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A comparative analysis of acitretin and methotrexate in the treatment of lichen planus

Liken planus tedavisinde asitretin ve metotreksatın karşılaştırmalı analizi

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Abstract

Background and Design: Lichen planus (LP) is a common inflammatory dermatosis affecting people of all ages. Acitretin is one of the first-line systemic treatments; however, certain circumstances limit its use and encourage the search for alternative therapies. We aimed to compare the efficacy and safety of methotrexate as an alternative to acitretin.
Materials and Methods: This study retrospectively evaluated the treatment response, clinical characteristics, and demographic features of patients who received methotrexate or acitretin for LP between January 2021-2024. Patients who showed clinical improvement and required continued treatment to maintain control were classified as "clinical responders". Patients who demonstrated a clinical response and remained clear after treatment discontinuation were classified as in "remission". Patients whose symptoms did not improve with treatment or who continued to develop new lesions were considered "non-responders".
Results: The study included 66 patients. The mean age of the patients was 53.4±9.6; 47 (71.2%) were female, and 16 (28.8%) were male. Thirty-one (46.9%) patients took methotrexate, and 35 (53.1%) took acitretin. The clinical response rate in patients receiving methotrexate (n=30; 96.7%) was significantly higher than in patients taking acitretin (n=28; 80%) ($p<0.05$). The predicted treatment response duration did not differ significantly ($p>0.05$) between the group taking methotrexate (15.9 weeks) and the group taking acitretin (13.8 weeks). There was no statistically significant difference in the number and duration of patients achieving remission and the side effect rate of the treatments ($p>0.05$).
Conclusion: Methotrexate and acitretin are effective and safe options in LP treatment. Multicenter randomized controlled trials are needed to develop treatment guidelines.
Keywords: Lichen planus treatment, acitretin, methotrexate, treatment efficacy

Öz

Amaç: Liken planus (LP) her yaştan insanı etkileyen yaygın görülen bir enflamatuvar dermatozdur. Asitretin sistemik tedavilerde birinci basamak tedavilerden biridir; ancak bazı durumlar kullanımını kısıtlamakta ve alternatif tedavi arayışlarını teşvik etmektedir. Çalışmamızda asitretin alternatifi olarak metotreksatın etkinliğini ve güvenliğini karşılaştırmayı amaçladık.
Gereç ve Yöntem: Ocak 2021-2024 tarihleri arasında LP tedavisi için metotreksat veya asitretin başlanan hastaların tedavi yanıtı, klinik ve demografik özellikleri retrospektif olarak incelendi. Hastaların metotreksat ve asitretin tedavilerine yanıtı analiz edildi. Klinik iyileşme gösteren, yeni lezyonları olmayan ve kontrolü sürdürmek için devam eden tedaviye ihtiyaç duyan hastalar "klinik yanıt" olarak sınıflandırıldı. Klinik yanıt gösteren ve tedavinin kesilmesinden sonra temiz kalan hastalar "remisyon" olarak sınıflandırıldı. Her iki tedaviyle semptomları gerilemeyen veya yeni lezyon çıkışları devam eden hastalar "tedaviye yanıtsız" kabul edildi.
Bulgular: Çalışmaya 66 hasta dahil edildi. Hastaların yaş ortalaması 53,4±9,6, kadın hasta sayısı 47 (%71,2) erkek hasta sayısı 16 (%28,8) idi. Hastaların 31'i (%46,9) metotreksat, 35'i (%53,1) asitretin kullanmaktaydı. Metotreksat 10-15 mg/hafta subkutan, asitretin 20-35 mg/gün

