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Research Article

Comparison of the Complications and Efficacy of Topical Clobetasol Ointment with *Salvia officinalis* Ointment in the Treatment of Plaque Psoriasis

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Abstract

Background: Psoriasis is an autoimmune and common disease that affects 1 to 3% of the world's population. The appearance and progress of psoriasis are influenced by genetic and environmental factors. Topical steroids have remained the first-line treatment for psoriasis. Long-term use of topical corticosteroids is associated with the risk of side effects. The purpose of this study was to compare the complications and efficacy of topical clobetasol ointment with *Salvia officinalis* ointment in the treatment of plaque psoriasis.

Methods: A topical ointment containing 20% Salvia officinalis was prepared in the pharmaceutical laboratory of Hormozgan University of Medical Sciences. After standardization, this experimental study was performed on 84 voluntary patients with mild plaque psoriasis for two weeks. One group was treated with the prepared *S. officinalis* ointment twice daily and the other group was treated with topical clobetasol ointment twice daily. In each group, psoriasis severity was assessed using the Psoriasis Area Severity Index (PASI) at determined time points including baseline and one and two weeks after treatment initiation.

Results: At the end of treatment (2 weeks), the mean PASI score changed from 2.36 to 1.55 in patients who received topical clobetasol ointment and this score reduced from 2.74 to 2.23 in patients who applied topical *S. officinalis* ointment. After 14 days of treatment, the mean percentage decrease in mean PASI score was greater in patients who applied topical clobetasol ointment.

Conclusion: This study provides evidence that topical clobetasol ointment is more effective than 20% *S. officinalis* ointment in the treatment of psoriasis. However, *S. officinalis* ointment can be used as an adjuvant therapy to the main treatments of mild plaque psoriasis.

Keywords: Psoriasis, Salvia officinalis, Dermatology

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Background

Psoriasis is a chronic inflammatory disease which is predominantly identified by skin, nail, and joint manifestations caused by an interaction between genetic and environmental factors. The mechanism of inheritance is not completely defined. It affects 1% to 3% of the world's population. There is no absolute gender predilection for psoriasis. Psoriasis is an immune-mediated skin inflammatory disease in which intralesional inflammation primes basal stem keratinocytes to hyper proliferate. Resolution of psoriasis is associated with decreased lesional infiltration of T cells, dermal dendritic cells, Langerhans cells, neutrophils and decreased expression of *tumor necrosis factor* alpha, Interferon *gamma*, and interleukin 12/23 dependent genes. Environmental factors including drugs, skin trauma (Koebner phenomenon), infection, and stress also play a role in the pathogenesis of psoriasis which in turn cause the appearance of itchy red plaques with scaling, especially on the extensor surfaces of the body. Psoriasis can be classified according to clinical appearance, morphology, and localization. Psoriasis may present as an acute, subacute, or chronic pustular eruption, erythrodermic psoriasis, guttate psoriasis, inverse psoriasis, localized psoriasis, plaque psoriasis, photosensitive psoriasis, generalized psoriasis, HIV-associated psoriasis (1,2).

Plaque psoriasis is the most common type of psoriasis (55% of psoriasis cases) (3) and the diagnosis of plaque psoriasis can be made by physical examination and history (1).

Plaque psoriasis lesions are sharply demarcated round erythematous plaques with silvery scales. Today, there are several treatments available for the optimal treatment of psoriasis patients that are categorized into three types including topical, phototherapy, and systemic (4). These treatments can be used together depending on patient conditions (5-7). Severe cases of psoriasis involve more

than 10% of the body and require systemic therapy such as cyclosporine, methotrexate, and acitretin (1), while topical therapy is used in mild psoriasis (1). Both systemic and phototherapy may cause various adverse reactions in comparison with topical therapy (1).

Most cases of mild plaque psoriasis should first be treated with topical treatments such as topical corticosteroids, tar compounds and vitamin D analogues such as calcipotriene and calcitriol (1). Additionally, intralesional corticosteroid injections may be beneficial (1).

The first-line treatment for plaque psoriasis is topical corticosteroids. However, long-term use of topical corticosteroids is associated with the risk of side effects such as atrophy, hypopigmentation, tachyphylaxis, and telangiectasia (8-10). Moreover, the effectiveness of topical corticosteroids may reduce over time. Therefore, the application of safer topical treatments besides topical corticosteroids would be beneficial to reduce the dose of corticosteroid medicines which in turn decline their associated side effects.

Today, researchers are looking for herbal remedies because they have fewer side effects and, if proven effective,they can be good alternatives to common chemical treatments.

Topical products from *S. officinalis* are among the recommended herbal remedies. S. officinalis ointment is an inexpensive and safe treatment for plaque psoriasis symptoms such as itching, skin erythema, scaling and thick plaques (11-12).

Salvia officinalis (derived from Latin word Salvus), common Sage, is an angiosperm with woody stems and purplish flowers which belongs to the Lamiaceae family. Based on recent studies, the leaf extract of Salvia has high amounts of phenolic diterpenes such as carnosic acid and rosmarinic acid, antibacterial contents such as safficinolide, pain killer, and also anti-inflammatory compounds such as ursolic acid and polysaccharide immunomodulators (13-20).

