ORIGINAL ARTICLE

Evaluation of Therapeutic Effect of Low Dose Enoxaparin in Treatment of Psoriasis: Pilot Study

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Abstract

Background: ***Psoriasis is an inflammatory skin condition that manifests as red, plaque-like lesions that are often covered with silvery-white scales. It is a chronic and recurrent immune-mediated skin disease.***

Aim and objectives: ***To assess the safety and effectiveness of treating plaque psoriasis with low doses of enoxaparin.***

Patients and methods: ***This study was conducted on 30 patients with plaque psoriasis(43.3%) males and(56.7%) females with a mean age of (37.7±13) years, ranging between(18-59) years, the patients had a mean disease duration (5.1±3.6) years, ranged between (1-16) years. Each patient was treated by 5mg enoxaparin(Clexane) as a subcutane-ous injection once a week for 12 weeks.***

Results: ***There was statistically significant improvement in clinical response as 6 patients(20%) showed significant change, 12 patients(40%) showed moderate change, 8 patients (26.7%) showed no significant change, and finally, 4 patients(13.3%) were worsened.***

Conclusion: ***The excellent side-effect profile of low-dose enoxaparin makes it a promising new therapeutic choice for psoriasis. Concerning efficacy, additional large-scale trials are needed to ascertain the optimal dose and length of treatment, the subgroup of psoriasis to be treated, and to compare enoxaparin to conventional psoriasis remedies.***

Keywords: Enoxaparin; Therapeutic effect; Psoriasis

1. Introduction

About 2% of people have psoriasis, an inflammatory skin condition that lasts for a long time. There is a wide range of phenotypic variants and severity levels associated with it. Eighty percent of patients experience mild to moderate disease, while twenty percent have moderate to severe disease.[1]

There is strong evidence that the anti-inflammatory benefits of enoxaparin are due to the non-anticoagulant fragments of the drug, but enoxaparin contains anticoagulant particles as well.[2]

According to Lider et al., T lymphocyte heparinase activity is suppressed, T cell migration and delayed-type hypersensitivity reactions are both inhibited, and low-dose heparin is effective in all three processes. [3]

There are numerous different types of polysaccharides that make up heparin's heterogeneous structure. The immunomodulatory effects of sulfated disaccharide groups in heparin are assumed to exist. Degradation of normal heparin chemically yields LMW heparins. Hence, immunologically active disaccharide molecules are present in only a subset of LMW heparins. Enoxaparin is a popular low-molecular-weight heparin that transmits heparin's immune-modulatory properties.[4]

Researchers Demircioğlu and Atakan found that 52% of psoriasis patients who received enoxaparin treatment saw improvements in their condition. There were no reported systemic adverse effects of enoxaparinved.[4]

This study was out to assess the safety and effectiveness of using low doses of enoxaparin to treat plaque psoriasis.

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2. Patients and methods

The study was prospective and randomized, carried out on 30 plaque psoriasis patients from March 2024 to November 2024 at El-Hussein University Hospital's outpatient clinic. All patients were asked to sign a document indicating their informed consent. Additionally, we received permission from Al-Azhar University's Medical Faculty's Research Ethics Committee.

Inclusion Criteria:

Participants must meet the following criteria: Participants' ages varied from 18 to 59 years old, have a confirmed diagnosis of plaque psoriasis, have the condition affecting more than 10% of their body surface, have not received systemic (oral, parenteral, photo-biological) or topical treatment for psoriasis in the past three months, and have given their approval to participate in the study by signing the "patient consent form".

Exclusion Criteria:

Experiencing bleeding diathesis, uncontrolled hypertension, a history of peptic ulcer, being pregnant or breastfeeding, having a hypersensitivity to heparin or its derivatives, or having a history of heparin-induced thrombocytopenia are all factors to be considered. Past three months involving a major surgical procedure; being on oral anticoagulants, acetylsalicylic acid, or another nonsteroidal anti-inflammatory medicine at the same time; having a history of bleeding diathesis or cerebrovascular accident in one's family; illness affecting the liver, as well as abnormalities in liver function tests; and abnormalities in kidney function tests.

Study Plan:

Prior to, during, and after treatment, all patients underwent a thorough history taking, physical examination (both internal and external), and photography to document any changes.