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oral olarak kullanılmıştı. Metotreksat kullanan hastalarda klinik yanıt oranı (n=30, %96,7), asitretin kullananlardan (n=28, %80) anlamlı olarak daha fazlaydı (p<0,05). Metotreksat kullanımı olan (15,9 hafta) grup ile asitretin kullanımı olan (13,8 hafta) olan grup arasında öngörülen tedavi yanıt süresi anlamlı farklılık göstermemiştir (p>0,05). Remisyona ulaşan hasta sayısı ve süresi, tedavilerin yan etki oranı açısından istatistiksel açıdan anlamlı fark yoktu (p>0,05).
Sonuç: Metotreksat ve asitretin LP tedavisinde etkili ve güvenli seçeneklerdir. Tedavi kılavuzlarının düzenlenmesi için çok merkez randomize kontrollü çalışmalara ihtiyaç vardır.
Anahtar Kelimeler: Liken planus tedavisi, asitretin, metotreksat, tedavi etkinliği

Introduction

Lichen planus (LP) is a chronic inflammatory dermatosis affecting the skin, nails, hair, and mucous membranes. In its classical form, cutaneous LP is characterized by purple, itchy, and polygonal papules. Cutaneous involvement may be accompanied by involvement of skin appendages and mucosa[1].

Different populations have reported varying rates ranging from 1 to 5%[2]. Although LP is more common between the third and sixth decades, it can occur at any age, regardless of gender or race[3].

The exact cause of LP has not been determined, but it has been associated with an impaired immune response triggered by genetic and environmental factors. Current data indicates that LP immunopathogenesis is predominantly mediated by cell-mediated immunological processes, with T-cells playing a critical role. Antigen-mediated stimulation of effector T-lymphocytes leads to their activation and differentiation. T helper 1 (Th1) and Th17 lymphocytes initiate and maintain inflammation by secreting key inflammatory cytokines such as interferon-gamma and interleukin-17[4].

LP is diagnosed by the typical morphology of the lesions and histopathological examination. Although different features can be observed in clinical variants, the classical form characteristically shows hyperkeratosis in the epidermis, wedge-shaped hypergranulosis, acanthosis, vacuolization of the basal layer, scattered apoptotic keratinocytes (Civatte bodies), and a dense, band-like lymphocytic infiltrate in the upper dermis[5].

The disease has a clear clinical definition, but the available treatments are based on anecdotal evidence or data from small sample-size studies. Numerous medications, including topical, intralesional, or systemic corticosteroids, topical calcineurin inhibitors, phototherapy, methotrexate, cyclosporine, acitretin, and mycophenolate mofetil, can be used to treat LP[1,5]. In our country, like in many other countries, there are no treatment guidelines for LP. In the European guideline published in 2020, acitretin was among the first-line systemic treatments in treating LP, while methotrexate was recommended as the third-line treatment due to the lack of studies with substantial evidence[5]. Few studies have been conducted on using methotrexate in treating LP[6] since the guideline was published, and the guideline has not yet been updated. The absence of national or international treatment guidelines presents a challenge for physicians, particularly in cases of resistance or recurrence.

The development of treatment options has led to more effective and safer solutions in treating diseases in dermatology, as in many other fields of medicine. Unfortunately, there are still many unmet needs in LP treatment[7]. In our study, we aimed to evaluate the efficacy of methotrexate and acitretin in treating LP and provide data on these two therapeutic choices to the literature.

Materials and Methods

This study retrospectively evaluated the treatment response, clinical characteristics, and demographic features of patients who received methotrexate or acitretin for LP between January 2021-2024. This study was approved by the Pamukkale University Non-Interventional Clinical Research Ethics Committee Local Ethics Committee (approval number: E-60116787-020-556309, date: 24.07.2024). Demographic characteristics, disease duration, mucosal involvement, comorbidities, and previous treatments were all recorded retrospectively. In an attempt to create a homogeneous distribution, patients with moderate-to-severe disease who had not responded to topical and systemic steroids and required systemic treatment were included. The study included patients who were followed up for an average of 9 months after starting treatment and at least 6 months after stopping treatment.

The inclusion criteria were 10% or more of the body surface area affected and morphologically compatible with classical cutaneous LP. Non-classical morphological variants such as atrophic, hypertrophic, inverse LP, and scalp and nail involvement were considered exclusion criteria.

