

Factors Affecting Topical Treatment Success in Pediatric Scabies Cases: A Cross-Sectional Study

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ABSTRACT Introduction: Scabies is a common disease that affects the pediatric population. Treatment failure and relapse occur frequently in children.

Objectives: We aimed to identify the factors that affect topical treatment success in pediatric scabies patients.

Methods: A multicenter cross-sectional study was conducted from April 2022 to December 2022. Pediatric scabies cases were classified as belonging to either the treatment failure (TF) group or the treatment success (TS) group.

Results: We enrolled 170 patients for the study. In the TF group, the presence of symptomatic household members and referrals from physicians other than dermatologists were more common (both $P < 0.001$), and relapse rates and total symptom duration were higher ($P = 0.007$, $P < 0.001$, respectively). Regarding treatment agents, 5% permethrin was more commonly used in the TF group (71.1% versus 25%; $P < 0.001$). The proportion of patients treated with sulfur preparations was significantly

higher in the TS group (60.7% versus 16.9%; $P < 0.001$). Misapplication of topical therapy was significantly more common in the TF group ($P < 0.001$), with statistically significant errors being (i) lack of treatment of close contacts ($p < 0.001$), (ii) single application ($P < 0.001$), and (iii) local application ($P = 0.027$). A multivariate analysis revealed that TS was mainly associated with (i) the presence of atopy (odds ratio [OR] 6.12, 95% CI: 1.39–27.04), (ii) the absence of symptomatic household members (OR 6.31, 95% CI: 2.14–18.63), and (iii) presentation to a dermatologist rather than another specialist (OR 6.51, 95% CI: 2.11–20.13). The use of permethrin negatively affected treatment success (OR 0.22, 95% CI: 0.07–0.71).

Conclusions: Pediatric scabies patients should be treated before other family members become infested and with topicals other than permethrin. In addition, awareness of scabies needs to be increased among non-dermatologists.

Introduction

Scabies is a significant global healthcare issue, with a rising incidence and reported outbreaks [1,2]. Treatment failure occurs in approximately one third of the cases of scabies, which possibly contributes to the increasing incidence of the disease in developed countries [3].

Epidemiologic data shows that the most common age range of scabies cases is 10–29 years [4]. Children represent a special population, as there are delays in their diagnosis, and they are frequently insufficiently treated [1]. Thus, treatment failure and relapse are frequent in children.

In clinical practice, authors have observed a growing number of pediatric scabies cases presenting to dermatology outpatient clinics. To improve treatment outcomes, risk factors for treatment failure should be identified and addressed.

Objectives

In this study, we aimed to identify the factors that affect topical treatment success in pediatric scabies patients presenting to dermatology outpatient clinics.

Methods

Study Design

A multicenter cross-sectional national study was performed from May 2022 to December 2022 on pediatric scabies cases presenting to dermatology outpatient clinics in five different cities. The study was approved by the ethics committee of Sancaktepe Sehit Prof.Dr.Ilhan Varank Research and Training Hospital (no. 38 12-04-2022) and performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from the legal representatives of the pediatric patients.

Patient Population

All consecutive pediatric scabies cases were prospectively enrolled to the study at the time of the outpatient dermatology visit. Patients were classified as belonging to either the treatment failure (TF) group or the treatment success (TS) group. Treatment failure cases were diagnosed both clinically and dermatoscopically by the presence of burrows despite topical therapies that had persisted for at least one month. The diagnosis of the treatment success group was made according to previous patient medical records along with patient history (eg, previous involvement of predilection sites and presence of postinflammatory changes).

Data Collection

During the dermatology outpatient visit, the following parameters were recorded for each enrolled patient: age, sex, presence of atopic diathesis, travel history, presence of pruritus, duration of symptoms, number of household members, number of children in the household, presence of symptomatic household members, prescribed treatment, referring physician, number of relapses, and application errors. The latter included lack of treatment of close contacts, lack of reapplication, local application of topical products, inappropriate concentration of topical products, inappropriate quantity of topical products, and lack of head and neck treatment of infants.

