Original Article | Annals of Dermatology 2023;35(2):124-131 • https://doi.org/10.5021/ad.22.114

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Prescription Patterns of Topical Medications in Patients with Atopic Dermatitis: An Investigative Review Using Big Data from the National Health Insurance Corporation

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Received July 22, 2022
Revised November 22, 2022
Accepted January 2, 2023

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Background: Topical medications play a crucial role in the treatment of atopic dermatitis (AD). Topical corticosteroids (TCSs) remain the main treatment of choice and topical antibiotics have also been used. However, with the new topical calcineurin inhibitors (TCIs), the prescription patterns of topical agents have changed over time.
Objective: To characterize the prescription patterns of topical medications in Korean patients with AD.
Methods: We investigated topical medications prescribed to Korean patients with AD using the National Health Insurance Sharing System (NHISS) database over a 14-year period (2002~2015). Additionally, the potency of prescribed TCSs was compared with AD and psoriasis patients.
Results: The annual prescription of TCSs showed a slightly decreasing trend without significant change. In particular, in terms of steroid class, prescription of moderate-to-low potency TCSs were increased and the use of high potency TCSs were decreased. TCSs were the most commonly prescribed topical medications for AD. Tertiary hospitals had a higher prescription rate for TCIs than secondary or primary hospitals (16.2%, 3.1%, and 1.9%, respectively). Additionally, dermatologists prescribed TCIs more frequently than pediatricians and internists (4.3%, 1.2%, and 0.6%, respectively). Among TCSs, Class 5 was prescribed the most (40.6%) followed by Class 7, 6, 4, 3, 1, and 2. When we compared the potency of TCSs prescribed for AD with psoriasis patients, moderate-to-low-potency TCSs were more commonly prescribed in AD.
Conclusion: Prescription patterns of topical medications had changed from 2002 to 2015 and differed according to the type of institution and specialty of the physician.

Keywords: Antibiotics, Atopic dermatitis, Calcineurin inhibitors, Corticosteroids, Topical agents

INTRODUCTION

Topical medications are the mainstay of treatments for atopic dermatitis (AD), especially in patients with mild AD. In 2015, the Korean Atopic Dermatitis Association (KADA) suggested topical medications, including topical corticosteroids (TCSs) and calcineurin inhibitors (TCIs), as primary medications for the active treatment of mild AD and supplementary treatment for moderate-to-severe AD[1]. In addition, long-term treatment of AD using intermittent application of tacrolimus, one of TCIs, has been demonstrated to prevent disease flare-ups, thus emphasizing the importance of topical agents in the treatment of AD[2].

TCSs are one of the most commonly used topical medica-

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tions for dermatologic diseases, including AD[3]. In addition, some patients are prescribed topical antibiotics for infective AD[4]. In early 2000s, when TCIs were first sold in Korea, they became a good treatment alternative for AD, owing to their relative safety and efficacy[1,5]. Thus, with the advent of TCIs, the prescription patterns of topical agents for AD patients have begun to change.

It is important to understand these pattern of changes to increase patient compliance and to provide structured long-term treatment. However, to date, most studies have focused on the individual efficacy of topical agents and there has been no comprehensive study on the overall prescribing patterns of topical medications for AD in Korea. Therefore, we analyzed the changes in prescription patterns according to institutions, specialties of physicians, and duration in years using a large database from the National Health Insurance Service (NHIS).

MATERIALS AND METHODS

Data source and subjects

We conducted a retrospective, population-based study to assess the prescription patterns of topical medications for AD in Korea from 2002 to 2015. We got permission to use the National Sample Cohort database of the National Health Insurance Sharing System (NHISS-NSC, https://nhiss.nhis.or.kr) which provides information on the medical resource utilization of approximately one million qualified health insurance subscribers and Medicare beneficiaries in Korea (Permission No. NHIS-2017-2-594, Permission period: November 28, 2017 to July 17, 2020).