Patients were analyzed according to their response to methotrexate and acitretin treatments. Patients who showed clinical improvement, no new lesion formation, and required ongoing treatment to maintain control were classified as "clinical responders". Patients who demonstrated a clinical response and remained clear for at least 12 weeks after treatment discontinuation were classified as "in remission". Patients whose symptoms did not improve with treatment or who continued to develop new lesions were considered "non-responders". Patients who were followed up for at least six months after cessation of treatment were included in the study.

Statistical analysis

Mean, standard deviation, median, minimum-maximum, frequency, and ratio values were used in the descriptive statistics of the data. The distribution of variables is measured by Kolmogorov-Smirnov and Shapiro-Wilk tests. An Independent sample t-test was used to analyze quantitative independent data with normal distribution. The Mann-Whitney U test was used to analyze quantitative independent data with non-normal distribution. The chi-square test was used to analyze qualitative independent data, and the Fisher's exact test was used when chi-square test conditions were not met. Cox regression and Kaplan-Meier were used in survival analysis. SPSS 28.0 software was used in the analyses.

Results

The study included 66 patients. The mean age of the patients was 53.4±9.6, the number of female patients was 47 (71.2%), and the number of male patients was 16 (28.8%). Twenty-one patients received oral methylprednisolone treatment at a dose of 0.5-1 mg/kg in addition to topical steroids in the first step. The clinical and demographic characteristics of the patients are summarized in Table 1. Thirty-one (46.9%) patients were using methotrexate, and 35 (53.1%) patients were using acitretin. Methotrexate was used in doses of 10-

15 mg/week subcutaneously, and acitretin was used in 20-35 mg/day doses. The clinical response rate in patients using methotrexate (n=30, 96.7%) was significantly higher than in those using acitretin (n=28, 80%, p=0.037) (Figure 1).

Age and gender distribution did not differ significantly between the groups using methotrexate and acitretin (p>0.05). Comorbidity rates did not differ significantly between the groups using methotrexate and acitretin (p>0.05). There was no significant difference in mucosal involvement and the presence of concomitant autoimmune disease between the groups using methotrexate and acitretin (p>0.05). The rate of concurrent phototherapy treatment in the group using acitretin was significantly higher than in the methotrexate group (p<0.05). There was no significant difference (p>0.05) in the systemic and topical steroid use rate between the groups using methotrexate and acitretin. The disease duration in the acitretin group was significantly (p<0.05) higher than in the methotrexate group. There was no significant difference (p>0.05) in the duration of clinical response between the groups using methotrexate and acitretin (Table 2).

The predicted treatment response duration did not differ significantly (p>0.05) between the group using methotrexate (15.9 weeks) and the group using acitretin (13.8 weeks) (Figure 2).

Side effect rates did not differ significantly (p>0.05) between methotrexate and acitretin groups (p>0.05) (Table 2). Side effects occurred in five (16.1%) patients using methotrexate, including nausea in four patients and a minimal increase in creatinine level in one patient. This side effect was tolerable for two patients with nausea, and treatment was continued. Treatment was discontinued for one of the other three patients with side effects because remission was achieved. One patient could not continue methotrexate because of nausea and was switched to hydroxychloroquine, resulting in remission. The patient with impaired renal function tests did not continue follow-up. As a result, two patients (6.1%) using methotrexate discontinued treatment due to side effects. Side effects were observed in nine (25%) patients using acitretin, including xerosis in two patients and hyperlipidemia in seven patients. In one patient who developed xerosis, the dose was reduced from 20 mg to 10 mg. No new lesions were detected in the 5-month follow-up, and the other patient did not continue with the follow-up. In four patients who developed hyperlipidemia, the dose was reduced from 20 mg to 10 mg, and since the clinical response was maintained, treatment was continued. At the end of the treatment, remission was achieved in three of these patients. While two of the other three patients who developed hyperlipidemia did not continue