Topical products from *S. officinalis* are among the recommended herbal remedies. *S. officinalis* ointment is an inexpensive and safe treatment for plaque psoriasis symptoms such as itching, skin erythema, scaling, and thick plaques (11,12).

Therefore, considering the importance of this issue, we decided to compare the effectiveness of 20% *S. officinalis* topical ointment with clobetasol topical ointment in the treatment of mild plaque psoriasis.

Materials and Methods

Preparation of Salvia officinalis Ointment

The dried hydroalcoholic extract of *S. officinalis* plant was purchased from the Research and Development Department of Barij Pharmaceutical Company. According to the certificate of analysis provided by Barij Pharmaceutical Company, the dried hydroalcoholic extract meet all the requirements of European Pharmacopoeia specifications.

To prepare *S. officinalis* ointment containing 20% w/w of total extract, the dried hydroalcoholic extract was triturated in a mortar and pestle. Then, a small amount of glycerin and distilled water was added to the dried extract at room temperature. In the next step, the mixture was gradually added to a sufficient amount of Eucerin to get a homogeneous semisolid mixture. In the last step, vaseline was added to the mixture by geometrical dilution method.

Clinical Study

This study was conducted in the Department of Dermatology, School of Medicine, Shahid Mohammadi Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran, from April 2021 to February 2022.

All patients with mild plaque psoriasis who have been pretreated or untreated were included in the study. The exclusion criteria were not having severe and systemic psoriasis, being pregnant, and being allergic to *S. officinalis* plant or clobetasol ointment.

A total of 84 voluntary patients (39 males and 45 females), of age ranging from 22 to 46 years old, with chronic plaque psoriasis were randomized to use one of the two treatments for 2 weeks.

One group (42 volunteers with a mean age of 32.02 ± 6.27) applied clobetasol ointment twice daily and the other group (42 volunteers with a mean age of 31.98 ± 6.98) used 20% *S. officinalis* ointment twice daily for 2 weeks.

Each group was advised to apply a thin layer of the assigned ointment to the affected areas every 12 hours and rub gently and completely. The volunteers were also instructed not to apply any formulation in the control area of the body. The severity of psoriasis was assessed in each patient at baseline and 1 and 2 weeks after treatment initiation based on the modified Psoriasis Area Severity Index (PASI) score. PASI score was measured and recorded for each patient. Then, *t* test was used to compare the mean PASI score.

The PASI is an index used to express the severity of psoriasis and measure the body surface area (0-6 scale), erythema, induration, and scaling (0-4 scale for each parameter) (21).

Statistical Analyses

All data were analyzed using IBM SPSS version 26.0. Descriptive statistics were expressed as percentages and means ± SD. The chi-square test and Mann-Whitney U test were used to compare mean PASI scores when the dependent variable was not normally distributed. Additionally, *t* test was used to compare two groups when data were normally distributed. The *P* value was set at 0.05.

Results

Table 1. Demographic Data of the Patients

Treatment	Female	Male	Age
Clobetasol	23	19	32.02 ± 6.27
Salvia officinalis	22	20	31.98 ± 6.98
Total	45	39	32.00

Table 2. Changes in Psoriasis Area Severity Index (PASI) in Two Experimental Groups

Treatment	Week	PASI (Mean ± SD)
Clobetasol (n = 42)	0	2.3667 ± 1.12069
	1	1.9167 ± 0.97578
	2	1.5500 ± 0.88490
	Total	1.9444 ± 1.04572
Salvia officinalis (n = 42)	0	2.7476 ± 1.42508
	1	2.5071 ± 1.35905
	2	2.2357 ± 1.31906
	Total	2.4968 ± 1.37358

Table 1 illustrates the demographic data of the patients included in this study. The statistical analyzes revealed no significant difference between the two treatment groups in terms of gender and age ($P > 0.05$).

As shown in Table 2 and Figure 1, the difference between the two treatment groups was not significant at the beginning of the study based on the results of the chi-square test ($P = 0.17$). The mean PASI score changed from 2.36 to 1.91 after 1 week of using topical clobetasol ointment and reduced from 2.74 to 2.50 after 1 week of using 20% *S. officinalis* ointment. According to the results of Mann-Whitney U test, the difference between the two treatments was significant ($P = 0.51$).

Table 2 shows the mean PASI score, at baseline (beginning of the treatment) and one and two weeks after the treatment initiation in the treatment groups. At baseline, both groups had high mean PASI scores. At the end of the treatment, the mean PASI score changed from 2.36 to 1.55 after 2 weeks of using topical clobetasol ointment and changed from 2.74 to 2.23 of using 20% *S. officinalis* ointment.

As shown in Figure 1, the decrease in mean PASI score was greater in patients who applied topical clobetasol ointment than in patients who applied the 20% *S. officinalis* ointment after 14 days.

