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Original Article

Efficacy and safety of simvastatin in chronic plaque psoriasis

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Abstract ***Objective*** To determine the efficacy and safety of simvastatin in chronic plaque psoriasis.

Patients and methods Sixty patients of either sex, aged between 18 and 70 years were included in the study. Efficacy was determined by percentage reduction in psoriasis area and severity index (PASI) score from baseline. Safety of simvastatin was evaluated by measuring serum alanine aminotransferase (ALT), creatinine phosphokinase (CPK) and bilirubin at baseline, 4^{th}, 8^{th} and 12^{th} week. The data were analyzed for variables like age, sex and percentage reduction in PASI score.

Results There was >50% reduction in PASI score in 20% patients. Out of these, 8 patients had moderate plaque psoriasis and 4 patients had severe psoriasis. In remaining 80% cases simvastatin did not prove to be efficacious. The drug was safe and well-tolerated.

Conclusion Simvastatin can be affective in patients with moderate disease as compared to cases with severe plaque psoriasis. The drug was safe and well-tolerated.

Key words
Psoriasis, simvastatin, efficacy, safety.

Introduction

Psoriasis is a common, chronic, inflammatory and proliferative disorder of skin, which is characterized by well-demarcated, erythematous, scaly, indurated plaques mostly present over extensor surfaces and scalp. The disease is enormously variable in duration, extent and periodicity of flare.[1] Both genetic and environmental factors have critical role in its initiation and aggravation.

The cardinal pathogenetic features of psoriasis are epidermal hyperproliferation, dilatation and proliferation of dermal blood vessels and accumulation of inflammatory cells in dermis and epidermis. Current research suggests that inflammatory mechanisms are immune based and most likely initiated and maintained by T cells, which are stimulated by leukocyte function antigen.[2,3]

Activated T cells cause release of different cytokines, like interferon gamma (IFN-γ), tumour necrosis factor alpha (TNF-α) and interleukins from them, which lead to inflammatory changes.[3]

Psoriasis is a complex inflammatory disorder, which presents as a therapeutic challenge to the dermatologists. Topical therapies like, coal tar, dithranol, calcipotriol, steroids etc. do improve the condition but they can be used for limited body involvement and milder forms of the disease. Patients with moderate to severe disease generally require phototherapy e.g. narrowband

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ultraviolet B radiation, photochemotherapy (oral psoralen plus ultraviolet A radiation) or systemic agents such as methotrexate, ciclosporin, oral retinoids, fumaric acid esters etc. to control the disease adequately. In general, these therapeutic modalities have proven to be highly effective in the treatment of psoriasis but potentially serious toxicity can limit their long-term use.

There is always search for new therapies aimed at good control of disease, cost effectiveness and fewer side effects.

Statins belong to lipid lowering group of drugs but recently their anti-inflammatory and immunomodulatory effects have been described which could be beneficial in psoriasis. Statins inhibit leukocyte function antigen-1 and decrease cytokine production by T-helper 1 cells, which are key mechanisms for persistent inflammation in psoriasis.[4,5]

Statins lipid lowering effect is of particular value in patients of psoriasis as these patients have an increased risk of cardiovascular morbidity.[2,6] Some studies have shown presence of high levels of serum lipoprotein (a) and triglycerides in psoriatic patients as compared to normal subjects.[2,7]

Simvastatin is one of the statins, which are studied for their immunomodulatory effects. Shirinsky and Shirinsky[8] in a pilot study treated seven patients of psoriasis with simvastatin for a period of 8 weeks and observed that 57.14% patients had a greater than or equal to 50% improvement in terms of reduction in psoriasis area and severity index score and only 14.2% patients developed rise in serum alanine amino transaminase level. Similar percentage of patients developed headache (14.2%) and arterial hypertension (14.2%) and it proved to be safe in 71.4% patients.

Till date there is no data on use of simvastatin in our population of psoriatic patients. This study was performed with the objective to determine efficacy and safety of the drug in moderate to severe plaque psoriasis.

Patients and methods

Patients presenting to the outpatient department of dermatology, Mayo Hospital, Lahore and fulfilling the inclusion criteria i.e. patients of either sex presenting between 18 and 70 years of age with psoriasis having PASI score > 12 diagnosed on the basis of history and clinical examination, were enrolled. Patients on any systemic therapy for psoriasis in the past 4 weeks, having acute or chronic liver disease, myopathies, family history of hereditary muscular disorders (assessed by history, clinical examination, raised serum alanine aminotransferase and creatinine phosphokinase twice the upper limit), having history of hypertension and pregnant and lactating females were excluded from the study.

After getting informed consent and explaining the risks and benefits of the treatment to the patient, the demographic data like name, age, address and telephone number was obtained. All patients were given simvastatin 40mg orally once a day for eight weeks. Efficacy of the drug was assessed by reduction in surface area involved and severity regarding erythema, thickness and scaling i.e. PASI score >50% at 12^{th} week of study. Safety of drug was assessed by measuring serum levels of alanine aminotransferase, creatinine phosphokinase and bilirubin at baseline, 4^{th}, 8^{th} and 12^{th} week.

