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Drug survival and safety profile of acitretin monotherapy in patients with psoriasis: A multicenter retrospective study

Asude Kara Polat[1] | Ilteris Oguz Topal[2] | Melek Aslan Kayıran[3] | Ayse Esra Koku Aksu[1] | Sema Aytekin[4] | Filiz Topaloglu Demir[5] | Tugba Ozkok Akbulut[6] | Ilknur Kıvanc Altunay[7] | Ezgi Ozkur[7] | Ayse Serap Karadag[8]

[1]Department of Dermatology, University of Health Sciences, Istanbul Training and Research Hospital, Istanbul, Turkey

[2]Department of Dermatology, Prof. Dr. Cemil Taşçıoğlu City Hospital, Istanbul, Turkey

[3]Department of Dermatology, Istanbul Medeniyet University, Göztepe Prof. Dr. Süleyman Yalçın City Hospital, Istanbul, Turkey

[4]Department of Dermatology, University of Health Sciences, Haydarpaşa Numune Training and Research Hospital, Istanbul, Turkey

[5]Department of Dermatology, Istanbul Medipol University, Faculty of Medicine, Istanbul, Turkey

[6]Department of Dermatology, University of Health Sciences, Haseki Training and Research Hospital, Istanbul, Turkey

[7]Department of Dermatology, University of Health Sciences, Şişli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey

[8]Department of Dermatology, Memorial Atasehir Hospital, Istanbul, Turkey

Correspondence
Asude Kara Polat, Department of Dermatology, University of Health Sciences, Istanbul Training and Research Hospital, Kasap İlyas Mah. Org. Abdurrahman Nafiz Gürman Cd. PK: 34098, Istanbul, Turkey.
Email: asudekara@yahoo.com.tr

Abstract

Acitretin is a nonimmunosuppresive systemic agent used in the treatment of psoriasis. Despite its frequent use, research on drug survival and adverse effects is limited. This study aims to evaluate drug survival, factors associated with survival, and adverse effects. Database of the six tertiary referral center for psoriasis patients treated with acitretin between November 2014 and April 2020 were retrospectively analyzed. Demographics of patients, adverse effects, and also drug survival were analyzed. Of 412 patients, 61.2% were male, and 38.8% were female. Common clinical adverse effects were cheilitis (71.4%), dry skin (62.5%), and palmoplantar skin peeling (37.2%). High triglyceride and high total cholesterol levels were observed in 50.0% and 49.5% of patients, respectively. Median survival time (95% confidence interval [CI]) was 18 (13.6-22.4) months. Statistically significant risk factors affecting drug discontinuation were having psoriatic arthritis, age under 65, and receiving previous systemic treatment. Drug survival rates were 56.6%, 25.9%, and 19.8% at 1, 5, and 8 years, respectively. Although mucocutaneous adverse effects of the acitretin were quite frequent, severe, life-treatining ones were infrequent. This old, relatively inexpensive and safe treatment remains a good alternative for the treatment of psoriasis.

KEYWORDS
acitretin, adverse effect, drug survival, psoriasis

1 | INTRODUCTION

Psoriasis is a chronic inflammatory disease with a frequency of 2% to 3% worldwide. Treatment differs according to severity. Systemic treatments are used in moderate and severe cases, including phototherapy and traditional and biological therapies.[1-3]

One of the conventional therapy recommended in guidelines for psoriasis treatment is a systemic retinoid.[4] The only systemic retinoid approved in the treatment of psoriasis in Turkey is acitretin, registered in 1995.[5] However, it has well-known potential adverse effects. These adverse effects may vary depending on the dose and duration of the drug with interindividual variations.[6] The most common adverse effect of acitretin is mucocutaneous. Other adverse effects are on the ophthalmological, neurological, musculoskeletal, gastrointestinal, and urogenital system. Acitretin may cause an increase in liver enzymes and lipid profiles.[2] There are still few studies in the literature evaluating the safety, drug survival, and adverse effects of acitretin treatment for psoriasis.[6-8] We aimed to investigate the adverse effects of acitretin, drug

survival, and factors associated with drug survival in psoriasis patients, designing a multicentered retrospective observational study.