Statistical Analysis

We used SPSS version 21 for the statistical analyses. Median and interquartile range (IQR) values were noted in descriptive analyses for continuous variables, and percentages were noted for categorical variables. A Mann–Whitney U test was performed to compare continuous variables between the two groups, whereas categorical variables were compared with the chi-square test and Fischer exact test when appropriate.

Using variables with P values < 0.25 in univariate analyses, factors affecting TS were analyzed with logistic regression analysis. A P value of less than 0.05 was considered significant.

Results

We enrolled 170 pediatric patients for the study, which included the TF group (N = 142, 83.5%) and the TS group (N = 28, 16.5%). All patients in the TF group had associated pruritus at referral, and severe pruritus was significantly more commonly present in the TF group (P < 0.001) than in the TS group. The TS group (25%) included significantly more patients with atopic diathesis than the TF group (9.2%; P = 0.026). The presence of symptomatic household members

was also more common in the TF group (85.9%) than the TS group (39.3%; P < 0.001). Sociodemographic factors, including number of household members and number of children in the household and duration of symptoms before the first therapy, did not seem to affect treatment results (Table 1). The TF group had significantly higher relapse rates and total symptom duration (P = 0.007 and 0.001, respectively; Table 1). Patients were also classified according to the specialty of the referring physicians. The proportion of patients treated solely by dermatologists was greater in the TS group than the TF group (71.4% versus 20.4%; P < 0.001; Table 2).

Regarding errors in application of topical therapy, 96.5% of the patients in the TF group had made at least one error, whereas all except one patient in the TS group had applied the prescription correctly (P < 0.01). A list of

Table 1. Patient characteristics.

	Treatment failure N = 142	Treatment success N = 28	P
Sex N (%)			
Female	71(50)	17(60.7)	0.3
Male	71(50)	11(39.3)	
Pruritus N (%)			
None	0	19(67.9)	<0.001
Mild	33(23.2)	7(25)	
Severe	109(76.8)	2(7.1)	
Travel history N (%)			
Yes	130(91.5)	25(89.3)	0.716
No	12(8.5)	3(10.7)	
Atopy N (%)			
No	129(90.8)	21(75)	0.026
Yes	13(9.2)	7(25)	
Symptomatic household members N (%)			
Present	20(14.1)	17(60.7)	<0.001
Absent	122(85.9)	11(39.3)	
Age (year) median (IQR)	7 (3.75-12)	6 (3.25-13.25)	0.784
Number of household members Median (IQR)	5(4-5)	4 (4-4)	0.081
Number of children in the household Median (IQR)	2 (2-3)	2(2-2)	0.141
Duration of symptoms before first therapy Median (IQR)	30 (15-30)	20 (11-30)	0.083
Total symptom duration Median (IQR)	60 (56.25-120)	60 (32.5-60)	0.007
Number of relapses Median (IQR)	1 (1-2)	0 (0-0)	<0.001

IQR = interquartile range

Table 2. Specialty distribution of pediatric patients treated for scabies.

	Treatment failure N = 142 N (%)	Treatment success N = 28 N (%)	P
Referring specialist before presentation to dermatology			
Emergency physician	24(16.9)	1(3.6)	0.082
General practitioner	53(37.3)	4(14.3)	0.018
Pediatrician	42(29.6)	4(14.3)	0.096
Dermatologist alone	29(20.4)	20(71.4)	<0.001

Table 3. Application errors of topical therapy.