Diagnostic codes from the Korea Standard Classification of Disease-7 (KCD-7) were used to extract specific data from patients with AD. Data from all patients diagnosed with AD (L20.*) as a principle diagnosis were analyzed and data from patients with the following comorbidities were excluded: psoriasis (L40.*), rosacea (L71.*), seborrheic dermatitis (L21.*), vitiligo (L80.*), lichen striatus (L44.2), and allergic contact dermatitis (L23.*)

Data analysis

We analyzed the trends and prescription patterns of topical medications in AD using either the period (annual alteration from 2002 to 2015) or subjects (type of medical institution or specialty of physician; convenience sample of three physician specialties: dermatologist, pediatrician, and internist). Topical medications used in patients were largely classified as TCSs, TCIs (tacrolimus and pimecrolimus), and antibiotics (mupirocin, fusidic acid). TCSs were divided according to the American classification system, which categorizes them into seven classes/groups[4-7]. In this system, potency is based on the activity and concentration of their molecules as well as the nature of the vehicle. Among the groups, Class 1 is the most potent while Class 7 is the least potent. Combination preparations of topical steroids and other agents were classified according to the components of the steroid. Shampoos and eye ointments that are frequently used to treat skin lesions on scalp and periorbital areas were included, but eye solutions and oral gargles that are thought to act on mucous membranes were excluded. We compared the prescription patterns of TCSs between AD and psoriasis patients (L40.* of the KCD-7). Statistical analyses were performed using SAS version 9.2; SAS Institute, Inc.). Chi-square test was used for categorical data and Wilcoxon rank-sum test for continuous data. *p*-values less than 0.05 were considered statistically significant.

Ethics statement

This study was approved by the Institutional Review Board of the Pusan National University Yangsan Hospital (IRB No. 04-2017-008).

RESULTS

Demographics characteristics of the subjects

Table 1 shows the demographic characteristics of the participants in this study. Over the past 14 years, from 2002 to 2015, the total number of subjects was 94,165; the annual number of subjects ranged from 5,743 to 9,340, thereby corresponding incident rates were 0.0055 and 0.0088/person·year of the entire sample research cohort, respectively.

Annual topical medications prescription patterns

TCSs (90.5%~95.4%) were the most commonly prescribed topical medications for the cohort period in AD patients, followed by topical antibiotics (3.8%~5.5%) and TCIs (0.2%~4.1%). Estimates indicated a slight decrease in prescription rates of TCSs from 95.4% to 92.0%, but there was no significant difference (Fig. 1).

Table 1. Demographics of the subjects

Characteristic	Year														Total
	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	
Sex															
Male	3,623	3,561	3,446	3,370	3,180	2,977	3,036	2,877	3,064	3,170	3,421	3,827	4,102	4,671	48,325
Female	3,045	3,062	3,097	3,014	2,842	2,844	2,828	2,866	3,034	3,263	3,370	3,745	4,161	4,669	45,840
Age (yr)															
<1	485	501	507	492	515	566	529	474	583	682	743	749	964	1,226	9,016
1~9	4,622	4,373	4,041	3,721	3,373	3,095	3,122	3,018	3,069	3,225	3,500	4,002	4,267	4,857	52,305
10~19	665	763	833	899	918	884	859	842	884	844	734	814	786	777	11,502
20~29	302	282	332	320	300	308	287	298	315	359	353	393	435	469	4,753
30~39	238	283	337	335	305	296	324	338	344	352	388	393	414	444	4,791
40~49	147	155	153	252	218	240	264	259	309	338	362	405	414	445	3,961
50~59	96	101	145	137	144	165	198	188	233	280	316	356	421	487	3,267
60~69	68	78	103	114	120	137	136	171	168	177	181	220	262	326	2,261
70~79	31	45	66	82	98	80	99	104	137	127	152	170	217	203	1,611
≥80	14	22	26	32	31	50	46	51	56	49	62	70	83	106	698
Total	6,668	6,623	6,543	6,384	6,022	5,821	5,864	5,743	6,098	6,433	6,791	7,572	8,263	9,340	94,165

Values are presented as number.