Two separate observers used the PASI scoring system to determine the amount and severity of the disease before therapy began. The first PASI score was the mean of these two scores. The laboratory tests that were ordered for all patients prior to treatment were complete blood counts, testing for liver and renal function, prothrombin time, active partial thromboplastin time, and INR. Patients were cautioned against taking many drugs at once, including pain relievers, unless their doctor has specifically approved the combination.

Methods:

Each patient had twelve sessions of treatment spaced one week apart, with pre-, mid-, and post-session photos taken. Thirty participants were given a subcutaneous injection of 5 mg enoxaparin (Clexane) once a week for twelve weeks as part of the trial. A 5 mg injectable dosage was made using 1/4 syringe of a commercially available enoxaparin solution (20 mg/0.2 ml).

Subcutaneous injections were administered into the abdomen. Nearly ten centimeters laterally to the midline, the injection was given to the abdominal wall. Each week, the injection site was switched; for example, if one dose was given to the right side, the other would be given to the left. Potential local and systemic side effects were inquired about in patients before each injection. An assessment of the patient's general health as well as the area around the injection site was carried out. A full blood count, aPTT, and INR were requested weekly, but liver function tests were rescheduled every six weeks. Two separate observers computed PASI scores six weeks and twelve weeks following treatment initiation, and the mean results were documented. Additional photographs were taken of the patients once the treatment was complete.

Evaluation criteria:

Prior to therapy, the study group's psoriasis area and severity index (PASI) scores were used to assess the area of affected body parts, the severity of the condition, and the patients' response to treatment. The four primary areas of the body—the head, the upper limbs, the trunk, and the lower limbs—are used to calculate the area in this scoring system. These areas were thought to make up 10%, 20%, 30%, and 40% of the entire body, respectively. A number between 0 and 6 was assigned to the psoriasis-affected area in each of the four locations based on the percentage of surface area involved. Every location was assessed independently for erythema (E), induration (I), and desquamation (D) using a score range of 0 to 4. We measured the response to enoxaparin treatment by tracking changes in PASI scores. A drop of 50% or more in the PASI score was considered a "significant improvement" after 12 weeks of treatment. As a "moderate improvement," a decrease of 25-49% was deemed acceptable. Positive treatment responses were defined as either a statistically significant improvement or a moderate improvement. A decrease in PASI score of less than 25% was considered to have "no significant change".

Patients' satisfaction:

To gauge whether a patient is happy or unhappy with a particular treatment, product, or overall experience, researchers utilize a satisfaction scale ranging from 1 to 5. extremely unsatisfied, dissatisfied, neutral, satisfied, and extremely satisfied are the five possible outcomes on the 5-point scale.

Statistical analysis:

Statistical Package for the Social Sciences (SPSS) version 25 was used for data analysis. The qualitative data were presented using percentages and frequencies. Quantitative and continuous data were presented as mean±standard deviation

(Mean±SD). The middle value of a discrete set of integers, calculated by dividing the sum of values by the number of values, is called the mean or average. As a measure of how widely distributed a set of values is, standard deviation (SD) is used. If the standard deviation is small, then the values are clustered around the set mean, and if it's large, then the values are more dispersed. We regarded a probability (P-value) to be significant if it was less than 0.05, highly significant if it was less than 0.001, and insignificant if it was greater than 0.05.

Compared samples. If you have two sets of continuous quantitative data from the same group, you may use a T-test to compare them. When comparing more than two groups (for continuous quantitative data), a one-way analysis of variance (F) is used. Non-parametric categorical data were compared using the chi-square test.

3. Results

Table 1. An explanation of the demographic information for each patient under study

DEMOGRAPHIC DATA		ALL PATIENTS (N=30)	
SEX	Males	13	43.3%
	Females	17	56.7%
AGE	Mean±SD	37.7±13	
	Min-max	18-59	
DURATION OF THE DISEASE	Mean±SD	5.1±3.6	
	Min-max	1-16	
FAMILY HISTORY	Positive	13	43.3%
	Negative	17	56.7%

As regard sex, there were 13 males (43.3%) and 17 females (56.7%) in all studied patients. As regard age, the mean was (37.7±13) years with range of (18-59) years in all studied patients. As regard disease duration, the mean was (5.1±3.6) years with range of (1-16) years in all studied patients. As regard family history, it was positive in 13 patients (43.3%) and negative in 17 patients (56.7%) in all studied patients, (table 1; figure 1).