	Treatment Failure N = 142 N (%)	Treatment Success N = 28 N (%)	P
Application error			
Present	137(96.5)	1(3.6)	<0.001
Application errors			
Close contacts not treated	73(51.4)	0(0.0)	<0.001
Lack of reapplication	57(40.1)	0(0.0)	<0.001
Local application	21(14.8)	0(0.0)	0.027
Inappropriate dosage	16(11.3)	1(3.6)	0.312
Inappropriate quantity	14(9.9)	0(0.0)	0.130
Lack of head-neck treatment of infants	6(4.2)	0(0.0)	0.591

application errors can be found in Table 3. In the TF group, statistically significant errors were the following: (i) close contacts were not treated ($P < 0.001$), (ii) reapplication in the first week was not performed ($P < 0.001$), and (iii) treatment was not applied to the whole body ($P = 0.027$). Regarding the referring physician, patients treated solely by dermatologists made significantly fewer application errors (Table 4). Patients without atopic diathesis (83.3%) were more prone to make errors in the application of topicals than atopic patients (65%), with a borderline statistical difference ($P = 0.066$).

Regarding treatment agents (Table 5), 5% permethrin lotion was more commonly used in the TF group than in the TS group (71.1% versus 25%; $P < 0.001$). However, the ratio of patients treated with sulfur preparations was significantly higher in the TS group (60.7% versus 16.9%; $P < 0.001$).

Univariate and Multivariate Analyses

Univariate and multivariate analyses were performed to identify the factors associated with treatment success (Table 6). The predictors of treatment success were (i) the presence of atopy (odds ratio [OR] 6.12, 95% CI: 1.39–27.04), (ii) the absence of symptomatic household members (OR 6.31,

95% CI: 2.14–18.63), and (iii) presentation to a dermatologist rather than another specialist (OR 6.51, 95% CI: 2.11–20.13). The use of permethrin lotion negatively affected treatment success (OR 0.22, 95% CI: 0.07–0.71).

Conclusions

The present study focuses on factors affecting treatment success of anti-scabietic topical treatments in pediatric population. We identified presence of atopy, absence of symptomatic household members and presentation to dermatologists rather than other specialties as predictors of treatment success whereas use of permethrin lotion negatively affected treatment success. Several studies have previously investigated risk factors of treatment failure in scabies, focusing on different treatment methods and clinical features. In a multicenter study conducted in France, monotherapy with topical benzyl benzoate and a single intake of oral ivermectin were identified as predictors of treatment failure in multivariate analyses [3]. Lee et al reported that limited mobility and topical steroid use before diagnosis were associated with treatment failure in topical permethrin treatment [5].

Boralevi et al studied the clinical characteristics of pediatric scabies according to age. They reported a history of

Table 4. Specialty distribution of pediatric patients treated for scabies according to presence of application errors.

	Application error		
	Absent N = 32 N (%)	Present N = 138 N (%)	P
Referring specialist before presentation to dermatology			
Emergency physician	1(3.1)	24(17.4)	0.05
General practitioner	5(15.6)	52(37.7)	0.017
Pediatrician	6(18.8)	40(29)	0.226
Dermatologist alone	21(65.6)	28(20.3)	<0.001

Table 5. Topical therapy agents used in treatment failure and treatment success groups.

	Treatment failure N = 142 N (%)	Treatment success N = 28 N (%)	P
Topical therapy agent			
Permethrin 5% lotion	101(71.1)	7(25)	<0.001
Permethrin 5% cream	9(6.3)	0(0.0)	0.358
Wilkinson ointment (sulfur 12.5%., tar 12.5%)	26(18.3)	5(17.9)	0.955
Sulfur in vaseline	24(16.9)	17(60.7)	<0.001
Other (benzyl benzoate, balsam of Peru)	4(2.8)	1(3.6)	1.000

Table 6. Factors associated with treatment success in univariate and multivariate analyses.