2 | MATERIALS AND METHODS

We conducted a retrospective observational study on psoriasis patients (18 years and above), while using oral acitretin (Neotigason 10 mg capsules/Neotigason 25 mg capsules [Actavis production company]) or (Psöretin 10 mg capsules/Psöretin 25 mg capsules [Farma-Tek production company]) between November 2014 and November 2019. Data was collected from computer-based records from six different dermatology outpatient clinics. Ethics committee approval was received from the University Scientific Research and Publication Ethics Board before the study (approval number: 25/10/2019-2035). Sociodemographic characteristics of the patients (age, gender, smoking, alcohol use, psoriasis in the family, body mass index [BMI], and concomitant disorders) and the disease-related features (type of psoriasis, duration, the presence of psoriatic arthritis, and previous treatments) were recorded.

In addition, the drug-related features (duration of use), adverse effects (mucocutaneous, ophthalmological, neuropsychiatric, musculoskeletal, gastrointestinal, genitourinary, and others), and laboratory parameters, such as lipid profiles and transaminase levels, were evaluated. Hepatotoxicity was defined as either serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels higher than 1.5-fold, the upper limit of the reference range. The reasons for discontinuing acitretin therapy were classified as follows: no satisfactory response (≥50% PASI score improvement at 12 weeks [primary failure]); loss of initial response over time (secondary failure); and others (cost and physician's or patient's decision).

Also, the mean survival time, predictors of drug survival, and 8-year drug survival were assessed.

2.1 | Statistics

"SPSS 15.0 for Windows" (SPSS Inc., Chicago, Illinois) was used for statistical analysis. Descriptive statistics for categorical variables were given as numbers and percentages (mean, SD, minimum, and maximum) for numerical variables. The rates in the groups were analyzed by Chi-Square Test. Survival rates and durations were calculated using the Kaplan Meier analysis. Risk factors were analyzed by Cox Regression analysis. Statistical alpha significance level was accepted as $P < .05$.

3 | RESULTS

(a) Sociodemographic characteristics and disease-related features of the patients (Table 1): Of 412 patients, 160 (38.8%) were female and 252 (61.2%) were male. The mean age of the patients was 50.2 ± 14.8 years. The most common type of psoriasis was plaque (83.0%). One hundred thirty-nine of patients (33.7%) had never received conventional systemic therapy.

(b) The drug-related features and adverse effects: The mean duration of use of acitretin was 18.2 ± 22.9 (min to max = 1-192) months. While 236 (57.3%) patients used the drug for <12 months, 176 (42.7%) used the drug for more than 12 months.

Adverse effects were observed in 384 (93.2%) patients. The most common clinical adverse effect in our study was cheilitis (69.2%), followed by dry skin (58.3%) pruritus (35.4%) and palmoplantar skin peeling (34.7%). Erythema (22.3%), dermatitis, (14.1%), dry mouth (13.6%), sticky skin (8.3%), increased sweating (2.2%), hyperesthesia (3.2%), and paresthesia (1.5%) were observed as other mucocutaneous adverse effects. Nail disorders (10.9%), periungual pyogenic granuloma (1.9%), and paronychia (3.2%) were observed frequently, while hair loss was observed in 86 patients (20.9%) and deterioration in hair structure in 14 patients (3.4%). Hair structure deterioration was found to be significantly higher in women than in men ($P = .002$).

The most common ophthalmologic adverse effect was xerophthalmia. Myalgia, back pain, headache, arthralgia, and nausea were among the adverse effects of other systems. Adverse effects due to the drug are demonstrated in Table 2.

In patients with an acitretin use period more than 12 months, adverse effects were significantly higher than those who used for <12 months ($P = .018$).

Cheilitis, skin peeling, erythema, telogen effluvium, xerophthalmia, and arthralgia were significantly higher, while hyperesthesia was significantly lower ($P < .001$, $P = .030$, $P < .001$, $P = .008$, $P = .047$, $P < .001$, $P = .002$, and $P = .006$) in patiens receiving acitretin treatment longer than 12 months.