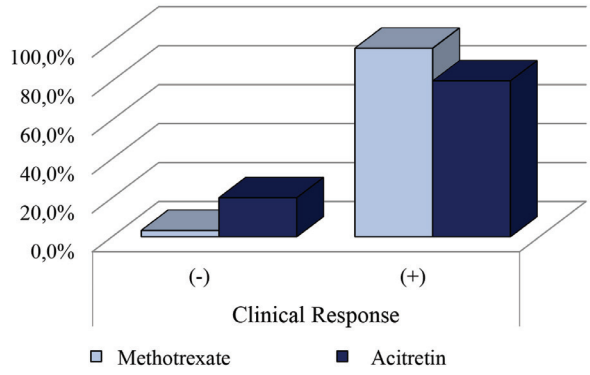


Figure 1. The clinical response rate in the methotrexate group was significantly higher than in the group receiving acitretin (p=0.037)

Table 1. Clinical and demographic characteristics of lichen planus patients

		Min.-Max.			Median	Mean ± SD			(n %)
Age (years)		23.0	-	72.0	50.0	49.4	±	12.0	
Gender	Female								47 (71.2%)
	Male								19 (28.8%)
Mucosal involvement	(-)								41 (62.1%)
	(+)								25 (37.9%)
Concomitant autoimmune disease	(-)								53 (80.3%)
	(+)								13 (19.7%)
Treatment	Acitretin								35 (53.0%)
	Methotrexate								31 (47.0%)
Accompanied phototherapy	(-)								59 (89.4%)
	(+)								7 (10.6%)
Systemic steroids	(-)								45 (68.2%)
	(+)								21 (31.8%)
Topical steroids	(-)					2		3.0%	2 (3.0%)
	(+)					64		97.0%	64 (97.0%)
Side effects	(-)								52 (78.8%)
	(+)								14 (21.2%)
Clinical response	(-)								8 (12.1%)
	(+)								58 (87.9%)
Clinical response duration (weeks)		4.0	-	36.0	12.0	14.1	±	7.3	
Disease duration (month)		2.0	-	120.0	12.0	22.1	±	24.1	
Min.: Minimum, Max.: Maximum, SD: Standard deviation									

follow-up, one patient was discontinued due to high lipid levels, and remission was achieved by switching to methotrexate. As a result, four patients (11.1%) using acitretin could not continue the treatment due to side effects. The clinical and demographic characteristics of patients using methotrexate and acitretin are summarized in Table 2.

When patients were classified by gender, the clinical response rate in female patients was 89.4%. The rate of female patients who achieved remission was 61.7%. In male patients, complete remission was achieved in all patients who achieved clinical response (84.2%). Data for female and male patients are summarized in Table 2.

Oral mucosa involvement accompanied cutaneous involvement in 25 patients (37.9%). The presence of oral mucosa involvement did not affect the response to treatment. Oral mucosa involvement was present in four of eight patients (50%) who did not respond to treatment.

We also analyzed demographic and clinical characteristics that may affect the clinical response levels to acitretin and methotrexate treatments. We found no significant effect of age, gender, presence of comorbidities, disease duration, or previous use of systemic steroids on the treatment response level (p>0.05), as presented in Table 3.

The most common comorbidity found in patients was hypertension. Autoimmune disease (hashimoto thyroiditis, Sjögren syndrome, rheumatoid arthritis) was found in 13 patients. The comorbidities of the patients are summarized in Table 4.

Discussion

The primary objective of LP treatment is symptom management. The choice of treatment should take the patient's comorbidities, the severity of the disease, and potential adverse effects of the medication into account[5]. The findings of our study showed that clinical response and remission rates were higher in patients using methotrexate than in patients using acitretin. In contrast, the rate of patients who

Table 2. Demographic and clinical characteristics of patients using acitretin and methotrexate

