent. Patients with liver disease, renal disease, Diabetes mellitus,

documented HIV infection, psoriasis, pregnancy or nursing women, who used systemic antibiotics, systemic antifungals, topical steroids, topical antifungals, selenium sulfide or zinc pyrithione within 15 days prior to the study, hypersensitivity to itraconazole, and on a drug which interfere with itraconazole were excluded from the study. Patients were treated with itraconazole capsule 100 mg twice a day for a week; then after a 3-week interval 100 mg capsule was given twice a day for 2 days of following months for two consecutive months. Four clinical parameters (Itching, burning erythema, scaling, and seborrhea) were assessed using a 0 to 3-point (0= absent, 1 = mild, 2 = moderate, 3 = severe) score. Mycological evaluation determined the presence of Malassezia spores in the scales using a direct smear. At the end of the initial treatment significant improvement was reported in four clinical parameters: Itching, burning erythema, scaling, and seborrhea.

Results:

The study was conducted in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka. Total 60 patients fulfilling the entry criteria were enrolled. No patients withdrew from study.

Sixty patients (36 males and 24 females) receiving Itraconazole completed study and were evaluated. Demographic data for these patients are summarized in table I with mean duration of disease.

Table I: Baseline characteristics of patients in the study.

Characteristic	Study group (n=60)
Age (years) mean ±SD	28.95 ± 7.87
Age range (years)	18-60
Male	36
Female	24
Mean duration of the disease in months (mean ±. SD)	32.4±22.84

Table II shows moderate and severe forms of seborrheic dermatitis present in 48 and 12 patients which is 80% and 20% of total study population respectively. Considering distribution of Seborrheic dermatitis in body areas shows involvement is highest in Scalp & forehead (Head) 43 cases (71.66 %), then in trunk 12 cases (20%), and the least involved area is the body folds 5 cases (8.33%).

Table II: Family history, forms and distribution of seborrheic dermatitis in study group (n=60)

Family History	Number of Patient	%
• Positive	16	26.66%
• Negative	44	73.33%
Forms		
• Moderate	48	80%
• Severe	12	20%
Distribution		
• Head(Scalp/Forehead/Eyebrows/Eyelids/Perinasal areas/ Chin/lips /Ears/ retro auricular areas	43	71.66%
• Trunk (anterior chest/ Interscapular Region/	12	20%
• Body Folds(Gluteal creases/ Axillae / Groins/ Umbilicus/Sub mammary region)	5	8.33%

Patients with moderate form of SD shows 54.15% good response, 31.25% moderate response, 14.58% no response. Whereas, patients with severe form show 25% good response, 41.66% moderate response and 33.3% no response. In total, the response was good in 48.33 % of cases, moderate response was found in 33.33% of cases, no response was observed in 18.33% of cases. (Figure-1)

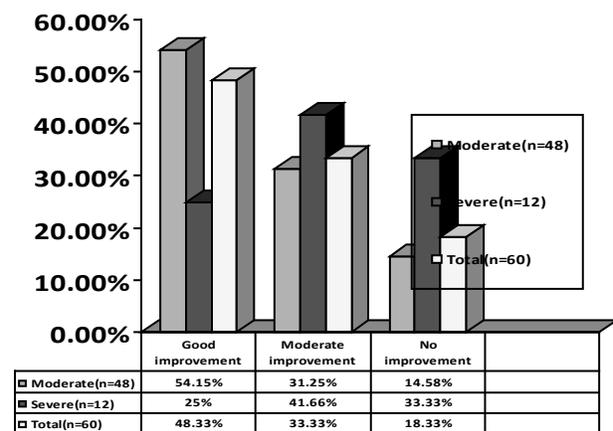


Figure 1. Bar-Diagram of Response of therapy in percentage at the end of the study.

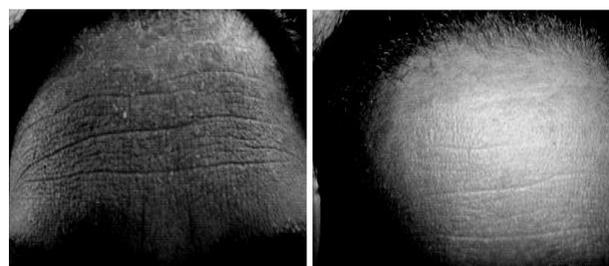




Figure 2. Before and after treatment of Seborrheic dermatitis with itraconazole.

