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Original Article

Efficacy Of Pulse Therapy Of Oral Fluconazole In The Treatment Of Seborrheic Dermatitis

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Abstract:

An interventional study was carried out for a period of total two years in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Total sixty five patients of seborrheic dermatitis were selected and were treated with oral fluconazole 150mg in a single dose per week for 4 weeks. Follow up were done at the end of 4th week and 8th week. Among the patients, 31-45 years age group was highest 44%, highest 54% males and 21(32%) had positive family history of seborrheic dermatitis. Regarding site of lesions, maximum patients of seborrheic dermatitis 92% had involvement of scalp; next 46% had involvement in the eyebrow. The study showed that the response was very good in 31.5 of cases, good response was found in 24.5% of cases, fair in 26% of cases and poor response was observed in 18.5% of cases. The study showed that 83% of study population was seen without clinical side-effect and only 17% were seen with side-effect(anorexia and dydpepsia) and it was showed that very good improvement 35% observed on the 1st follow up visit at the fourth week, 30% had good, 15% fair and poor improvement 20% respectively. On the 2nd follow up visit at the end of eight week, very good improvement was 39% cases; good, fair and poor improvement was 26%, 20% and 17% respectively. The results of this study indicate that fluconazole provides benefit for the therapy of seborrheic dermatitis. However, larger studies using different dosages and durations of therapy, fluconazole may provide a rationale for systemic use of fluconazole in seborrheic dermatitis.

Key words: Pulse therapy of oral fluconazole, seborrheic dermatitis.

Introduction:

Seborrheic dermatitis is a common chronic superficial papulo-squamous dermatosis that is often associated with increased sebum production (seborrhea) of the scalp and the sebaceous follicle-rich areas of the face and trunk. Seborrheic dermatitis, also known as Seborrheic eczema, occurring in 2% to 5% of the population.[1] The affected skin is erythematous and covered with yellow-brown scales and crusts. The disease varies from mild to severe; including psoriasiform patterns and erythroderma.[2] Patients with human immunodeficiency virus (HIV) infection have an increased risk of seborrheic dermatitis.[3] Consequently, it is included in the spectrum of premonitory lesions and should be carefully evaluated in high-risk patients.[3] The skin commensal yeasts Malassezia is 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.[4] Although there is no definitive care, topical corticosteroids, tar, sulfur, pyrithione sulfide,

ciclopiroxolamine, terbinafine, butenafine, azoles such an ketoconazole, bifonazole, itraconazole, metronidazole, fluconazole; tacrolmus, pimecrolimus, lithium succinate and cinnamic acid may be used. However, the relapse rate is high and the duration of remission generally short. In severe disease, systemic antifungals that are used in the treatment of seborrheic dermatitis are ketoconazole, itraconazole and terbinafine.[5] Fluconazole is distinguished from the other azole medications by its water solubility and good cerebrospinal fluid penetration. So an excellent bioavailability can be gained by oral administration. Drug interaction are also less common because fluconazole has the least effect on hepatic microsomal enzymes. For this reason and also for better gastrointestinal tolerance, fluconazole has the widest therapeutic index of the azole, permitting more aggressive dosing in a variety of fungal infections.[6] Since seborrheic dermatitis is a relapsing condition, use of topical agents may not be suitable 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. [4]

Materials and methods:

The interventional study was carried out for a period of total two years from January 2009 to December 2010 in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka in Bangladesh. Total sixty five patients of seborrheic dermatitis were selected considering exclusion criteria like patient with known hypersensitivity to any ingredients of the fluconazole, pregnancy/ lactation, impaired hepatic function, impaired renal function and severe systemic illness. The inclusion criteria of patient selection were both male and female patient of age 15-60, patient willing to give consent to take part in the study, patient expected to be available for the duration of study and able to comply with the study visit and patient received no topical treatment for 2 weeks prior to the study and no systemic antifungal intake. Purposive type non-probability sampling technique was followed in this study. After collection of data, these were screened by checking consistency, edited and were finally analyzed by software SPSS (Statistical Package for Social Science) method.

Procedure of Treatment

The patient of seborrheic dermatitis was identified first. The diagnosis was made on the clinical basis by assessing morphology of lesions, age of onset and their distribution sites. To reach a clinical diagnosis detailed history and thorough physical examination done. Then clinical conditions of the patient were recorded by us. Skin biopsy was also performed for histopathological examination, along with hematological and biochemical profile, like blood for total count, differential count, ESR, platelet count, bleeeding time, clotting time, random blood sugar, serum for cholesterol and triglyceride level, serum for ALT and serum creatinine level. Then verbal and written concent was taken from the selected patient and were interviewed by asking questions. Finally, all patients with seborrheic dermatitis were treated by oral fluconazole 150mg in a single dose per week for 4 weeks. The cases were divided as mild from (dandruff, red and flaky skin),moderate form (thick,oily and yellow scales) and severe from (generalized exfoliative erythroderma) and patient's subjective assessment of pruritus and burning sensation were evaluated before and after treatment. A final medical assessment of efficacy is made at the end of the treatment period using a three point scale (categories: very good- more than 75% clearing, good-50-75% clearing, fair- 25-50% clearing, poor less than 25% clearing) and the assessment result is recorded and analyzed to prepare the final result. Follow up were done at the end of 4th week and 8th week.

