Research Article (Araştırma Makalesi)

Evaluation of The Effects and Side Effects of Topical Clobetasol 0.05% and Topical Anthralin Treatment in Alopecia Areata with Phototricogram

Alopesi Areata'da Fototrikogram ile Topikal Klobetasol 0.05% ve Topikal Antralin Tedavisinin Etki ve Yan Etkisinin Takibi

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Özet

Amaç: Alopesia areata (AA) skarsız saç kaybıyla karakterize kronik inflamatuar bir hastalıktır. AA'lı hastalara uygulanan topikal anthralin ve topikal klobetasol propiyonat tedavisinin etki ve yan etkilerini fototikogramla araştırmayı amaçladık.

Gereç ve yöntemler: Alopesia areata'lı 40 hasta çalışmaya alındı ve randomize olarak iki gruba ayrıldı. 20 hasta topikal % 0.05 klobetasol 17 propionat losyon, 20 hasta topikal antralin tedavisi kullandı. Tedavi öncesi ve sonrası değerlendirme fototrikogram ile yapıldı.

Bulgular: Üç ay sonunda tedavi yanıtı değerlendirildiğinde, klobetasol 17-propiyonat %0,05 uygulanan hastaların 7'sinde (%35) yetersiz yanıt, 8'inde (%40) kısmi yanıt, 5'inde (%25) kozmetik yanıt olduğu görüldü. Lokal antralin grubundaki hastaların 4'ünde (%20) yetersiz yanıt, 8'inde (%40) kısmi yanıt, 8'inde (%40) kozmetik yanıt gözlendi. Lokal antralin grubunda kozmetik yanıt oranı daha yüksek olmasına rağmen anlamlı fark yoktu (p=0,470). Topikal antralin grubunda tedaviye yanıt vermeyen hasta oranı daha düşüktü ancak anlamlı fark saptanmadı (p<0,05). Tedavisi 6 ay boyunca değişmeyen hastalarda lokal klobetasol 17-propiyonat %0,05 alan 13 (%65) hastanın 6'sında (%46,1) ve 10 (%62,5) hastada kozmetik yanıt gözlendi. Lokal antralin alan 16 (%80) hastada gruplar arasında anlamlı fark saptanmadı (p=0,379). Lokal klobetasol 17-propiyonat %0,05 tedavisine yanıt vermeyen ve antralin tedavisine geçen hastalarda tedavi başarısı, tedavi değişikliği yapılan diğer hastalara göre istatistiksel olarak anlamlı derecede yüksekti (p=0,026). Öte yandan 6 aylık süre sonunda her iki ilacın da mm2 başına saç kökü sayısı (NH), saç yoğunluğu (HD), anagen oranı (AR) ve telojen oranı (TR) artışına anlamlı bir etkisinin olmadığı ortaya çıktı (p=0,148).

Sonuç: Topikal klobetasol 17 propiyonat %0,05 losyon ve topikal antralin tedavisi, yama tarzı AA tedavisinin güvenli ve etkili bir şeklidir. Her iki ilaç karşılaştırıldığında topikal klobetasol 17 propiyonat %0,05 losyona yanıt vermeyen hastalarda topikal antralin tedavisine geçildiğinde tedavi başarısının istatistiksel olarak üstün olduğu görüldü. Çalışmamızın sonuçları ve literatür taramaları bu iki ilacın etkinliği açısından daha geniş hasta serileri ile çalışmaların gerekliliğini göstermektedir.

Anahtar kelimeler: Alopesia areata, topikal anthralin, topikal klobetasol, fototrikogram

Abstract

Objective: Alopecia areata (AA) is a chronic inflammatory disease characterized by non-scarring hair loss. In this study, we aimed to investigate the effects and side effects of topical anthralin and topical clobetasol propionate treatment in patients with AA using a phototrichogram.

Material and methods: The study included 40 patients with AA who were randomly divided into two groups: topical anthralin (n=20) and clobetasol 17-propionate 0.05% (n=20). Phototrichogram values were assessed before and after treatment.