The adverse effects observed in terms of laboratory parameters are indicated in Table 3. In our study, the most common laboratory adverse effect due to acitretin was increased triglyceride levels. Among the observed adverse effects, increased triglyceride, total cholesterol, and LDL cholesterol levels were found to be statistically significantly higher in women than in men ($P = .011$, $P = .010$, and $P = .001$), but low HDL levels did not differ ($P = .720$).

Total cholesterol and LDL cholesterol levels were significantly higher in patients using acitretin for more than 12 months compared to those <12 months ($P = .005$ and $P = .007$). However, no significant difference was found between duration and increased triglyceride and decreased HDL cholesterol levels ($P = .292$ and $P = .397$).

Hepatotoxicity was observed in 12.9% of patients. There was no significant difference between hepatotoxicity, and gender and duration of the treatment ($P = .182$ and $P = .686$).

There was no significant correlation between the dose and the frequency of adverse effects ($P = .866$), difference between the type of psoriasis and the frequency of adverse effects ($P = 0{,}564$), and also PASI and the frequency of adverse effects. As PASI increased, the frequency of adverse effects decreased.

A significant difference was found in the frequency of adverse effects in women compared to men ($P < 0.001$) and in the frequency of adverse effects in alcohol abstainers and smokers ($P = .044$ and $P = .011$), and between the dose and the increased triglyceride levels ($P = .021$). There was no decrease in HDL cholesterol ($P = .892$) levels. We found a correlation between dose and increased total cholesterol

TABLE 1 Sociodemographic characteristics and disease-related features of the patients

Characteristics	Mean ± SD or n (%)
Age, years (mean ± SD)	50.2 ± 14.8
Gender	
Female	160 (38.8)
Male	252 (61.2)
Smoking habits	
Active smoker	221 (53.6)
Nonsmoker	166 (40.3)
Former-smoker	25 (6.1)
Alcohol habits	
Chronic alcohol use	48 (11.7)
BMI, (mean ± SD)	27.9 ± 8.6
BMI in details	
Underweight (BMI < 18.5)	7 (1.7)
Normal (BMI 18.5-24.9)	125 (30.3)
Overweight (BMI 25.0-29.9)	164 (39.8)
Obesity (BMI 30.0 and above)	116 (28.1)
Comorbidities	
Hyperlipidemia	129 (31.3)
Hypertension	96 (23.3)
Diabetes	88 (21.4)
Hepatosteatosis	58 (14.1)
Tyroid dysfunction	56 (13.6)
Metabolic syndrome	33 (8.0)
Depression	26 (6.3)
Others (breast cancer, lymphoma, bladder cancer, skin cancer, asthma, vitiligo, cerebrovascular disease, glaucoma)	27 (6.6)
Coronary heart disease	18 (4.4)
Type of psoriasis	
Plaque psoriasis	342 (83.0)
Generalized pustular psoriasis	26 (6.3)
Palmoplantar psoriasis	16 (3.9)
Guttate psoriasis	11 (2.7)
Palmoplantar pustular psoriasis	7 (1.7)
Invers psoriasis	7 (1.7)
Erythrodermic psoriasis	3 (0.7)
Psoriatic arthritis	62 (15.0)
Family history of psoriasis	145 (35.2)
Duration of disease (mean ± SD) (years)	16.2 ± 12.6
Previous treatments	
Topical therapies	139 (33.7)
Phototherapy	97 (23.5)
Methotrexate	63 (15.3)
Methotrexate + phototherapy	63 (15.3)
Cyclosporine	19 (4.6)
Methotrexate + cyclosporine	10 (2.4)
Cyclosporine + phototherapy	13 (3.2)
Methotrexate + cyclosporine + phototherapy	8 (1.9)

(Continues)

TABLE 2 The drug-related features and adverse effects that occur while using the drug