Results:

The study was carried out for a period of total two years from January 2009 to December 2010 in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka in Bangladesh. Total sixty five patients of seborrheic dermatitis were selected. Among them, 31-45 years age group was 44%, 15-30 years was 38% and 46-60 years age group was 12%, regarding sex,35 (54%) males and 30 (46%) females between15-60 years aged patients with seborrheic dermatitis and regarding family history, 21(32%) had positive family history and 44(68%) had negative family history of seborrheic dermatitis(Table I). Regarding occupation among the patients, 50% were outdoor worker, 38% were involved in indoor service and rest 12% involved in other occupation(Figure I).Among the sixty five patients of seborrheic dermatitis in table II, mild form was 54%, moderate was 22% and severe was 12%. Regarding duration of lesions, highest patients of seborrheic dermatitis 51% had the duration 1 to 3 years and next 38% had the duration 4 to 6 years. Regarding site of lesions, maximum patients of seborrheic dermatitis 92% had involvement of scalp, next 46% had involvement in the eyebrow, 41% had involvement in back etc.

Table III showed that 43% patients of seborrheic dermatitis had very good response, 28% good response, 20% fair response and 9% poor response in mild form of seborrheic dermatitis. Patients with moderate form show that 23% had good response, 27% good response, 36.5% fair response and 3% poor response. And patients with severe form showed no very good response and good response but 2% fair response and 6% poor response in treating patients of seborrheic dermatitis. In total, the response was very good in 31.5 of cases, good response was found in 24.5% of cases, fair in 26% of cases and poor response was observed in 18.5% of cases. Table IV showed that 83% of study population were seen without clinical side-effect and only 17% were seen with side-effect like anorexia and dyspepsia which was not significant. Nobody had discontinued therapy for side-effects and not required any additional treatment for side-effect.

Figure II showed that very good improvement 35% observed on the 1st follow up visit at the fourth week, 30% had good, fair 15% and poor improvement 20% respectively. On the 2nd follow up visit at the end of eight week, very good improvement was 39% cases, good, fair and poor improvement was 26%, 20% and 17% respectively.

Table I: Distribution of the patient by epidemiological profile (n=65).

Epidemiological profile	Frequency
Age(in years)	
15-30	25(38%)
31-45	28(44%)
46-60	12 (18%)
Sex	
Male	35(54%)
Female	30(46%)
Family History	
Positive	21(32%)
Negative	44(68%)

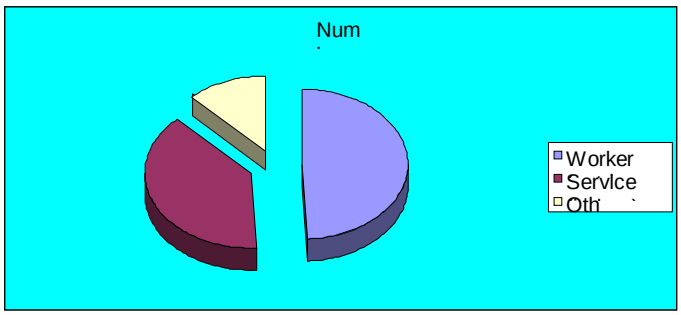


Figure I: Distribution of the patient by occupation.

Table II: Distribution of the patient by different form of disease, duration of lesions and site of lesions (n=65).

Parameters	Frequency
Different forms	
Mild	35(54%)
Moderate	22(34%)
Severe	8(12%)
Duration of lesion	
Less than 1 year	5(8%)
1 to 3 years	33(51%)
4 to 6 years	25(38%)
More than 6 years	2(3%)
Site of lesion (multiple response may exceed hundred)	
Scalp	60(92%)
Forehead	20(31%)
Nasolabialfold,	25(38%)
Eyebrow	30(46%)
Ear	22(34%)
Back	27(41%)
Chin	25(38%)
Intermammary	19(29%)

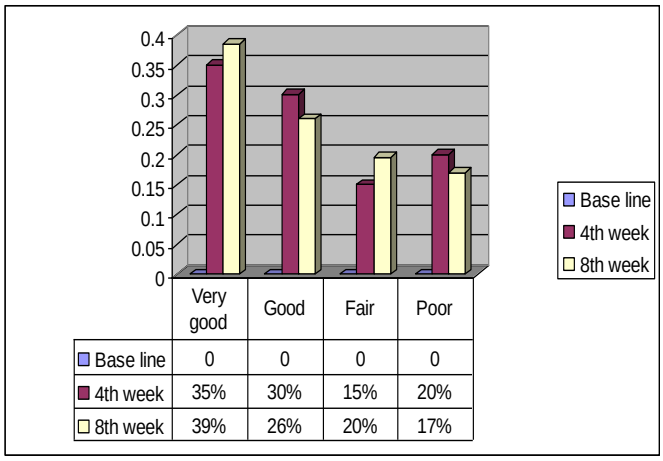
Table III: Distribution of the patient by response of therapy at the end of the study (n=65).