Results: An evaluation of treatment response at the end of three months indicated inadequate response in 7 (35%), partial response in 8 (40%), and cosmetic response in 5 (25%) of the patients in the clobetasol 17-propionate 0.05% group as opposed to inadequate response in 4 (20%), partial response in 8 (40%), and cosmetic response in 8 (40%) of the patients in the local anthralin group. Although the cosmetic response rate was higher in the local anthralin group, there was no significant difference (p=0.470). The rate of patients unresponsive to treatment was lower in the topical anthralin group, while no significant difference was established (p<0.05). In patients whose treatment was not changed throughout the 6 months, cosmetic response was observed in 6 (46.1%) out of 13 (65%) patients who received local clobetasol 17-propionate 0.05% and in 10 (62.5%) out of 16 (80%) patients who received local anthralin and no significant difference was found between the groups (p=0.379). Statistically, treatment success was significantly higher in patients who did not respond to local clobetasol 17-propionate 0.05% treatment and were converted to anthralin treatment than those who underwent a treatment change (p=0.026). On the other hand, at the end of the 6 months, it was revealed that both drugs had no significant effect on the increase in the number of hair follicles per mm2 (NH), hair density (HD), anagen rate (AR), and telogen rate (TR) values (p=0.148).

Conclusion: Topical clobetasol 17 propionate 0.05% lotion and topical anthralin treatment is a safe and effective form of patchy AA treatment. When both drugs were compared, treatment success was statistically superior when switched to topical anthralin treatment in patients who did not respond to topical clobetasol 17 propionate 0.05% lotion. The results of our study and literature reviews indicate the necessity of studies with larger patient series in terms of the effectiveness of these two drugs.

Keywords: Alopecia areata, topical anthralin, topical clobetasol, phototricogram

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INTRODUCTION

Alopecia areata (AA) is an organ-specific autoimmune disease characterized by progressive, non-scarring hair loss, affecting both genders equally. Although environmental factors and genetic predisposition are considered to be effective in the onset of the disease, its exact etiology remains unknown. AA is a T cell-mediated autoimmune phenomenon that may affect all hair follicles. Factors affecting the response of the disease to treatment include age of onset, diffuseness of hair loss, family history, and presence of comorbidities, ophiasis, and atopy. All the treatments given to AA patients control the disease and provide a palliative effect. In contrast, all the local treatments of AA have no systemic effect on the disease and have a limited effect on the disease area (1-4).

Phototrichogram has become popular as a noninvasive method in the differential diagnosis of hair diseases, allowing for differentiation of vellus and terminal hair, assessment of hair density, easy calculation of the anagen-to-telogen ratio, and detection of drug-related side effects (5). Topical and intralesional steroids and topical immunotherapy are recommended as the first choice therapies in the treatment of mild and moderate AA in numerous evidence-based and consensus-based guidelines (6-8). Studies conducted on topical clobetasol propionate have suggested this drug as an effective treatment for AA (9,10). Likewise, anthralin was proposed as a viable option for the treatment of AA after the discovery of its effect on local irritant dermatitis in 1979. Moreover, despite its local side effects, this drug is used locally in the treatment of AA (11-13).

In this study, we compared the effects and side effects of topical anthralin and clobetasol 17-propionate 0.05% in patients with AA, using phototrichogram.

MATERIALS AND METHODS

The study designed as experimental. 40 patients with multilocular AA were included in the study. Clobetasol 17-propionate 0.05% was used by 20 patients (Group I) and anthralin was used by 20 patients (Group II). Patients were selected from among those who had no history of topical or systemic treatment, regardless of age and disease duration. Patients with alopecia totalis (AT) and alopecia universalis (AU) were not included in the study. In all patients, presence of atrophy was investigated by clinical examination. All the patients applied their treatments at home. Prior to the treatment, the initial phototrichogram of the alopecia area (round, bald patch on the scalp) was obtained with Grimed Microsoft WDM Image Capture (Win 32) and Scalar USB microscope M2 macrolens of the dermatoscope. For phototrichogram imaging, using a patch punched out into 1-cm by 1-cm squares at a thickness of 1 mm, the hair follicles were cut 1 mm above the skin, dyed with a dye within three days, made to rest for 12 minutes, and then cleaned with an alcohol-containing substance and photographed. After the initiation of the treatment, both patient groups were evaluated in terms of increase in parameters including number of hair follicles per mm^2 (NH), hair density (HD), anagen rate (AR), and telogen rate (TR) at month 3 and 6. The treatment response was classified as inadequate (absence of change along with persistence of alopecic patch, growth of vellus hair alone, or presence of sparse, sporadic pigmented or non-pigmented hair), partial (terminal hair growth of less than 75% in the alopecia area), and cosmetic (terminal hair growth of more than 75% in the alopecia area).