		Methotrexate group (n=31)		Acitretin group (n=35)		p
		I.Q-3.Q	Median	I.Q-3.Q	Median	
Age		41.0-60.0	50.0	41.0-58.0	48.0	0.681[t]
Mucosa	(-)	22 (71.0%)		19 (54.3%)		0.163[X²]
	(+)	9 (29.0%)		16 (45.7%)		
Accompanied phototherapy	(-)	31 (100.0%)		28 (80.0%)		**0.008[X²]**
	(+)	0 (0.0%)		7 (20.0%)		
	(+)	13 (41.9%)		8 (22.9%)		
Topical steroids	(-)	2 (6.5%)		0 (0.0%)		0.217[X²]
	(+)	29 (93.5%)		35 (100.0%)		
Side effects	(-)	26 (83.9%)		26 (74.3%)		0.342[X²]
	(+)	5 (16.1%)		9 (25.7%)		
Clinical response	(-)	1 (3.2%)		7 (20.0%)		**0.037[X²]**
	(+)	30 (96.8%)		28 (80.0%)		
Clinical response duration (weeks)		8.0-24.0	12.0	8.0-16.0	12.0	0.451[m]

[t]Independent sample t-test, [m]Mann-Whitney U test, [X²]Ki-kare test (Fisher's exact test)

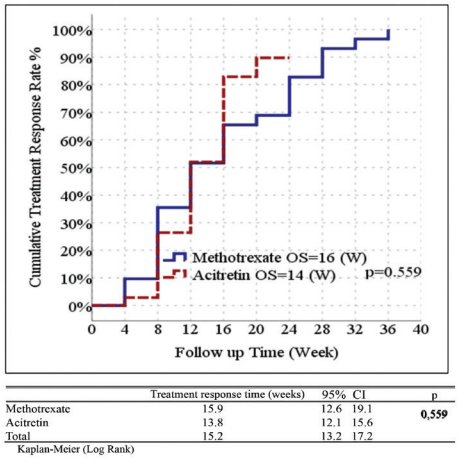
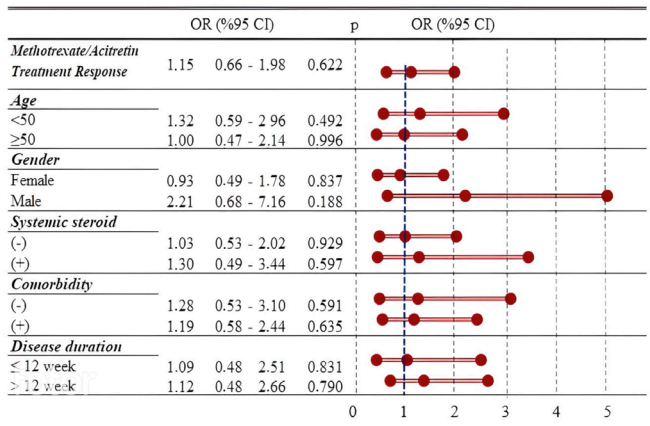


Figure 2. The Kaplan-Meier curve demonstrates the cumulative probability of clinical response in patients receiving methotrexate and acitretin

Table 3. The relationship between clinical response levels of acitretin and methotrexate treatments and demographic and clinical characteristics



OR: Odds ratio, CI: Confidence interval

Table 4. Comorbidities detected in lichen planus patients

Comorbidity	Frequency (n, %)
Hypertension	15 (22.7%)
Hashimoto's thyroiditis	10 (15.1%)
Coronary artery disease	7 (10.6%)
Hyperlipidemia	5 (7.6%)
Sjögren's syndrome	2 (3%)
Anxiety	2 (3%)
Depression	2 (3%)
Rheumatoid arthritis	1 (1.5%)
Hepatitis C	1 (1.5%)
Cervical intraepithelial neoplasia	1 (1.5%)

discontinued treatment due to side effects was lower.