	N (%)
Duration of drug use (month; mean ± SD; Minimum–Maximum)	18.2 ± 22.9 (1–192)
Number of patients reported one or more adverse event	384 (93.2)
Mucocutaneous adverse effects	
Dermatologic effects	
Skin	
Dry skin	240 (58.3%)
Pruritus	146 (35.4%)
Palmoplantar skin peeling	143 (34.7%)
Eryhtema	92 (22.3)
Dermatitis	58 (14.1)
Sticky skin	34 (8.3%)
Hyperesthesia	13 (3.2%)
Increased sweating	9 (2.2%)
Paresthesia	6 (1.5%)
Photosensitivity	6 (1.5%)
Hair	
Alopecia	86 (20.9%)
Deterioration in hair structure	14 (3.4%)
Nail	
Nail changes	45 (10.9%)
Onycholysis	38 (9.2%)
Paronychia	13 (3.2%)
Periungual pyogenic granuloma	8 (1.9%)
Oral	
Cheilitis	285 (69.2%)
Dry mouth	56 (13.6%)
Nose	
Epistaxis	20 (4.9%)
Rhinitis	4 (1.0%)
Ophthalmological findings	
Xerophthalmia	62 (15.0%)
Visual problems	10 (2.4%)
Blepharitis	4 (1.0%)
Pseudotumor cerebri	2 (0.5%)

(Continues)

TABLE 2 (Continued)

	N (%)
Neuropsychiatric	
Headache	29 (7.0%)
Depression	17 (4.1%)
Agitation	4 (1.0%)
Amnesia	2 (0.5%)
Musculoskeletal system	
Myalgia	74 (18.0%)
Back pain	40 (9.7%)
Arthralgia	30 (7.3%)
Gastrointestinal manifestations	
Nausea	27 (6.6%)
Constipation	10 (2.4%)
Rectal bleeding	6 (1.5%)
Pancreatitis	1 (0.2%)
Gastritis	2 (0.5%)
Genitourinary system manifestations	
Vaginal dryness[a]	11 (6.9%)
Hypertrichosis[a]	1 (0.6%)
Vulvovaginal candidiasis[a]	1 (0.6%)
Penil bleeding[b]	1 (0.4%)
Sexual dysfunction	4 (1.0%)
Others	
Weight gain	23 (5.6%)
Fatigue	13 (3.1%9
Weight loss	9 (2.2%)
Unusual thirst	3 (0.7%)
Urticaria	1 (0.2%)
Maculopapular drug eruption	1 (0.2%)

[a]Adverse effects in female population (n = 160).
[b]Adverse effect in male population (n = 252).

TABLE 3 Laboratory changes in the use of acitretin

	N (%)
Increased triglycerides levels	206 (50.0%)
Increased total cholesterol levels	204 (49.5%)
Increased LDL cholesterol levels	195 (47.3%)
Decreased HDL cholesterol levels	123 (29.9%)
Increased transaminases levels	53 (12.9%)
Increased uric acid levels	8 (1.9%)

and increased LDL (*P* = .011 and *P* = .043). There was no significant difference in dose and hepatotoxicity (*P* = .105).

(c) Drug Survival: Median survival time (95% confidence interval [CI] min-max) was 18 (13.6-22.4) months (Figure 1). The drug was discontinued in 227 patients. In 185, treatment continued uninterrupted. Drug survival rates were 56.6%, 25.9%, and 19.8% at 1, 5, and 8 years, respectively (Table 4). In our study, patients stopped their