Based on these phototrichogram images, the effects and side effects of drugs (itching, erythema, discoloration, burning for anthralin); (papules, pustules telangiectasia and atrophy for clobetasol 17-propionate [0.05%]) were evaluated for each patient.

Clobetasol 17-propionate applied both in the morning and evening to the patients whose skin involvement area less than 20%. Anthralin 0.5% in petrolatum was applied an average amount of 0.5-1 fingertip units (FTUs) onto the alopecia area so as to form a layer on the area and then to wait for 20 minutes before washing the area with plenty of water, with the total application time limited to 120 min. The patients' treatment responses were evaluated at the end of 3 months.

In patients using anthralin, the concentration was increased to 1% after observing partial and cosmetic response to topical anthralin 0.5% for another 3 months. If partial or cosmetic response was achieved in patients using topical clobetasol 17-propionate 0.05%, this treatment was applied for another 3 months.

At the end of 3 months, the treatment was changed in the patients with inadequate response. In patients using anthralin treatment was converted to clobetasol 17-propionate. In the other group clobetasol 17-propionate was converted to anthralin 0.5% for 3 months. We evaluated side effects of antralin and clobetasol 17-propionate during the treatment.

Statistical Analysis

Data were analyzed using SPSS for Windows version 13.0 (SPSS Inc., Chicago, IL, USA). Descriptives were expressed as mean ± standard deviation (SD). In the comparison of continuous variables, t-test was used for data with normal distribution and Mann-Whitney U test was used for data with nonnormal distribution.

Categorical variables were compared using Pearson's Chi-squared test. Phototrichogram values obtained at month 3 and 6 were compared using Wilcoxon signed-rank test and the changes between these two time points were evaluated using univariate covariance analysis. A p value of <0.05 was considered significant.

Our study was reviewed according to the "Helsinki Declaration" and "Good clinical practice guideline" and was prepared "duly" according to the guideline. Ethics committee approval was granted from Selçuk University Meram Faculty of Medicine Ethics Committee (Decision no: No: 2007/070; date: 02/05/2007).

RESULTS

The study included 40 patients who completed the treatment and follow-up periods. The results indicated no significant difference between the two groups with regard to age and gender and disease duration. No significant difference was found between the two disease duration means, according to the paired sample t test results (t:-.831;df:19; p>0.000). Demographic characteristics of the patients are shown in **Table 1**.

An evaluation of treatment response at the end of three months indicated inadequate response in 7 (35%), partial response in 8 (40%), and cosmetic response in 5 (25%) of the patients in the clobetasol 17-propionate 0.05% group as opposed to inadequate response in 4 (20%), partial response in 8 (40%), and cosmetic response in 8 (40%) of the patients in the local anthralin group. Based on the findings, it was observed that the local anthralin group exhibited a higher rate of cosmetic response. In contrast, the topical anthralin group exhibited a lower rate of inadequate response compared to the other group. However, the partial response rate was similar in both groups. Nevertheless, there was no statistically significant difference observed between the treatment types and the patients' responses to these treatments (p>0.05, Chi-Square =1.510; df.=2).

Table 2 presents the four parameters assessed before the treatment and at three months of the treatment in both groups, including number of hair follicles per mm^2 (NH), hair density (HD), anagen rate (AR), and telogen rate (TR). In both groups, all four parameters showed a significant increase (p<0.05 for all).