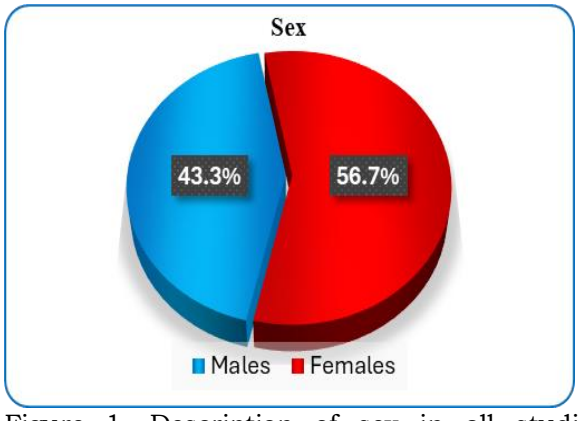

Figure 1. Description of sex in all studied patients.

Table 2. Description of PASI score in all studied patients.

PASI SCORE		ALL PATIENTS (N=30)
BEFORE TREATMENT	Mean±SD	17.9±7.6
	Min-max	5.9-32.7
AFTER 12 SESSIONS	Mean±SD	12.3±8.1
	Min-max	0.8-32.2
VALUE OF CHANGE	Mean±SD	-5.6±6.5
	Min-max	-28.8-4.6
PERCENTAGE OF CHANGE	Mean±SD	-33±31.4
	Min-max	-92.3-26.3

As regard PASI score before treatment, the mean was (17.9±7.6) with range of (5.9-32.7). While after 12 sessions of treatment, the mean became (12.3±8.1) with range of (0.8-32.2). The value of change was (-5.6±6.5) with range of (-28.8-4.6). While the percentage of change was (-33±31.4) with range of (-92.3-26.3) in all studied patients, (table 2; figure 2).

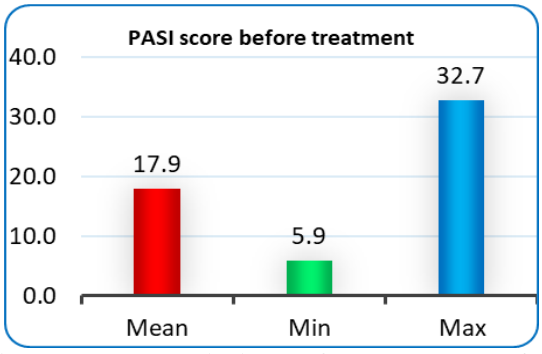

Figure 2. Description of PASI score before treatment in all studied patients.

Table 3. Comparison of PASI score before treatment and after 12 sessions in all studied patients

		BEFORE TREATMENT (N= 30)	AFTER 12 SESSIONS (N= 30)	T	P-VALUE
PASI SCORE	Mean±SD	17.9±7.6	12.3±8.1	4.8	<0.001 HS
	Min-Max	5.9-32.7	0.8-32.2		

T: Paired sample T-test. HS: P<0.001 is considered highly significant.

High statistically significant (P<0.001) decreased PASI score after 12 sessions of treatment {(12.3±8.1) with range of (0.8-32.2)} when compared with that before treatment {(17.9±7.6) with range of (5.9-32.7)} in all studied patients, (table 3; figure 3).

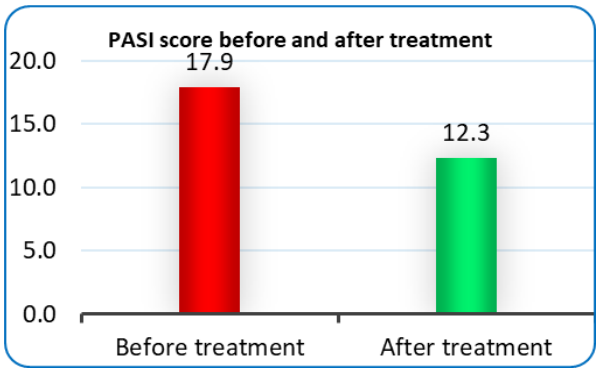

Figure 3. Comparison of PASI score before treatment and after 12 sessions in all studied patients.