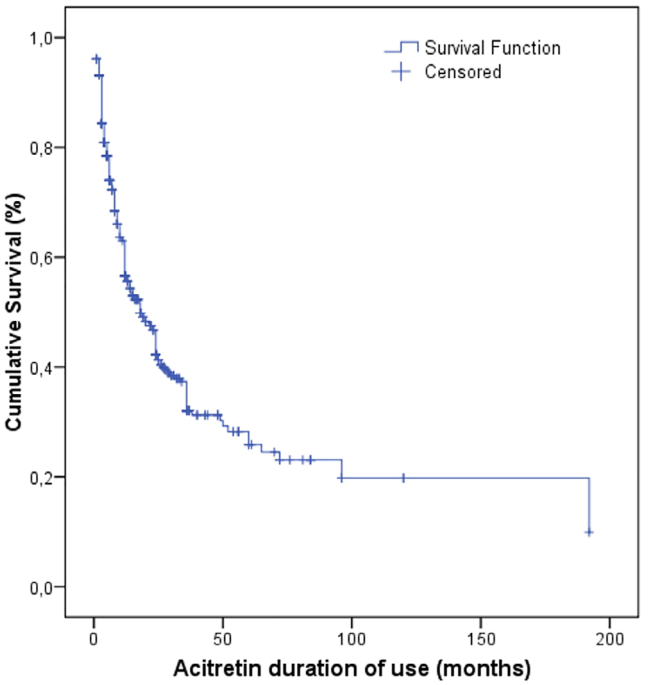

FIGURE 1 Drug survival chart

TABLE 4 Drug survival rates

N = 412	
Median for survival time (95 CI)	18 (13.6–22.4)
Drug survival rate	%
1 years	56.6 (SE:2.6)
2 years	42.2 (SE:2.8)
3 years	32.1 (SE:3.0)
5 years	25.9 (SE:3.3)
8 years	19.8 (SE:4.3)

TABLE 5 Reasons for treatment cessations

Reasons	n	% of all patients
Primary failure	44	10.7
Secondary failure	62	15.0
Psoriatic arthritis	*47*	*11.4*
Adverse events	69	16.7
Patients' wish	40	9.7
Cost	9	2.2
Exacerbation	1	0.2
Others (remission, family planning)	2	0.5

treatment mostly due to adverse events (16.7%, n = 69) (Table 5). The factors affecting drug discontinuation were examined with univariated analysis; being under the age of 65 (*P* = .036, and HR or OR = 1.50 [95% CI: 1.03-2.19]), having psoriatic arthritis (*P* = .001, and HR or OR = 1.72 [95% CI: 1.25-2.37]), and receiving previous systemic

treatment ($P < .001$, and HR or OR = 1.73 [95% CI: 1.28-2.33] were determined as significant risk factors. When we examined with a multivariate analysis, factors affecting drug discontinuation were as follows: being under the age of 65 ($P = .025$, and HR or OR = 1.57 [95% CI: 1.06-2.32]), having psoriatic arthritis ($P = .007$, and HR or OR = 1.60 [95% CI: 1.14-2.26]), and receiving previous systemic treatment ($P < .001$, and HR or OR = 1.89 [95% CI: 1.35-2.64]) (Table 6).

4 | DISCUSSION

Acitretin is a retinoid derivate that is used safely at low doses, with adverse effects at high doses (>25 mg/day) for psoriasis treatment.[9]

Almost all patients experience adverse effects; the most common adverse effect of acitretin is mucocutaneous, such as dryness of the skin and mucous membranes.[3,4,10,11] Among them, the most common adverse effect, cheilitis, is especially dose-dependent, observed in between 10.9% and 75%.[12-15] In our study, all patients received acitretin treatment at a dose of 10 to 50 mg/day. The most common adverse effect was cheilitis (69.2%), which is similar in the literature. The frequency of palmoplantar skin peeling (34.7%) was similar in our study, whereas dry skin (58.3%) was higher than the literature (15-25%).[15] In another study the most common adverse effect was dry mouth, at 27.9%, which was higher than our study (13.6%).[16] The less frequent adverse effect was increase in sweating, which was observed with a frequency of 2.2% in our study.[11] The frequency of sticky skin was reported at 10% to 25% in the literature and was found to be higher (8.3%) in our study.[8,17,18] Nose bleeding is another mucocutaneous adverse effect.[12] In our study, epistaxis was detected in 4.9%.