Photographs were taken at each visit. All the information was collected on especially designed pro forma, which is attached.

Data were entered and analyzed through SPSS (version 11). The quantitative data like age were presented as the mean and standard deviation. Qualitative outcome variables like sex, efficacy and safety were presented as frequency and percentage.

Results

Out of 60 enrolled patients, 40 were males and 20 females. The mean age of the patients in the study was 35.47±12.39 years (range 18-70). The mean age of the males and females is given in **Table 1**. Most of the patients were between 20-50 years.

Table 2 summarizes the mean PASI score in the study population. Results of study showed more than 50% reduction in PASI score in 12 (20%) patients. Out of these 8 patients had moderate plaque psoriasis (PASI score less than 20) and 4 patients had severe disease. In remaining 48 (80%) patients simvastatin did not prove efficacious. Mean percentage reduction in PASI score at the end of treatment was 22.5% which did not meet the criteria for simvastatin to be proved efficacious. There was no significant difference between males and females regarding improvement in disease in response to simvastatin.

Simvastatin was not efficacious as most of the patients did not have >50% reduction in PASI score. It was safe and well-tolerated as none of the patients showed rise in serum transaminases and creatinine phosphokinase and bilirubin.

Table 1 Age distribution of patients according to gender (n=60).

Age range (years)	18-70
<20	4 (6.7%)
21-30	13 (21.6%)
31-50	39 (65.0%)
>50	4 (6.7%)
Mean age (years)	35.47±12.39
Male (n=40)	
Mean age (years)	34.75 ±12.38
Female (n=20)	
Mean age (years)	36.90±12.59

Discussion

This is the first study regarding the efficacy and safety of simvastatin in psoriasis in Pakistan. Internationally a pilot study by Shirinsky and Shirinsky[8] from Russia used oral simvastatin alone for psoriasis. Another study by Naseri *et al.*[10] from Nigeria was published in 2010 in which simvastatin was used with topical betamethasone.

Regarding improvement in PASI score in our study, only twelve patients had reduction in PASI score >50%. Out of these, 33% patients had severe form of disease and 67% cases had moderate plaque psoriasis. Cases of moderate form of disease responding to simvastatin were twice as compared to those having severe plaque psoriasis. Though the drug seems to be more useful in moderate illness, more number of patients is required to find whether this is statistically significant or not.

Table 3 Baseline and end of treatment PASI score in variables of study population (n=60).

Variable	*Baseline PASI (Mean±SD)*	*End of treatment (week 12) PASI (Mean±SD)*
Male (n=40)	28.12 ± 11.52	20.84 ± 11.48
Female (n=20)	31.09 ± 14.30	24.23 ± 19.49
Total study population	29.11 ± 12.47	21.97 ± 14.56

SD = standard deviation

In comparison with international studies simvastatin did not prove to be efficacious in our present study. Shirinsky and Shirinsky[8] enrolled seven patients having PASI score >12 at presentation. Three patients out of seven were using topical fluocinolone concomitantly. Mean reduction in PASI score at the end of study was 47.34% while in our study it was 24.5%. In study by Naseri *et al.*[10] 30 patients were enrolled. All were given topical betamethasone and 50% were given oral simvastatin. The group of patients who received simvastatin in addition to topical betamethasone showed greater reduction in PASI score as compared to the one using topical treatment alone. Better results of these two studies as compared to ours, regarding efficacy of simvastatin, may be due to concomitant use of topical corticosteroids in these two trials. It is known that simvastatin has anti-inflammatory and immunomodulatory effects. Coupled with corticosteroids, simvastatin may have enhanced anti-inflammatory action, thus showing good results.

Psoriasis is associated with hyperlipidemias, metabolic syndrome and diabetes mellitus.[11] As simvastatin has lipid lowering properties, it can be used as adjuvant therapy in patients of psoriasis.

In our present dosage regimen, safety and tolerability of simvastatin were very good. No known side effects (myopathy, rise in liver transaminases, and ichthyosis) were encountered in any patient. The tolerability and safety of simvastatin at the dose used in this study were in line with the other two studies. Trial done in Russia[8] showed mild rise in liver transaminases in one patient and arterial hypertension in other, while study from Nigeria[10] did not report a single side effect of simvastatin in any patient.

The use of simvastatin should be avoided in patients with known hepatic disease, myopathies and old age. It should not be used concomitantly with certain other drugs like fibrates, erythromycin, itraconazole and immunosuppressive drugs like cyclosporine because these can increase blood levels of statins and consequently increase the risk of myopathies.

Simvastatin has proved beneficial regarding its good tolerability and minimal side effects. It may have better results in patients having mild to moderate psoriasis as compared to severe disease.

Conclusion

Simvastatin did not prove efficacious as in only 20% of patients, there was >50% reduction in PASI score. It was not effective in severe plaque psoriasis as all the cases who responded had moderate plaque psoriasis. Simvastatin was well-tolerated and safe, as there was no significant rise in serum alanine aminotransferase and creatinine phosphokinase. It is a safe drug which can be used as an adjunct treatment in moderate plaque psoriasis when other therapies are not effective but studies with larger number of patients are required to confirm this.

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