Table 4. Description of clinical response and satisfaction in all studied patients

DEMOGRAPHIC DATA		ALL PATIENTS (N=30)	
CLINICAL RESPONSE	No significant change	8	26.7%
	Moderate change	12	40.0%
	Significant change	6	20.0%
	Worse	4	13.3%
PATIENTS' SATISFACTION	Mean±SD	2.2±1.4	
	Min-max	0-5	

As regard clinical response to treatment, 8 patients (26.7%) showed no significant change, 12 patients (40%) showed moderate change, 6 patients (20%) showed significant change and finally, 4 patients were worsened. As regard patients' satisfaction, the mean was (2.2±1.4) wit range of (0-5) in all studied patients, (table 4; figure 4).

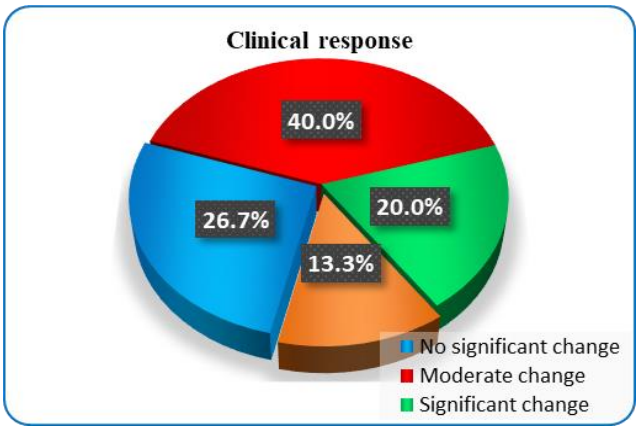

Figure 4. An explanation of the clinical reaction in each subject under study.

Table 5. An explanation of each patient's side effects

SIDE EFFECTS	ALL PATIENTS (N=30)	
SYSTEMIC BLEEDING	0	0.0%
PAIN AT INJECTION SITE	5	16.7%
ECCHYMOSIS AT INJECTION SITE	3	10.0%
NAUSEA	2	6.7%

As regard side effects after treatment, pain at site of injection was developed in 5 patients (16.7%), ecchymosis at site of injection was developed in 3 patients (10%) and nausea was present in 2 patients (6.7%) in all studied patients, (table 5; figure 5).

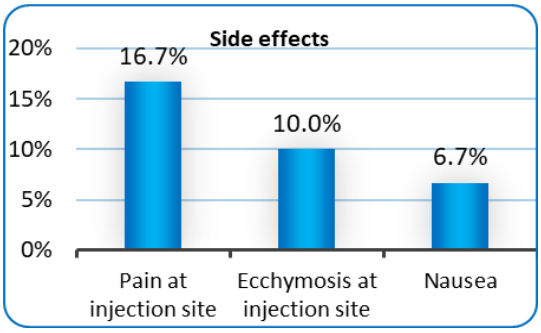

Figure 5. An explanation of the adverse effects experienced by every patient in the study.

Table 6. Clinical response and demographic information for each patient under study

		NO SIGNIFICANT CHANGE (N=8)		MODERATE CHANGE (N=12)		SIGNIFICANT CHANGE (N=6)		WORSE (N=4)		STAT. TEST	P-VALUE
SEX	Males	2	25.0%	7	58.3%	1	16.7%	3	75.0%	X2=5.6	0.14NS
	Females	6	75.0%	5	41.7%	5	83.3%	1	25.0%		
AGE	Mean±SD	39.8±14.2		38.6±12.3		33±13.5		38±15.5		F=0.32	0.81NS
	Min-Max	18-56		19-59		18-51		18-53			
DURATION	Mean±SD	5.3±2.4		4.5±3.2		6.8±5.4		3.8±3.8		F=0.76	0.53NS
	Min-Max	3-8		1-13		2-16		1-9			
FAMILY HISTORY		4	50.0%	5	41.7%	3	50.0%	1	25.0%	X2=0.81	0.85NS

F: Value of ANOVA test. NS: P>0.05 is considered non-significant. X2: value of chi-square test.