TABLE 6 Factors affecting drug discontinuation

	Discontinuated		Univariate		Multivariate	
	n (%)	Estimate Survival Median Time	HR (95% CI)	*P*	HR (95% CI)	*P*
Age						
<65 years	196/343 (57.1)	16 (2.2)	1.50 (1.03–2.19)	.036	1.57 (1.06–2.32)	.025
≥65 years	31/69 (44.9)	29 (8.7)	1			
Gender						
Female	95/160 (59.4)	14 (2.2)	1.24 (0.95-1.61)	.119	1.20 (0.91-1.58)	.207
Male	132/252 (52.4)	24 (2.5)	1			
GPP						
No	210/386 (54.4)	19 (2.4)	1	.266		.101
Yes	17/26 (65.4)	15 (4.1)	1.32 (0.81-2.18)		1.54 (0.92-2.59)	
Psoriatic arthritis						
No	180/350 (51.4)	23 (2.3)	1	.001		.007
Yes	47/62 (75.8)	10 (1.6)	1.72 (1.25–2.37)		1.60 (1.14–2.26)	
Obesity						
No	163/296 (55.1)	20 (2.3)	1.02 (0.76-1.36)	.900	1.14 (0.82-1.57)	.434
Yes	64/116 (55.2)	12 (4.6)	1			
Metabolic syndrome						
No	193/354 (54.5)	18 (2.3)	1	.788		.945
Yes	34/58 (58.6)	16 (7.1)	1.15 (0.73-1.51)		1.01 (0.67-1.53)	
Hepatosteatosis						
No	197/356 (55.3)	19 (2.2)	1.06 (0.72-1.56)	.754	1.13 (0.75-1.72)	.559
Yes	30/56 (53.6)	12 (7.2)	1			
Previous treatments						
Topical	60/139 (43.2)	36 (12)	1	<.001		<.001
Systemic	167/273 (61.2)	12 (1.6)	1.73 (1.28–2.33)		1.89 (1.35–2.64)	
Number of treatments[a]						
<2	165/307 (53.7)	20 (2.3)	1	.376		.152
≥2	62/105 (59.0)	13 (2.9)	1.14 (0.85-1.53)		0.79 (0.57-1.09)	

Note: Cox regression analysis.
Abbreviation: GPP, generalized pustular psoriasis.
[a]Not included in the multivariate analysis.

Hair and nail changes are also seen with acitretin treatment.[10,19] Hair loss is again a dose-dependent adverse effect, especially shortly after the initiation of treatment.[10] In various clinical studies, it has been reported with different frequencies, such as 2.9%, 13%, 10% to 25%, and 50% to 75%.[13-18] In our study, alopecia was observed in 20.9% (n = 86). Nail adverse effects, paronychia, periungual pyogenic granulomas, nail fragility, and other nail changes could be observed. In our study, 10.9% of patients had nail disorders. Unlike the literature, in our study paronychia was found to be higher, with a frequency of 3.2%.[16]

Other cutaneous adverse effects due to acitretin are hyperesthesia and paresthesia, which is rare. In the study of Murray et al,[8] they detected hyperesthesia in four patients (6%). In our study, hyperesthesia (3.2%) and paresthesia (1.5%) were observed with a low frequency compared to the literature.[8,17,18]

When evaluated in terms of ophthalmological adverse effects, in our study, xerophthalmia, also considered a mucous adverse effect, was found to be higher with a frequency of 15.0% (n = 62) compared to the study of Borghi et al[13] (n = 2, 10.9%). Also, visual problems, blepharitis, and pseudotumor cerebri were observed at 2.4%, 1.0%, and 0.5%, respectively. Pseudotumor cerebri may occur rarely with systemic retinoids such as acitretin.[20] This effect is generally seen in patients using concomitant tetracycline. We observed pseudotumor cerebri in two patients.

Neuropsychiatric adverse effects can occur with acitretin: headache, polyneuropathy, thrombotic stroke, and depression.[21-23] Depression is a relevant entity. For patients' safety, the Food and Drug Administration (FDA) packaged inserts warning about depression/suicide with acitretin.[23] When the literature is examined, there is no convincing suicide case associated with acitretin treatment. Depression while using acitretin was reported in three patients (5%) in the study of Murray et al and one patient (2.2%) in Borghi et al.[8,13] In our study, depression was detected in 17 patients, and this rate (4.1%) was similar to the range reported in the literature.

Headache, one of the neurological adverse effects of acitretin, may appear.[12] In our study, headache was observed with a frequency of 7.0%. Chroni et al reported cases with sensorimotor polyneuropathy after chronic 1-month and 3-month oral acitretin treatment in plaque psoriasis.[22,24] Polyneuropathy was not detected in our study.

Musculoskeletal system adverse effects, such as myalgia and arthralgia, can be observed with acitretin treatment.[9] Also, tendonitis, back pain, diffused interstitial skeletal hyperostosis (DISH), or osteoporosis may occur.[15] Chularojanamontri et al reported myalgia as 1% and Borghi et al 4.4% (n = 2) in patients using acitretin.[13,16] Murray et al[8] detected arthralgia and back pain in four patients (6%), too. In our study, myalgia (18.0%), arthralgia (7.3%), and back pain (9.7%) rates were found to be high compared to the literature.[8,13,16] However, tendonitis was not seen in our study.