A review of the current literature reveals that acitretin is among the first-line systemic treatments, although the evidence base is limited[1,5,8]. The first significant data on the use of acitretin in the treatment of LP were obtained from the multicenter placebo-controlled study by Laurberg et al.[9] The study, which included 65 patients, demonstrated that at the end of 8 weeks, the 30 mg/day acitretin group exhibited a significantly higher rate than the placebo group (64% and 13%, respectively). Acitretin, a synthetic retinoid, is used in the treatment of diseases such as psoriasis, palmoplantar pustulosis, LP, lamellar ichthyosis, and hidradenitis suppurativa with its antiproliferative, immunomodulatory, and anti-inflammatory activities. Common side effects include mucocutaneous dryness and elevated triglycerides. Teratogenicity and the need for long-term contraception make it inappropriate for women of childbearing age[10]. Due to limited data on the effectiveness of acitretin in real life and the existence of conditions that restrict its use, the search for alternative first-line treatments continues. There are no direct comparative studies of acitretin with methotrexate in the literature. In a retrospective study, cutaneous LP patients receiving different treatments were compared. Intramuscular triamcinolone, hydroxychloroquine, and methotrexate were reported as the most successful agents, with response rates of 79%, 61%, and 42%, respectively[11].

Methotrexate, an analog of folic acid, is used to treat a range of dermatological conditions such as psoriasis, atopic dermatitis, LP, vasculitis, connective tissue diseases, and lymphoproliferative disorders due to its antiproliferative and anti-inflammatory properties[12]. It is used subcutaneously or orally at low doses (5-25 mg weekly) for immune-mediated diseases[13]. Commonly reported side effects at low doses are nausea, anorexia, fatigue, and weakness, and they usually occur at the beginning of treatment. In general, severe side effects with low-dose methotrexate, such as hepatotoxicity, bone marrow suppression, and nephrotoxicity, are idiosyncratic and related to dosage errors or interactions with other drugs[12,13].

There are relatively few studies in the literature on the use of methotrexate in cutaneous LP[6,14-16]. A recent randomized controlled trial reported that 95% of patients responded to 7.5 mg/week of methotrexate, achieved complete remission in 55%, and no patients dropped out of treatment due to side effects. They found the mean time to achieve remission to be 10.17±2.33 weeks[7]. While the rate of patients achieving a clinical response was similar to our study, we believe that the slightly lower remission rate and the lack of side effects are related to taking lower doses of methotrexate. In the study by Turan et al.[16] from Türkiye, 11 patients were included in the study in which methotrexate was used at 15-20 mg/week, and complete remission was achieved in 10 patients (90.9%) in the fourth week, and treatment was discontinued in the other patient due to side effects. Kanwar and De[15] reported that they achieved complete remission in 58% of the patients at week 24 using methotrexate at a dose of 15 mg/week in their prospective study including 25 patients. In a study of 18 patients by Malekzad et al.[17], they reported clinical improvement in 25% of cases by the end of week 4 and in 75% of cases by the end of week 8 with methotrexate at a dose of 7.5 mg in 12 patients and 10 mg in 6 patients. In another study, patients treated with 7.5 mg/week methotrexate achieved clinical improvement in 20% of 20 patients at 4 weeks, 40% at 8 weeks, and 80% at 12 weeks[18]. While studies indicate that methotrexate dosage does not influence the time to achieve remission, this comparison is difficult due to the absence of disease severity scores for LP.

Methotrexate treatment was generally well tolerated in our study group, and only 6.1% of patients had to discontinue treatment due to side effects. In the study by Turan et al.[16], one in 11 patients was reported to have discontinued treatment after 4 weeks due to side effects[15]. Malekzad et al.[17] reported that laboratory findings deteriorated in two patients. More et al.[18] reported no side effects in 20 patients. Current literature data supports the findings of our study and indicates that methotrexate is a safe option for treating LP.

In our patient population and some studies, there is a noticeable predominance of females despite data indicating that gender distribution is insignificant in cutaneous LP[1,14,17]. A recent meta-analysis reported the prevalence of hepatitis C in LP patients as 9.42%, whereas it was detected in only 1.5% of our patients[18]. This outcome might have been impacted by the study's retrospective design and the fact that we only evaluated a limited number of participants.