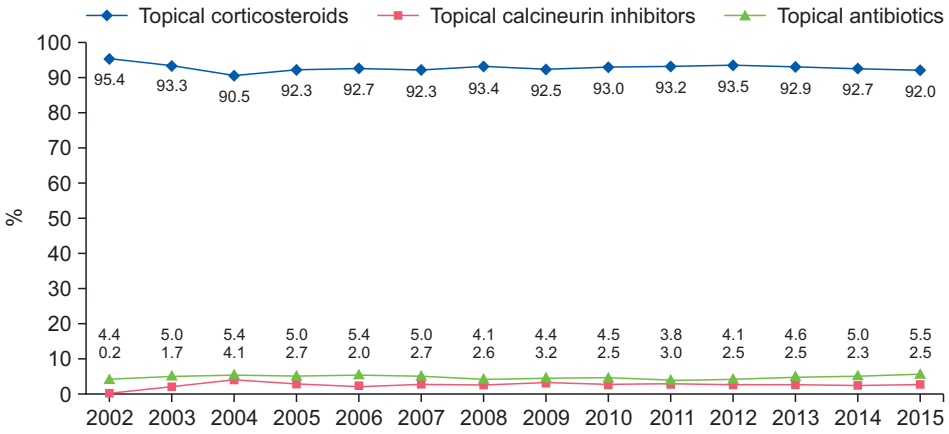


Fig. 1. Alteration of annual topical medication prescription pattern from 2002 to 2015. Although prescription pattern of topical corticosteroids tended to mildly decrease, it remained as the mainstay of topical therapy in atopic dermatitis. No significant increase of topical calcineurin inhibitors or topical antibiotics prescriptions was observed over time.

Prescription patterns of topical medication by medical institutions

The prescription distributions of patients with AD stratified by medical institutions in 2015 are presented in Fig. 2A. The proportion of TCSs prescribed in primary medical institutions was higher than that in secondary or tertiary institutions (93.1% vs. 88.7% in secondary or 74.7% in tertiary institutions). In addition, a marked increase was observed in the use of TCIs in secondary (3.1%) and tertiary (16.2%) medical institutions and in the use of antibiotics in secondary (8.3%) and tertiary (9.2%) medical institutions.

Prescription patterns of topical medication by prescriber specialty

TCSs were the most common topical medications used in patients with AD in 2015 (90.8%~94.8%). However, according to the prescribing physician's specialty, the distribution of prescription patterns of topical medications was significantly different. Overall, TCIs were used most prescribed by dermatologists (4.3%), pediatricians (1.2%), and internists (0.6%). Moreover, topical antibiotics were prescribed most often by pediatricians (6.5%), dermatologists (5.0%), and internists (4.5%). Lastly, TCSs were prescribed most often by internists (94.8%), pediatricians (92.3%), and dermatologists (90.8%) (Fig. 2B).

Annual TCSs prescription patterns

As classified based on their potency, moderate-to-low potency TCSs, such as those in Class 5 (40.6%), 7 (21.2%), and 6 (13.4%), were most often prescribed in AD patients. In contrast, the proportion of patients prescribed with high potency TCSs, including Class 3 (13.3% to 6.4%), 1 (10.8% to 3.6%), and 2 (6.5% to 1.7%), annually decreased from 2002 to 2015 (Fig. 3).

TCSs prescription pattern by medical institutions

The most commonly prescribed TCS group was Class 5 in primary (41.3%) and secondary (40.8%) medical institutions and Class 7 in tertiary (28.4%) medical institutions. The proportion of non-mid strength potency TCSs (Classes 1, 2, 6, and 7) was high in tertiary institutions (54.9%), followed by secondary (44.9%) and primary institutions (38.6%) (Fig. 4A).