One of the gastrointestinal manifestations with this drug is nausea. Cave et al[25] found that nausea was 1.7% in the pediatric population, whereas this rate was found to be high at 6.6% in our study. The other is pancreatitis, a rare adverse effect associated with acitretin.[26] In our study, pancreatitis was observed in 0.2% of patients.

Fatigue is another adverse effect of acitretin. In a study by Borghi et al[13] in 46 patients, fatigue was detected in 10.6%. In our study, fatigue was observed in 3.1%, which is lower when compared to the literature.

Laboratory manifestations with the use of acitretin were common, such as increased liver enzyme levels and idiosyncratic hepatotoxic reaction. Severe hepatotoxic reactions are less common. Roenigk et al[27] evaluated liver biopsies of patients with psoriasis who received acitretin before and after, which showed no change in 49 patients (59%) and worsening in 14 (17%). Of these 14 psoriasis patients, most changes were mild in biopsies. Borghi et al[13] reported an increase in transaminases in one patient (2.2%). In our study, increased transaminase levels were detected with a frequency of 12.9% (n = 53).

With retinoid therapy, serum lipid profiles may change in patients. Increase in serum triglyceride and cholesterol levels may be the most common abnormal laboratory parameters due to acitretin treatment, according to Gupta et al.[14,17] In a study of 525 patients who received acitretin treatment at 10 to 75 mg/day doses, 66% of them had increased triglyceride and 33% of them had increased total cholesterol levels. HDL levels decreased in approximately 40% of patients.[17,18] Hyperlipidemia was seen 8.7% of patients during the treatment of acitretin, according to Borghi et al.[13] Hypercholesterolemia, hypertriglyceridemia, and hepatitis were seen 27.3%, 18.9%, and 9.6% of patients, respectively, in Chularojanamontri et al's study. In those using acitretin treatment more than 1 year, these rates changed: hypercholesterolemia (33.8%) and hypertriglyceridemia (22.4%).[16] In our study, increased triglyceride levels were seen in 50.0% of patients, which was higher than Chularojanamontri et al.[16] Besides, increased total cholesterol levels was also seen in 49.5% of patients in our study. Karadağ et al[28] observed an increase in total cholesterol and triglyceride levels after acitretin treatment.

Drug survival is critical in chronic diseases such as psoriasis. In a study conducted with psoriasis patients, it was evaluated that the rate of drug survival with biological treatments was higher than conventional treatments. The highest drug survival in these patients has been reported with ustekinumab. It has been observed that most patients quit the treatment of acitretin and cyclosporine.[29] In another study, drug survival levels of acitretin and methotrexate were compared, and no significant difference was found between them.[30] In our study, the median survival time (95% CI min-max) was 18 (13.6-22.4) months, which is similar in Shalom et al's study.[30]

The studies conducted by Shalom et al, Arnold et al, Davila-Seijo et al, and Chularojanamontri et al showed 1-year acitretin survival rates of 55.7%, 37%, 42.3%, and 79%.[16,29-31] The 5-year survival rates were approximately 20%.[29-31] However, in Chularojanamontri et al's[16] study the 5-year survival rate was 53.5%. In our study, survival rates were 56.6% and 25.9% at 1 and 5 years, respectively.

Drug discontinuation is an important problem in psoriatic patients. In the studies conducted, it is determined that the patients stop the treatment due to side effects, ineffectiveness, cost, etc.

There are few studies on this issue related to acitretin.[16,29,30] In our study, patients commonly stopped their treatment because of adverse effects. Secondary failure, primer failure, patients' wish, cost, exacerbation, and other reasons (remission, or family planning) were other reasons. In Chularojanamontri et al's study, 11.5% of patients cessated their treatment because of remission, with 8.7% because of adverse events. In another study, 34.9% of patients stopped their treatment because of inefficacy.[16,29] As factors affecting drug discontinuation, in our study, similar to Shalom et al's study, psoriatic arthritis was observed as a significant risk factor. Again, in our study, being under the age of 65 and using systemic treatment before was determined as a risk factor in drug discontinuation, which is different from Chularojanamontri et al.[16] Obesity, metabolic syndrome, presence of pustular psoriasis, and the number of systemic treatments more than two were not considered as risk factors in our study, similar to the study of Chularojanamontri et al.[16]

5 | LIMITATIONS

Although our study is a multicenter study, there are some limitations.