No significant (P=0.14) correlation between clinical response to treatment and sex in all studied patients. In patients with no significant change there were 2 males (25%) and 6 females (75%). While in patients with moderate change there were 7 males (58.3%) and 5 females (41.7%). In patients with significant change there was 1 male (16.7%) and 5 females (83.3%). Finally, in patients who worsened, there were 3 males (75%) and 1 female (25%).

No significant (P=0.81) correlation between clinical response to treatment and age in all studied patients. In patients with no significant change, the mean was (39.8±14.2) with range of (18-56). While in patients with moderate change, the mean was (38.6±12.3) with range of (19-59). In patients with significant change, the mean was (33±13.5) with range of (18-51). Finally, in patients who worsened, the mean was (38±15.5) with range of (18-53).

No significant (P=0.53) correlation between clinical response to treatment and disease duration in all studied patients. In patients with no significant change, the mean was (5.3±2.4) with range of (3-8). While in patients with moderate change, the mean was (4.5±3.2) with range of (1-13). In patients with significant change, the mean was (6.8±5.4) with range of (2-16). Finally, in patients who worsened, the mean was (3.8±3.8) with range of (1-9).

No significant (P=0.85) correlation between clinical response to treatment and family history in all studied patients. It was positive in 4 patients (50%) among patients with no significant change, 5 patients (41.7%) among patients with moderate change, 3 patients (50%) among patients with significant change and 1 patient (25%) of patients who worsened after treatment, (table 6; figure 6).

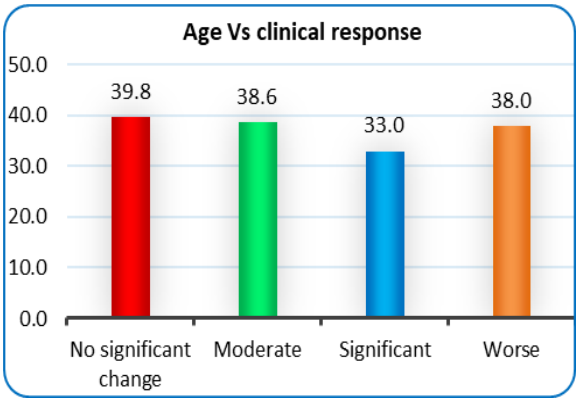

Figure 6. Correlation between clinical response and age in all studied patients.

Case presentation

Cases(1):

Female patient 18-years old with plaque psoriasis of 10-years duration with –ve family history.

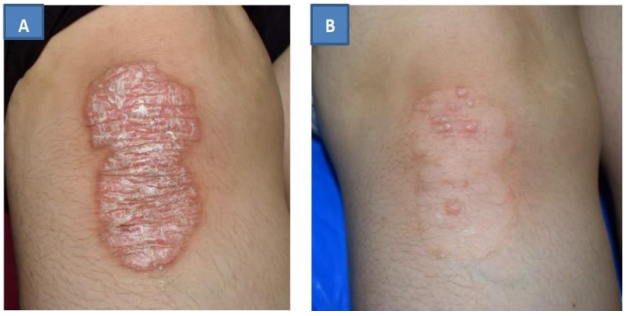

Figure 7. (A) Frontal view of right knee before treatment. (B) Frontal view of right knee after 12th session of treatment showing clearance of psoriatic plaque after 3 months of treatment.

Case (2):

Female patient 21-years old with plaque psoriasis of 2-years duration with +ve family history.

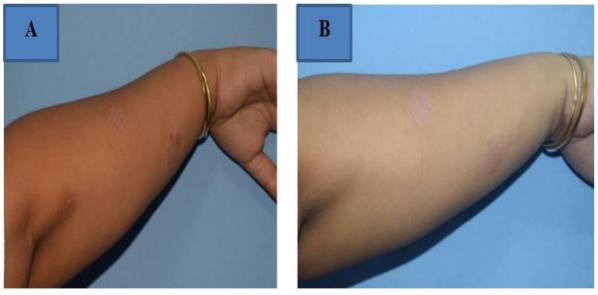

Figure 8. A) Dorsal of right forearm before treatment. B) Dorsal of right forearm after 12th session of treatment showing clearance of psoriatic plaque.