In the current study, oral mucosa involvement accompanied cutaneous involvement in 37.9% of the patients. In patients with cutaneous LP, oral mucosa involvement may occur at rates as high as 75%[19]. This means that oral mucosal involvement should be considered in treating cutaneous LP for many individuals. There is data in the literature that both methotrexate and acitretin are effective in the treatment of oral LP. Two recent prospective studies have demonstrated that topical triamcinolone acetonide combined with methotrexate or acitretin is superior to topical monotherapy for oral LP[20,21]. Mucosal lesions of LP have a risk of transformation into squamous cell carcinoma (SCC) in 1 to 5% of patients, especially erosive ones. There is evidence that smoking and hepatitis C infection increase this risk, but there is no evidence of drug-related immunosuppression[19]. Methotrexate may treat head and neck SCCs at low doses, such as 15 mg/week, which varies from other immunosuppressive treatments[22]. However, rare case reports regarding possible associations of SCC with methotrexate necessitate careful treatment selection and follow-up in oral LP cases[23].

Study Limitations

Retrospective design and lack of assessment of disease severity with objective scoring systems are limitations of the study. The current literature shows no universally accepted clinical severity scoring system for LP. However, since the study population was selected only from

patients requiring systemic treatment, it can be assumed that they are in the moderate-severe disease group and have relatively similar severity. Additionally, the follow-up period in the study may not have been sufficient to assess the long-term prognosis of the disease entirely. Longer-term follow-up studies are necessary, particularly to determine recurrence rates. The study's strengths include using real-life data, including patients with various comorbidities, and the direct comparison of two prominent agents in the literature by comparing the effectiveness of acitretin and methotrexate in treating LP.

Conclusion

LP can affect many people of all ages and may occur with various comorbidities. Studies on individualized treatments are needed in LP treatment. In-depth knowledge of the available drugs is essential for selecting the right drug for the right patient. Our study demonstrated that methotrexate and acitretin, which have been used in different dermatological indications for many years, are highly effective in achieving remission in more than 60% of LP patients. These two agents are invaluable in that they provide physicians with effective alternatives based on patient-based factors such as existing comorbidities, the desire to have children, and the preference to use oral or injection drugs.

In subsequent research, creating validated severity scores to assess treatment response objectively and developing reliable treatment guidelines for clinicians in treatment selection using these scales should be a priority.

Ethics

Ethics Committee Approval: This study was approved by the Pamukkale University Non-Interventional Clinical Research Ethics Committee Local Ethics Committee (approval number: E-60116787-020-556309, date: 24.07.2024).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: Ö.S.K.B., Design: Ö.S.K.B., Data Collection or Processing: R.E., Analysis or Interpretation: Ö.S.K.B., R.E., Literature Search: Ö.S.K.B., R.E., Writing: Ö.S.K.B.

Conflict of Interest: The authors declared that they have no conflict of interest.