At the end of treatments, the mean PASI score changed from 2.36 to 1.55 after two weeks of using topical clobetasol ointment and reduced from 2.74 to 2.23 after two weeks of using 20% *S. officinalis* ointment. The difference between the two treatments was significant based on the results of Mann-Whitney U test ($P = 0.019$).

The mean percentage decrease in PASI score was greater in patients who applied topical clobetasol ointment (34.32%) than in patients who applied 20% *S. officinalis* ointment (18.61%).

There was a significant association between the use of clobetasol ointment and decreased mean PASI score after two weeks of treatment ($P = 0.001$) and it was more effective than 20% *S. officinalis* ointment.

There was not a significant difference between the mean PASI score and the use of 20% *S. officinalis* ointment after two weeks of treatment ($P = 0.098$)

No side effects including sensitivity, itching, atrophy, hypopigmentation, tachyphylaxis, and telangiectasia were reported.

Discussion

Psoriasis is an autoimmune and common disease, and for most patients, it is more emotionally than physically disabling (1).

This randomized hospital-based cross-sectional clinical trial study aimed to compare the complications and efficacy of topical clobetasol ointment with *S. officinalis* ointment in the treatment of mild plaque psoriasis.

In folk medicine, *S. officinalis* has been used for the treatment of different kinds of disorders including

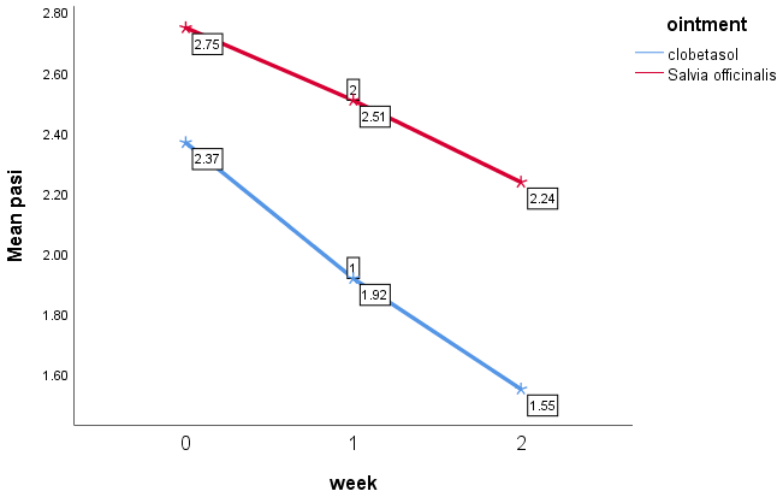

Figure 1. Mean PASI Scores of the Two Experimental Groups at Three Time Points

seizure, ulcers, gout, rheumatism, inflammation, dizziness, tremor, paralysis, diarrhea, and hyperglycemia (22,23).

The pharmacological findings that have been frequently reported for *S. officinalis* include anticancer, anti-inflammatory, antinociceptive, antioxidant, antimicrobial, antimutagenic, antidementia, hypoglycemic, and hypolipidemic effects (24). Moreover, *S. officinalis* essential oil has antifungal and anti-inflammatory effects (25).

The result of the current study was consistent with previous studies in which an anti-inflammatory effect was reported for *S. officinalis* as the prepared 20% *S. officinalis* ointment showed some positive effects on decreasing the mean PASI score. Corticosteroids are a mainstay of topical therapy for psoriasis. In a clinical study by Horn et al, it was reported that skin atrophy and adrenal suppression have been associated with excesses in potency, prolonged or widespread use (26).

This study provided evidence that topical clobetasol ointment is more effective than 20% *S. officinalis* ointment in the treatment of psoriasis after two weeks. At the first evaluation (baseline), the difference between the two experimental groups was not significant because the two groups had an equal situation with no treatments but the difference became significant over time. This result also confirmed that topical corticosteroids are still the most efficient treatments for plaque psoriasis.

Conclusion

Although the statistical analyzes revealed no significant difference between the mean PASI score using 20% *S. officinalis* ointment for a duration of two weeks but it has positive effects on decreasing the mean PASI score and may be more effective at higher concentrations or longer periods of time. Overall, according to the results, 20% *S. officinalis* ointment is not recommended as the main treatment for mild plaque psoriasis but can be used as an adjuvant therapy.

Finally, further studies are needed to prove the efficacy and complications of *Salvia officinalis* ointment use in the treatment of mild plaque psoriasis.

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Authors' Contribution

Sedighe Tavakoli and Amir Hossein Mosalman Haghighi: concepts/design/definition of intellectual content/literature search/clinical and experimental studies/data acquisition/data analysis/statistical analysis/manuscript preparation/manuscript editing/manuscript review/guarantor.

Competing Interests

The authors declare that they have no conflict of interest.

Ethical Approval

This study was approved by the Research Ethics Committee of Hormozgan University of Medical Sciences. (IR.HUMS.REC.1399.489). It was registered in the Iranian Registry of Clinical Trials website (identifier: IRCT20210202050214N1; https://www.irct.ir).

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