Table 1. Demographic characteristics

Variable		**Clobetasol 17-propionate 0.05%**		**Topical Anthralin**	
Age (years)	Mean ± SD Median Range	26.04±9.86 24.5 7-50		20.4±9.53 20 7-40	
Variable		n	%	n	%
Gender	Female	11	55	10	50
	Male	9	45	10	50
Family history	Yes	4	20	5	25
	No	16	80	15	75
Disease duration (days)	Mean ± SD Median Range	122.8±210.33 45 3-720		78.7±77.54 60 15-360	

Table 2. Clinical parameters

Clobetasol 17-propionate 0.05%				**Topical anthralin**		
	Pre-treatment	**Month 3**	***p***	**Pre-treatment**	**Month 3**	***p***
NH	19.6±5.1	29.8±11.4	<0.001	20.1±5.8	32.8±11.9	<0.001
HD	31±7.7	44.7±18.7	0.005	30.9±9.0	55.1±20.1*	<0.001
AR	11.0±8.1	22.6±12.2	0.002	12.0±7.5	24.6±10.8	<0.001
TR	88.9±8.1	77.3±12.2	0.002	88.0±7.5	75.9±10.6	<0.001

NH: Number of hair follicles per mm^2, HD: Hair density, AR: Anagen rate, and TR: Telogen rate, p<0.05

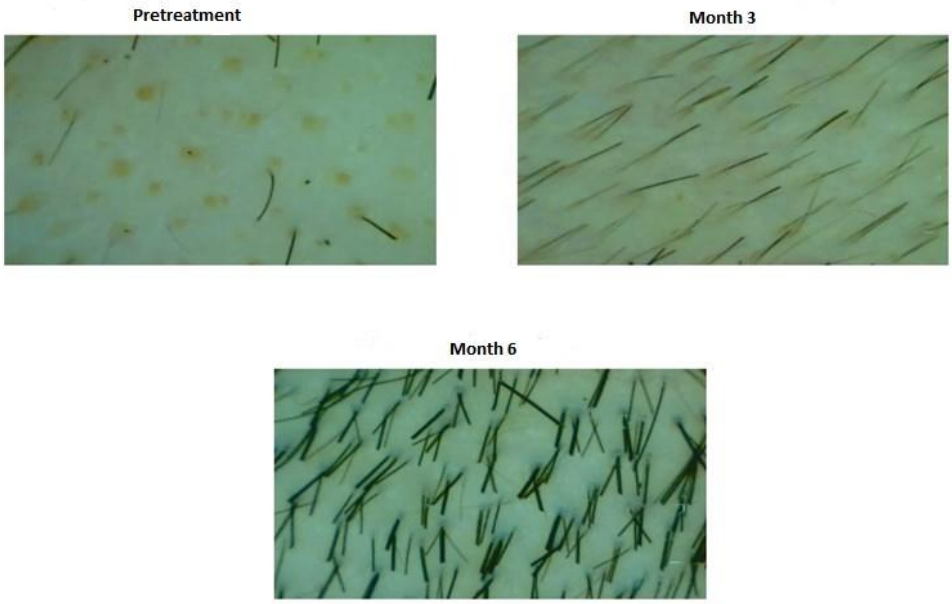

Figure 1. Phototrichogram images showing cosmetic response in a patient

In patients whose treatment was not changed throughout the 6-month period, cosmetic response was observed in 6 (46.1%) out of 13 (65%) patients who received local clobetasol 17-propionate 0.05% and in 10 (62.5%) out of 16 (80%) patients who received local anthralin and no significant difference was found between the groups (p=0.379).

A total of four patients (20%) who did not exhibit a positive response to local anthralin treatment were afterwards switched to clobetasol 17-propionate 0.05% treatment. Among these patients, one of them (25%) had a partial response following the treatment shift. In contrast, a total of 7 patients, accounting for 35% of the sample, who did not exhibit a reaction to the application of topical clobetasol 17-propionate 0.05%, were then switched to topical anthralin. Among these patients, a cosmetic response was noted in 2 individuals, representing a response rate of 28.6%. According to statistical analysis, there was a substantial increase in treatment success among patients who did not exhibit a response to local clobetasol 17-propionate 0.05% treatment and then switched to anthralin treatment, in comparison to other patients who underwent a shift in treatment ($p<0.05$, Chi-Square =7.399; df.=2).