1. Retrospective design of the study.
2. Limitation in accessing detailed data.

6 | CONCLUSION

Our study is a multicenter study to evaluate the adverse effects related to acitretin and drug survival. Like the literature, the most common adverse effects were mucocutaneous effects, especially cheilitis, dry skin, palmoplantar skin peeling, and alopecia. Hyperlipidemia and hepatotoxicity were also observed in high rates, consistent with the literature, but did not require discontinuation of treatment. Unlike the literature, urticaria, maculopapular drug eruption, penile bleeding, and vulvovaginal candidiasis were also observed in our study. Since psoriasis is a chronic disease, treatments are used for a long time. There is limited data related to drug survival rate in acitretin treatment, which is an important and safe alternative due to its non-immunosuppressive and protective effect against malignancy. In our study, approximately half of the patients could continue with the drug in the first year. This rate gradually decreased in a 5-year follow-up. The most important factors affecting this were psoriatic arthritis, age, and previous systemic treatments. These factors can be taken into consideration while choosing the psoriasis treatment. In today's costly and highly effective biological era, this drug appears systemically safe, excluding the risk of teratogenicity. Acitretin is also protective against malignancy and does not predispose to infection; it is a powerful alternative. Informing patients about common mucocutaneous adverse effects and taking preventive measures will increase compliance. Also, with appropriate patient selection and laboratory monitoring, drug survival can increase.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Conception: Asude Kara Polat, Ilknur Kıvanc Altunay, Ayse Serap Karadag. Design: Asude Kara Polat; Ilknur Kıvanc Altunay, Ayse Serap Karadag. Supervision: Asude Kara Polat; Ilteris Oguz Topal, Ayse Esra Koku Aksu, Filiz Topaloglu Demir; Ilknur Kıvanc Altunay, Ayse Serap Karadag. Data collection and/or processing: Asude Kara Polat; Ilteris Oguz Topal; Melek Aslan Kayıran; Sema Aytekin; Filiz Topaloglu Demir; Tugba Ozkok Akbulut; Ezgi Ozkur; Ayse Serap Karadag. Analysis and/or interpretation: Asude Kara Polat; Ilteris Oguz Topal; Ayse Esra Koku Aksu; Filiz Topaloglu Demir; Ilknur Kıvanc Altunay; Ezgi Ozkur; Ayse Serap Karadag. Literature review: Asude Kara Polat; Melek Aslan Kayıran; Ayse Esra Koku Aksu; Ilknur Kıvanc Altunay; Ezgi Ozkur; Ayse Serap Karadag. Writing: Asude Kara Polat, Ilknur Kıvanc Altunay; Ezgi Ozkur; Ayse Serap Karadag. Critical review: Asude Kara Polat; Ilteris Oguz Topal; Melek Aslan Kayıran; Ayse Esra Koku Aksu; Sema Aytekin; Filiz Topaloglu Demir; Tugba Ozkok Akbulut; Ilknur Kıvanc Altunay; Ezgi Ozkur; Ayse Serap Karadag.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Asude Kara Polat https://orcid.org/0000-0002-5040-6901
Ilteris Oguz Topal https://orcid.org/0000-0001-8735-9806
Melek Aslan Kayıran https://orcid.org/0000-0003-4347-3134
Ayse Esra Koku Aksu https://orcid.org/0000-0002-3457-1958
Sema Aytekin https://orcid.org/0000-0003-1376-1573
Filiz Topaloglu Demir https://orcid.org/0000-0002-2049-1316
Tugba Ozkok Akbulut https://orcid.org/0000-0001-9995-2543
Ilknur Kıvanc Altunay https://orcid.org/0000-0002-1354-7123
Ezgi Ozkur https://orcid.org/0000-0002-9136-7021
Ayse Serap Karadag https://orcid.org/0000-0003-4333-8274

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