Case(3):

Female patient 25-years old with plaque psoriasis of 6-years duration with +ve family history.

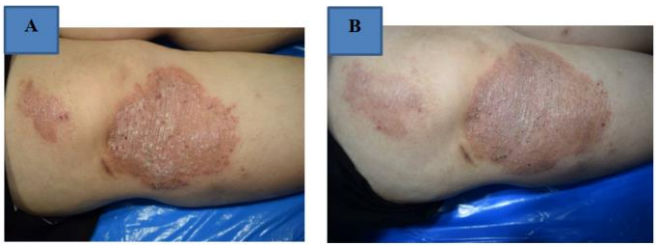

Figure 9. (A) Ventral aspect of right knee before treatment. (B) Ventral aspect of right knee after 12th session of treatment showing mild improvement of psoriatic plaque after 3 months.

Case(4):

Female patient 33-years old with plaque psoriasis of 4-years duration with -ve family history.

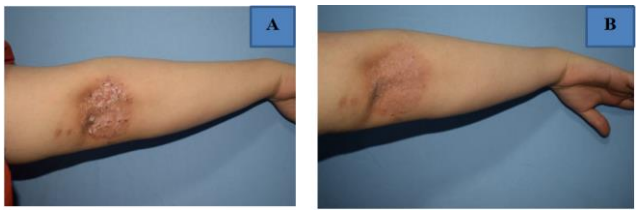

Figure 10. (A) Dorsal aspect of right elbow before treatment.(B) Dorsal aspect of right elbow after 12th session of treatment showing moderate improvement of psoriatic plaque after 3 months of treatment.

4. Discussion

Sharply defined, erythematous papules or plaques covered in silvery-white scales are the clinical hallmark of psoriasis, a chronic, recurring, immune-mediated, inflammatory skin disease. The most prevalent inflammatory skin condition, after atopic dermatitis, is psoriasis, whose prevalence has been marginally rising over the past three decades.[5]

Although psoriasis can develop at any age, it is more frequent in adults than in children. A comprehensive global study found that the prevalence of psoriasis ranged from 0.5 to 11.4% in adults and 0 to 1.4% in children. An estimated 60 million people worldwide suffer from psoriasis. It is more common in places with an older population and high incomes.[6]

Our study's patients were between the ages of 18 and 59, which closely matched a study by Demircioğlu and Atakan[4] in which the oldest patient was 57 years old, and the youngest was 19.

Despite some research suggesting that psoriasis is more prevalent in men, there is no obvious gender preference for the condition.[7] Our analysis revealed a female predominance, with women making up 56.7% of our patients (17 out of 30). Our results are consistent with research that found that women are somewhat more likely than men to have psoriasis.[8]

All of the patients in our study had disease durations ranging from 1 to 16 years, which was consistent with what was found by Mahajan and Singla[9] where the illness's length varied from one and a half months to fifteen years, the research by Chakravdhanula et al.,[10] where the length of the illness ranged from one to ten years, and research by Demircioğlu and Atakan4 where the duration of the disease ranged between (0-35 years).

Thirteen patients (43.3%) in our study had a positive family history of psoriasis. Our research aligns with the findings of Mohd Affandi et al.,[11] where 23.1% of patients reported having a good family history. An additional investigation by Zhang et al.,[12] found that a positive family history was present in 29.4% of psoriasis vulgaris participants.

Six patients (20%) showed substantial change, twelve patients (40%) demonstrated moderate change, eight patients (26.7%) demonstrated no meaningful change, and four patients (13.3%) showed worsening, indicating a statistically significant improvement in clinical response in our study. This closely matched a research conducted by Demircioğlu and Atakan[4] Four patients (17%) showed considerable improvement, eight patients (35%), five patients (22%), and no meaningful change occurred. Lastly, six individuals (26%) experienced worsening.

The PASI ratings of patients at baseline (before therapy) and at the end of treatment (following the 12th dose of enoxaparin) differed significantly ($P<0.001$) in our study. This closely matched a research conducted by Demircioğlu and Atakan[4] where there was a statistically significant distinction among the patients' pre-treatment and post-treatment PASI scores (following the sixth enoxaparin dose) ($p=0.008$).