On the other hand, at the end of the 6-month period, it was revealed that both drugs had no significant effect on the increase in NH, HD, AR, and TR values (p=0.148).

When the patients were evaluated with respect to side effects due to anthralin at the end of 6 months; in 20 patients discoloration, in 8 patients erythema, in 7 patients burning, in one patient papule were detected. Erythema, burning and papule were disappeared during the treatment. When topical clobetasol 17-propionate 0.05% using patients were assessed in 2 patients atrophy, in 2 patients papule, in 2 patients pustule and in 2 patients telangiectasia were detected. No serious side effects were detected in any of the patients that would require interrupting the treatment.

DISCUSSION

Alopecia areata (AA) is an autoimmune disease that targets hair follicles in the anagen phase and is characterized by non-scarring hair loss (14). All topical treatments in AA affect only the treatment area and do not have systemic effects (6-8). In the present study, we compared the efficacy and side effects of topical clobetasol 17-propionate 0.05% and topical anthralin (0.5-1%) were compared in patients with patch-type AA.

Numerous studies have reported on cosmetic improvement in AA patients receiving topical anthralin treatment (11,15,16). In a retrospective study conducted in pediatric patients, at least 50% regrowth of hair was observed in 68% of the patients (13). In another prospective study conducted in patients receiving anthralin 1%, partial or complete response was observed in 70% of patients at 12-month follow-up (17). In our local anthralin group, cosmetic improvement occurred in 40%, partial improvement occurred in 40%, and inadequate response was observed in 20% of the patients at the end of three months. These rates implicate that local anthralin achieved remarkably high response rates within a short period of time.

Durdu *et al.* reported that the combination of dinitrochlorobenzene (DPCP) and 0.5% anthralin was more effective than the use of DPCP alone (18). In a retrospective study, Nasimi et al. detected 41% hair regrowth following the addition of anthralin to the treatment in patients that did not respond to DPCP (19). In our study, cosmetic response was obtained in 2 (28.5%) out of 7 patients (35%) that did not respond to topical clobetasol 17-propionate 0.05% treatment after 3 months of anthralin treatment. Taken together, these findings suggest that topical anthralin therapy can be recommended as a combination therapy in refractory patients.

To our knowledge, there have been very few studies using anthralin alone. Moreover, in studies with anthralin, significant differences have been observed in terms of the efficacy of anthralin (11,15-29). These differences could be associated with the different definitions of cosmetic improvement proposed in those studies and also with the evaluation of different patients groups in a single study. In our study, we treated patients with patch-type AA alone.

Although side effects such as excessive itching, desquamation, local pyoderma, and regional lymphadenopathy have been reported in some studies in the literature (16,20,21), no such side effects or irritation that could cause cessation or termination of the treatment were observed in our patients. Additionally, in the local anthralin group, no allergic reaction occurred in any patient, while only mild irritation symptoms were observed at the beginning of the treatment and all of them disappeared after the treatment.

Literature reviews indicate that there are few studies on the effects of topical corticosteroids in the treatment of AA and the effects of these drugs remain controversial (9,10,23,24,28). In our study, the cosmetic response rate was higher in the local anthralin group compared to the topical clobetasol 17-propionate 0.05% group, though no significant difference was established . However, the partial response rate was the same in both groups. Some authors argue that the effect of anthralin is not superior to that of placebo (22,23). In a study conducted with patients that applied fluocinolone acetonide cream twice a day for six months, successful results were reported in 61% of the cases. Additionally, no irritant or allergen dermatitis developed in any patient, while localized acneiform eruptions developed in 18% of the patients (22). Accumulating evidence suggests that very potent topical corticosteroids should be used for at least three months and continued if effective (7,8). In a multicenter study with limited patch-style AA (less than 26% hair loss), it was reported that applying Betamethasone Valerate 0.12% foam twice a day for 12 weeks provided significantly better outcomes compared to Betamethasone Dipropionate 0.05% lotion and that Betamethasone Valerate 0.12% foam achieved a hair regrowth rate of 27% at the end of 8 weeks (24). In our study, in line with the literature, cosmetic response was achieved in 25% in the local clobetasol 17-propionate 0.05% group.