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References

1. Boch K, Langan EA, Kridin K, Zillikens D, Ludwig RJ, Bieber K: Lichen planus. Front Med (Lausanne). 2021;8:737813.
2. Leasure AC, Cohen JM: Prevalence of lichen planus in the United States: a cross-sectional study of the all of US research program. J Am Acad Dermatol. 2022;87:686-7.
3. Solimani F, Forchhammer S, Schloegl A, Ghoreschi K, Meier K: Lichen planus - a clinical guide. J Dtsch Dermatol Ges. 2021;19:864-82.
4. Vičić M, Hlača N, Kaštelan M, Brajac I, Sotošek V, Prpić Massari L: Comprehensive insight into lichen planus immunopathogenesis. Int J Mol Sci. 2023;24:3038.
5. Ioannides D, Vakirlis E, Kemeny L, et al.: European S1 guidelines on the management of lichen planus: a cooperation of the European Dermatology Forum with the European Academy of Dermatology and Venereology. J Eur Acad Dermatol Venereol. 2020;34:1403-14.
6. Gamal Alsakaan NA, Abd-Elsalam S, Fawzy MM, Elwan NM. Efficacy and safety of oral methotrexate versus oral mini pulse betamethasone therapy in the treatment of lichen planus: a comparative study. J Dermatolog Treat. 2022;33:3039-46.
7. Ujiie H, Rosmarin D, Schön MP, et al.: Unmet medical needs in chronic, non-communicable inflammatory skin diseases. Front Med (Lausanne). 2022;9:875492.
8. Atzmony L, Reiter O, Hodak E, Gdalevich M, Mimouni D: Treatments for cutaneous lichen planus: a systematic review and meta-analysis. Am J Clin Dermatol. 2016;17:11-22.
9. Laurberg G, Geiger JM, Hjorth N, et al.: Treatment of lichen planus with acitretin. A double-blind, placebo-controlled study in 65 patients. J Am Acad Dermatol. 1991;24:434-7.
10. Guenther LC, Kunynetz R, Lynde CW, et al.: Acitretin use in Dermatology. J Cutan Med Surg. 2017;21:2-12.
11. Hunt KM, Klager S, Kwak YJ, Sami N: Successful systemic treatment outcomes of lichen planus: a single-center retrospective review. Dermatol Ther. 2021;34:14903
12. Shen S, O'Brien T, Yap LM, Prince HM, McCormack CJ. The use of methotrexate in dermatology: a review. Australas J Dermatol. 2012;53:1-18.
13. Hajar T, Latour EJ, Haynes D, et al.: Low-dose methotrexate in dermatology: the utility of serological monitoring in a real-world cohort. J Dermatolog Treat. 2022;33:2161-67.
14. Bakhtiar R, Noor SM, Paracha MM: Effectiveness of oral methotrexate therapy versus systemic corticosteroid therapy in treatment of generalised lichen planus. J Coll Physicians Surg Pak. 2018;28:505-8.
15. Kanwar AJ, De D. Methotrexate for treatment of lichen planus: old drug, new indication. J Eur Acad Dermatol Venereol. 2013;27:410-3.
16. Turan H, Baskan EB, Tunali S, Yazici S, Saricaoglu H: Methotrexate for the treatment of generalized lichen planus. J Am Acad Dermatol. 2009;60:164-6.
17. Malekzad F, Saeedi M, Ayatollahi A: Low dose methotrexate for the treatment of generalized lichen planus. Iran J Dermatol. 2012;14:131-5.
18. More YE, Khatu SE, Chavan DC, Mahajan P, Pawar S, Gokhale N: Evaluation of safety and efficacy of low-dose methotrexate as an alternative treatment option to systemic corticosteroids in generalized lichen planus. Medical Journal of Dr. DY Patil University. 2017;10:149-55.
19. Daye M, Temiz SA, Isık B: The relationship between lichen planus and metabolic syndrome. J Cosmet Dermatol. 2021;20:2635-9.
20. García-Pola M, Rodríguez-Fonseca L, Suárez-Fernández C, Sanjuán-Pardavila R, Seoane-Romero J, Rodríguez-López S: Bidirectional association between lichen planus and hepatitis C-an update systematic review and meta-analysis. J Clin Med. 2023;12:5777.
21. Louisy A, Humbert E, Samimi M: Oral lichen planus: an update on diagnosis and management. Am J Clin Dermatol. 2024;25:35-53.
22. Chauhan P, De D, Handa S, Narang T, Saikia UN: A prospective observational study to compare efficacy of topical triamcinolone acetonide 0.1% oral paste, oral methotrexate, and a combination of topical triamcinolone acetonide 0.1% and oral methotrexate in moderate to severe oral lichen planus. Dermatol Ther. 2018;31.
23. Vinay K, Kumar S, Dev A, et al.: Oral Acitretin plus topical triamcinolone vs topical triamcinolone monotherapy in patients with symptomatic oral lichen planus: a randomized clinical trial. JAMA Dermatol. 2024;160:80-7.
24. Kamal MV, Rao M, Damerla RR, et al.: A Mechanistic review of methotrexate and celecoxib as a potential metronomic chemotherapy for oral squamous cell carcinoma. Cancer Invest. 2023;41:144-54.
25. Choudhary R, Singh A, Chhabra N, Gupta AK: Oral squamous cell carcinoma following acute methotrexate toxicity in a psoriasis patient: a causal association or mere co-incidence. Curr Drug Saf. 2023;18:580-3.