	OR	Univariate	P	Multivariate		
		%95CI		OR	%95CI	P
Sex (ref. Female)						
Male	0.65	0.28-1.48	0.302	0.37	0.12-1.20	0.098
Age (year)	1.02	0.94-1.10	0.683	1.05	0.95-1.16	0.364
Atopy (ref. Present)						
Absent	3.31	1.18-9.25	0.023	6.12	1.39-27.04	0.017
Symptomatic household members (ref. Present)						
Absent	9.43	3.86-23.04	<0.001	6.31	2.14-18.63	0.001
Presentation to dermatologist alone (ref. No)						
Evet	9.74	3.9-24.34	<0.001	6.51	2.11-20.13	0.001
Use of permethrin lotion (ref. No)						
Yes	0.14	0.53-0.34	<0.001	0.22	0.07-0.71	0.011

CI = 95% confidence Interval; OR = odds ratio; ref. = reference category. Nagelkerke R²:0,491, Hosmer and Lemeshow:0,689

atopic dermatitis in 12.8% of 323 pediatric patients, mainly in patients under 15 years of age. A very similar proportion of pediatric patients in our cohort (11.8%) had atopy. These children with atopic diathesis were found to respond better to therapies. We hypothesized that parents of atopic children would have better compliance with topical therapies. In fact, in our series, patients with atopic diathesis made fewer errors in the application of topical therapies than non-atopic patients.

Our study showed that the presence of symptomatic household members decreased treatment success. In addition, total symptom duration was significantly longer in the TF group. We can conclude that the identification and treatment of the disease before its propagation is associated with better treatment outcomes. In this regard, prompt and correct recognition of the disease by all specialists is important, as scabies patients also present to general practitioners, pediatricians, and emergency departments [6,7]. In

our cohort, the majority of patients (71.8%) were referred to dermatology outpatient clinics by non-dermatologists. However, patients treated solely by dermatologists had better treatment outcomes than those referred by other specialists. Treatment application errors were also less common in patients treated solely by dermatologists. We stress that awareness of the proper treatment of scabies needs to be increased among general practitioners, pediatricians, and emergency physicians.

At the time of the study, oral ivermectin was unavailable in our country; thus, all patients in our study cohort were only treated with topical therapies. Topical permethrin is the first-line therapy for scabies in children [8]. Although in vitro results prove its effectiveness [9], longer exposure times are required for its effectiveness, and widespread clinical resistance is frequently reported [10]. In fact, the observations of Mazzatenta et al in daily practice led them to modify the standard treatment regimen of permethrin 5% cream at days 0 and 7 to twice or thrice the weekly regimen [11]. Even with the latter modified permethrin regimen, the authors report treatment failure in 2 out of 3 patients. Thus, it seems necessary to change or at least modify the first-line treatment of scabies [11]. Combined therapy with oral ivermectin and topical benzyl benzoate seems to be the best therapeutic approach, with 100% treatment success in newly diagnosed patients and patients unresponsive to permethrin [12]. In infants weighing less than 15 kg, topical ivermectin is recommended [13]. According to our data, permethrin lotion negatively affected treatment success. We suggest that sulfur-containing topicals should be preferred over permethrin lotion in pediatric scabies cases.

Improper application of topical agents is a common problem in scabies. In a prospective study that included 21 young patients who were clearly instructed on how to apply topical therapies, all patients made application errors. Of note, predilection sites such as ankles, interdigital spaces, and the sacral region were insufficiently treated in 62%, 33%, and 24% of patients, respectively [14]. This study shows the important pitfall of topical therapies, as the rates of misapplication could be higher in children. In our study, 81% of our patients had made at least one application error with topical treatment. Statistically significant errors were the lack of treatment of close contacts, lack of reapplication on first week, and local application of the treatment. Our results were consistent with a descriptive study involving 31 scabies patients with treatment failure in which persistence of infestation was linked to insufficient treatment of close contacts, absence of a repeated treatment, and insufficient efficacy of the available treatments [15].

The limitations of our study include a lack of longitudinal follow-up with the patients and a relatively small TS group, as patients typically present to dermatology outpatient clinics with persistent infection.

In conclusion, in line with previous reports of permethrin resistance, pediatric scabies cases should be prescribed with topicals other than permethrin, preferably sulfur containing preparations. Pediatric patients should be treated promptly before other family members are affected. Special care should be taken in topical treatment of scabies patients without atopic diathesis as they are more prone to make application errors. In addition, awareness of scabies treatment needs to be increased among non-dermatologists.

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