In our study, an evaluation of the correlation between the duration of disease and response rate showed that as the duration of the disease increased, the response rate decreased in both drug groups and that the effect of drug on NH, HD, AR, and TR decreased as the duration of disease increased. In similar studies, dinitrochlorobenzene (DNCB), topical minoxidil, intralesional corticosteroid, and topical azelaic acid have been shown to provide a response rate of 22-68%, 0-52%, 65-95%, and 53.3%, respectively (16,20,25-28). Although these rates are higher than those obtained by topical anthralin and topical clobetasol 17-propionate 0.05% in our study, they are contradictory and the use of those drugs is limited due to their side effects, application difficulties, and high financial costs. By contrast, both topical anthralin and topical clobetasol 17-propionate 0.05% have been shown to be safe and effective treatment options in patch-type AA and it has also been suggested that better results can be obtained by adding different formulations and occlusion procedures that promote skin penetration and access to the hair bulb to topical corticosteroid application (28).

In our study, no statistical superiority could be determined between topical clobetasol 17-propionate 0.05% and topical anthralin for the treatment of patch-type AA. Despite this, the anthralin treatment that was applied to patients unresponsive to topical clobetasol 17-propionate 0.05% treatment was found to be partially superior over topical clobetasol 17-propionate 0.05% treatment that was applied to patients unresponsive to anthralin treatment. Accordingly, it is advisable that topical anthralin may be preferred as a treatment option for patients that do not respond to topical clobetasol 17-propionate 0.05% treatment.

In conclusion, the treatment to be applied in AA patients should be an effective, easy to apply, and cost-effective treatment with minimal side effects. Accordingly, topical clobetasol 17-propionate 0.05% and topical anthralin patch seem to be viable options in AA treatment. Additionally, topical anthralin treatment may be a useful option in patients unresponsive to topical clobetasol 17-propionate 0.05% treatment. Based on these results and literature reviews, further studies with larger patient series are needed to substantiate the effectiveness of these two drugs.

Conflicts of Interest: The authors declare no conflict of interest.

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Ethical Approval: Ethics committee approval was granted from Selçuk University Meram Faculty of Medicine Ethics Committee (Decision no: No: 2007/070; date: 02/05/2007) and International Helsinki Principles were followed. An informed consent was obtained from the participants.