Forms of seborrheic dermatitis	Very good	Good	Fair	Poor
Mild (n=35)	43%	28%	20%	9%
Moderate(n=22)	23%	27%	36.5 %	3%
Severe(n=8)	0%	0%	2%	6%
Total(n=50)	31%	24.5 %	26%	18.5%

Table-IV: Distribution of the patients by side effect.

Safety	Number	Percentage
With out side-effect	54	83%
With side-effect	11	17%

Figure II: Distribution of the patient by follow up after fluconazole therapy.



	Very good	Good	Fair	Poor
Base line	0	0	0	0
4th week	35%	30%	15%	20%
8th week	39%	26%	20%	17%

Discussion:

The study was carried out for a period of total two years from January 2009 to December 2010 in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Total sixty five patients of seborrheic dermatitis were selected. In this study, regarding occupation among the patients, 50% were outdoor worker, 38% were involved in indoor service and rest 12% involved in other occupation. Fifty percent of total patients are outdoor worker used to exposure in sunlight and hot humid climate for their nature of occupation. This reflects the precipitating factor of seborrheic dermatitis.

The study showed that 43% patients of seborrheic dermatitis had very good response, 28% good response, 20% fair response and 9% poor response in mild form of seborrheic dermatitis. Patients with moderate form show that 23% had very good response, 27% good response, 36.5% fair response and 3% poor response. And patients with severe form showed no very good response and good response but 2% fair response and 6% poor response in treating patients of seborrheic dermatitis. In total, the response was very good in 31.5 of cases, good response was found in 24.5% of cases, fair in 26% of cases and poor response was observed in 18.5% of cases.

The study by Robert, Schwartz and Christopher showed that short-term fluconazole treatment may improve the clinical features of mild-to-moderate seborrheic dermatitis. Several topical and systemic antifungals had been used in the treatment of seborrheic dermatitis with varying success rates.[7] The efficacy of oral antifungals was attributable to their antifungal and/or anti-inflammatory effects by Gupta, Nicol and Batra. [8] Systemic use of ketoconazole, itraconazole, and terbinafine has been associated with good clinical response in the treatment of seborrheic dermatitis. However, the efficacy of oral fluconazole which was highly effective against a wide spectrum of dermatophytes and yeasts, had been tried in seborrheic dermatitis and showed marked improvedment. [9.10] In one study, oral fluconazole 150 mg as a single dose per week was given for 4 weeks. This dosage was chosen because it has been used effectively and safely in the treatment of tinea versicolor. Furthermore, the long-term safety of fluconazole has been established in patients with onychomycosis receiving 150–300mg weekly dosages for 6–12 months by Coldiron B. [11] During therapy with fluconazole, the drug concentration in skin reaches ten times that in plasma and the drug is eliminated from the skin very slowly. This allows once-weekly administration, improving patient compliance and reducing costs compared with daily administration, seen by Montero-Gei and Perera. [12]

The study showed that very good improvement 35% observed on the 1st follow up visit at the fourth week, 30% had good, fair 15% and poor improvement 20% respectively. On the 2nd follow up visit at the end of eight week, very good improvement was 39% cases, good, fair and poor improvement was 26%, 20% and 17% respectively. 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 safety profile of fluconazole when used on a long term basis, its efficacy against yeasts, and the cost effectiveness of pulse therapy make fluconazole a therapeutic option in 'recalcitrant cases' of seborrheic dermatitis.[8]

It was showed that 83% of study population was seen without clinical side-effect and only 17% were seen with side-effect like anorexia and dyspepsia, which was not significant. Nobody had discontinued therapy for side-effects and not required any additional treatment for side-effect.

Our study had several limitations. First, no fungal culture was performed and the clinical outcome could not therefore be correlated with Malassezia yeast colonization. Consequently, a possible anti-inflammatory effect of fluconazole could not be evaluated. In addition, the self-remitting course of the disease, the number of patients and the duration of treatment in this study may have been insufficient to evaluate drug-related improvement. The current study was an attempt to develop a

short, cost-effective, convenient, and safe treatment protocol, which is strongly needed for seborrheic dermatitis.

Conclusion:

The results of this study indicate that fluconazole provides benefit for the patients of seborrheic dermatitis. However, larger studies using different dosages and durations of therapy may provide a rationale for systemic use of fluconazole in seborrheic dermatitis.

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