Our study found no significant relationship between the clinical response at the end of treatment and age, gender, length of disease, or prior psoriasis therapies, which was in good agreement with a study by Demircioğlu and Atakan[4] where the change (increase or decrease) in the PASI score at the end of treatment did not significantly correlate with age, gender, length of disease, or prior psoriasis therapies.

Family history of psoriasis and clinical response at the end of treatment did not significantly correlate in our study ($P=0.85$), which did not concur with research conducted by Demircioğlu and Atakan[4] where the change in PASI score and family history were shown to be statistically correlated ($p=0.06$). All six individuals whose PASI scores rose at the end of treatment had positive family histories.

Our study group did not experience any systemic side effects associated with the medication. Laboratory testing conducted both during and after the treatment revealed no abnormalities. Five patients (16.7%) experienced discomfort at the injection site, three patients (10%) developed ecchymosis at the injection site, and two patients (6.7%) experienced nausea as the sole local side effects. This closely matches research conducted by Demircioğlu and Atakan.[4] While these results indicate that low-dose enoxaparin treatment is relatively safe, it is important to remember that uncommon adverse effects, like hypersensitivity reactions, can occur regardless of dosage.

4. Conclusion

Low-dose enoxaparin has a good side-effect profile and is a potential innovative therapy option for psoriasis. To ascertain the target psoriasis subgroup, the proper dosage and duration of therapy, and the efficiency of enoxaparin in comparison to conventional psoriasis treatments, more extensive research is necessary.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

References

1. Golbari NM, Porter ML, Kimball AB. Current guidelines for psoriasis treatment: a work in progress. Cutis. 2018;101(3S):10-12.
2. Shastri MD, Stewart N, Horne J, et al. Non-Anticoagulant Fractions of Enoxaparin Suppress Inflammatory Cytokine Release from Peripheral Blood Mononuclear Cells of Allergic Asthmatic Individuals. PLoS One. 2015;10(6):e0128803. Published 2015 Jun 5.
3. Lider O, Mekori YA, Miller T, et al. Inhibition of T lymphocyte heparanase by heparin prevents T cell migration and T cell-mediated immunity. Eur J Immunol. 1990;20(3):493-499.
4. Demircioğlu D, Atakan N. The Efficacy of Low-Dose Enoxaparin in Psoriasis. Acıbadem Üniversitesi Sağlık Bilimleri Dergisi. 2022;13:352-359.
5. Vičić M, Kaštelan M, Brajac I, et al. Current Concepts of Psoriasis Immunopathogenesis. Int J Mol Sci. 2021;22(21):11574.
6. Branisteanu DE, Cojocaru C, Diaconu R, et al. Update on the etiopathogenesis of psoriasis (Review). Exp Ther Med. 2022;23(3):201.
7. Parisi R, Symmons DP, Griffiths CE, et al. Identification and Management of Psoriasis and Associated ComorbidiTy (IMPACT) project team. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol. 2013;133(2):377-385.
8. Vena GA, Altomare G, Ayala F, et al. Incidence of psoriasis and association with comorbidities in Italy: a 5-year observational study from a national primary care database. Eur J Dermatol. 2010;20(5):593-598.
9. Mahajan BB, Singla M. Evaluation of intralesional 5% 5-fluorouracil in resistant localized plaque psoriasis. Indian Dermatol Online J. 2014;5(3):287-290.
10. Chakravdhanula U, Anbarasu K, Verma VK, et al. Clinical efficacy of platelet rich plasma in combination with methotrexate in chronic plaque psoriatic patients. Dermatol Ther. 2016;29(6):446-450.
11. Mohd Affandi A, Khan I, Ngah Saaya N. Epidemiology and Clinical Features of Adult Patients with Psoriasis in Malaysia: 10-Year Review from the Malaysian Psoriasis Registry (2007-2016). Dermatol Res Pract. 2018;2018:4371471.
12. Zhang X, Wang H, Te-Shao H, et al. The genetic epidemiology of psoriasis vulgaris in Chinese Han. Int J Dermatol. 2002;41(10):663-669.