REFERENCES

1. Braun-Falco O, Plewig G, Wolf HH, Burgdorf WHC. Disease of hair. Dermatology, 2nd ed. Berlin: Springer-Verlag; 2000.p.1099-140.
2. Dawber RPR, Berker de D. Disorders of hair. In: Rook A, Wilkinson DS, Ebling FJG (eds.). Textbook of dermatology. 6th ed. Oxford: Blackwell Scientific Publications; 1998. p.2869-973.
3. Forslind B. Structure and function of the hair follicle. In: Camacho FM, Randall VA, Price VH, editors. Hair and its disorders. Biology, pathology and management. 1st ed. London, Martin Dunitz Ltd; 2000.p.3-15.
4. Sinclair R, Banfield C, Dawber RPR. Handbook of disease of the hair and scalp, Blackwell Science; 1999.p.3-23.
5. Hoffmann R. TrichoScan, a GCP-validated tool to measure hair growth. JEADV 2008; 22: 101–136.
6. Olsen E, Hordinsky M, Price V, et al. Alopecia areata investigational assessment guidelines–part II. Jaad. 2004;51(3):440-447.
7. Messenger A, Mckillop J, Farrant P, McDonagh A, Sladden M. British Association of Dermatologists' guidelines for the management of alopecia Areata 2012. Br J Dermatol. 2012;166(5):916-926.
8. Ramos M, Anzai A, Duque-Estrada B, et al. Consensus on the treatment of alopecia areata – Brazilian society of dermatology. An Bras Dermatol. 2020;95:39-52
9. Nassar A, Elradi M, Radwan M, Albalat W. Comparative evaluation of the efficacy of topical tacrolimus 0.03% and topical calcipotriol 0.005% mixed with betamethasone dipropionate versus topical clobetasol 0.05% in treatment of alopecia areata: A clinical and trichoscopic study. J Cosmet Dermatol. 2023;22:1297-1303.
10. Ucak H, Kandi B, Cicek D, Halisdemir N, Dertlioğlu SB. The comparison of treatment with clobetasol propionate 0.05% and topical pimecrolimus 1% treatment in the treatment of alopecia areata. J Dermatol Treat. 2012;23:6, 410-420.
11. Schmoeckel C, Weissmann I, Plewig G, Braun Falco O. Treatment of alopecia areata by anthralin-induced dermatitis. Arch Dermatol. 1979;115(10):1254-1255
12. Sehgal VN, Verma P, Khurana A. Anthralin/dithranol in dermatology. Int J Dermatol. 2014;53(10):e449-e460.
13. Özdemir M, Balevi A. Bilateral half-head comparison of 1% anthralin ointment in children with alopecia areata. Pediatr Dermatol. 2017;34 (2):128-132
14. Hordinsky MK. Overview of alopecia areata. J Investig Dermatol Symp Proc 2013;16:S13–5.
15. Nelson DA, Spielvogel RL. Anthralin therapy for alopecia areata. Int J Derm 1985;24: 606-7.
16. Fiedler-Weiss V, Buys C. Evaluation of anthralin in the treatment of alopecia areata. Arch Dermatol 1987;123:1491-3.
17. Wu SZ, Wang S, Ratnaparkhi R, Bergfeld WF. Treatment of pediatric alopecia areata with anthralin: A retrospective study of 37 patients. Pediatr Dermatol. 2018;35:817–820.
18. Durdu M, Özcan D, Baba M, Seçkin D. Efficacy and safety of diphenylcyclopropenone alone or in combination with anthralin in the treatment of chronic extensive alopecia areata: A retrospective case series. J Am Acad Dermatol. 2015;72:640–50.
19. Nasimi M, Ghandi N, Abedini R, Mirshamsi A, Shakoei S, Seirafi H. Efficacy and safety of anthralin in combination with diphenylcyclopropenone in the treatment of alopecia areata: A retrospective case series. Arch Dermatol Res. 2019;311:607–13.
20. Saşmaz Sezai, Arıcan Ö. Comparison of azelaic acid and anthralin for the therapy of patchy alopecia areata. Am J Clin Dermatol 2005;6:403-6.
21. Fiedler VC, Wendrow A, Szpunar GJ et al. Treatment of resistant alopecia areata. Arch Dermatol 1990;126:756
22. Bolduc C, Shapiro J. The treatment of alopecia areata. Dermatologic Therapy 2001;14:306- 16.
23. Charuwichitratana S. Randomized double-blind placebo-conrolled trial in the treatment of alopecia areata with 0.25% desoximetasone cream. Arch Dermatol 2000;136:1276-7
24. Mancuso G, Balducci A, Casadio C, et al. Efficacy of betamethasone valerate foam formulation in comparison with betamethasone dipropionate lotion in the treatment of mild-to- moderate alopecia areata: a multicenter, prospective, randomized, controlled, investigator- blinded trial. Int J Dermatol 2003;42:572–5.
25. Fiedler VC: Alopecia areata: A review of therapy, efficacy, safety and mechanism. Arch Dermatol 1992;128:1519
26. Rokhsar CK, Shupack J L, Vafai J J, Washenik K: Efficacy of topical sensitizers in treatment of alopecia areata. J Am Acad Dermatol 1998; 39:751-61.
27. White SI, Friedmann PS. Topical minoxidil lacks efficacy in alopecia areata. Arch Dermatol 1985;121:591.
28. Tosti A, Iorizzo M, Botta GL, Milani M. Efficacy and safety of a new clobetasol propionate %0.05 foam in alopecia areata: a randomized, double-blind placebo-controlled trial. J Eur Acad Dermatol Venereol 2006;20:1243-7.