Discussion:

SD is an inflammatory disorder of the skin characterized by erythema and scaling over the areas rich in sebaceous glands, the scalp, face, chest, back, and flexural areas. The enigma of SD is yet unsolved. Probably the organism *Pityrosporum ovale*, *Pityrosporum* lipase activity, skin surface lipids, and lastly immune dysfunction may play a role. It has been suggested that SD is an inflammatory response to these organisms⁵. *Malassezia restricta/globosa*, which plays an important role in the pathogenesis of SD⁶, stimulates cytokine production by keratinocytes. Many studies showed that antimycotics are effective in clearing lesions with a reduction in the number of *Malassezia* yeasts. The efficacy of azole and imidazole antimycotics may be due to their anti-inflammatory action and antimycotic activity. They inhibit the cell wall lipid synthesis of the organisms (antifungal activity of the azoles is via inhibition of lanosterol 14 α demethylase) and may have some effects on the skin surface lipids. Itraconazole is anti-inflammatory primarily because of its inhibitory effect on the synthesis of 5 lipo-oxygenase metabolites, which are involved in several inflammatory diseases such as SD⁷.

In our study, response of the treatment of seborrheic dermatitis have been observed that moderate form showed 54.15% good response, 31.25% moderate response, and 14.58% no response. Patients with severe form showed good response in 25%, moderate response in 41.66% and no response in 33.3%. In total the response was good in 48.33 % of cases, moderate response was found in 33.33% of cases, and no response was observed in 18.33% of cases. In our study 98% patient was in 3rd and 4th decade. This occurs with the observation that seborrheic dermatitis is most common in these age groups. In our study 60% of total patients were male, which reflects seborrheic dermatitis is more common in males. In our study 61.66% of total patients were outdoor worker used to exposure in sunlight and hot humid climate for their nature of occupation. This reflects the precipitating factor of

seborrheic dermatitis. In our study 15% (9 number) of total patients reported anorexia, nausea and abdominal pain which was not significant. Nobody discontinued therapy for side-effects, and not required any additional treatment for side-effect. No hematologic or biochemical abnormalities were observed. These findings were consistent with other studies⁸.

Vahide Baysal et al conducted a study in the Department of dermatology, School of Medicine, University of Suleyman Demirel, Isparta, Turkey where thirty-two adult patients with SD, who applied topical corticosteroids for at least 1 month with no response, were recruited for this study. The treatment was administered in three different periods: first period, 1% hydrocortisone cream twice daily for 4 weeks and itraconazole 200 mg daily, during the first week of the first month; the patients were instructed to apply the cream to the scalp, face, and sternum twice a day; second period (maintenance period), 1% hydrocortisone cream was discontinued and itraconazole 200 mg daily was given on the first 2 days of every month for 11 months; third period (follow-up period), untreated follow-up for 2 months. No other topical or oral medication was allowed as therapy for SD. The global evaluation included complete clearing (71%), marked improvement (51-70%), moderate improvement (26-50%), and slight improvement (25%)⁸.

Caputo, et al conducted an open, single center study involving 160 patients with seborrheic dermatitis. Itraconazole 200 mg/day was administered for 7 consecutive days. Patients were evaluated at baseline, day 7 and day 37 following the end of therapy. The parameters evaluated were itching, burning, erythema, desquamation, and each was rated as: absent (0), mild (1), moderate (2), and intense. Mycological examination for *Malassezia* yeasts was also performed at baseline, and at days 7 and 37 following therapy. The treatment was judged to be effective by 148 patients (92.5%), with clinicians rating overall improvement as excellent in 55 patients (34.3%), good in 64 patients (40.0%), and moderate in 30 patients (18.7%)⁹.

Jayasree Nath et al did an open non comparative clinical trial in the Department of Dermatology, Calcutta School of Tropical Medicine, CR Avenue, Kolkata - 700 073, West Bengal India in which 30 patients were evaluated. The patients were clinically evaluated according to the following items: Itching, burning erythema, scaling, and seborrhea. In the treatment protocol, itraconazole capsule 100 mg twice a day was given for 1 week; then after a 3-week interval 100 mg capsule was given twice a day for 2 days of following months for two consecutive months. The evaluation of results was performed on day 15, day 30, day 60, and day 90. The clinical response was graded

as markedly effective, effective, or ineffective. The mycological examination was done after treatment to evaluate further. Thirty patients were enrolled in the study. Out of these 30 patients, 21 were male and 9 were female. In all of these patients, response to conventional therapy was very unsatisfactory. The evaluation of clinical improvement showed at the end of 90 days that a markedly effective result was seen in 18 patients (60%). A moderate response was seen in 7 patients (23.3%) and in 5 patients (16.6%) no improvement was seen. None of the patients showed any adverse effect with itraconazole¹⁰.

Conclusion:

Since seborrheic dermatitis is a relapsing condition, use of topical agents may be unsuitable on a long-term basis and oral treatment is preferred by patients who are refractory to topical treatment, relapse frequently, or have disease that affects large areas.

The results of this study indicate that Itraconazole is effective for the therapy of moderate to severe cases of seborrheic dermatitis. However, larger studies using different dosages and/or durations of Itraconazole therapy may provide a rationale for systemic use of Itraconazole in seborrheic dermatitis.

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