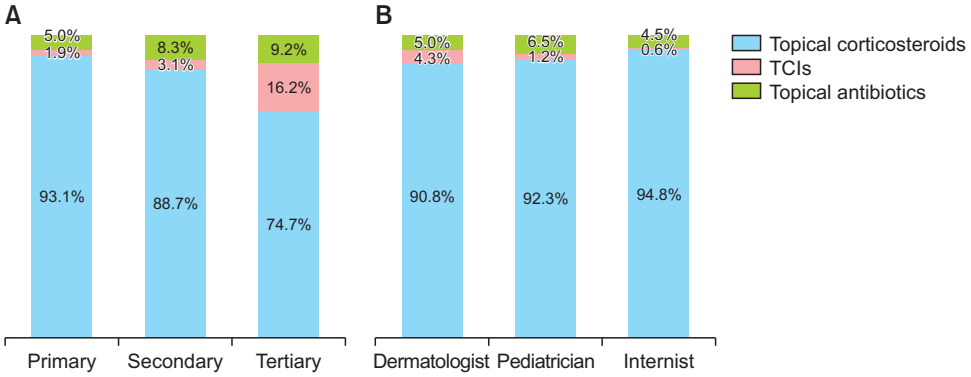


Fig. 2. Prescription patterns of topical medication by medical institutions and prescribers' specialty in 2015. (A) Compared to other institutions, tertiary institutions prescribed topical calcineurin inhibitors (TCIs) and topical antibiotics the most, followed by secondary and primary institutions. (B) Compared to other specialists, TCIs were prescribed the most by dermatologists, whereas topical antibiotics were prescribed the most by pediatricians.

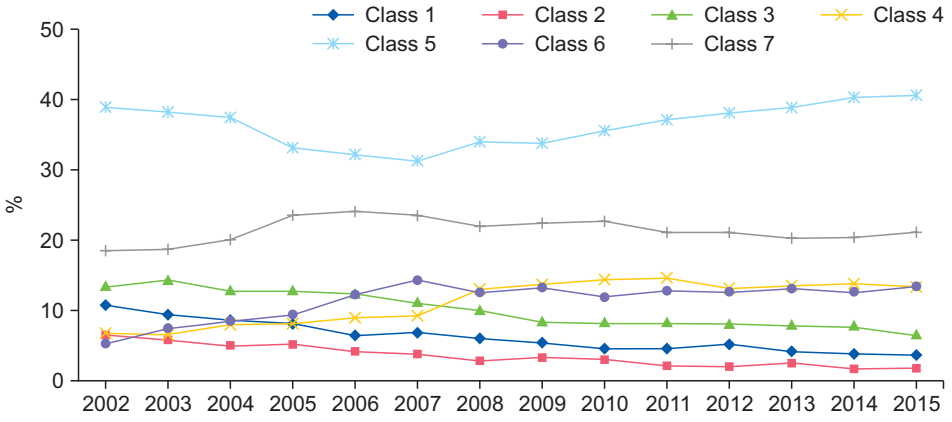


Fig. 3. Annual topical corticosteroids (TCSs) prescription patterns according to potency of TCSs. Moderate-to-low-potency TCSs (Classes 5 and 7) were mainly prescribed.

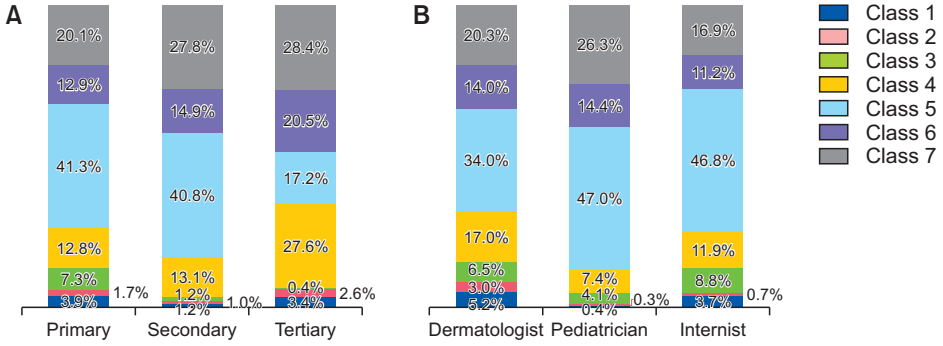


Fig. 4. Topical corticosteroids (TCSs) prescription pattern by medical institutions and prescribers' specialty in 2015. (A) Primary institutions prescribed moderate-potency TCSs (Class 5) the most, while tertiary institutions prescribed TCSs with more diverse potencies. (B) Dermatologists tend to prescribe more diverse potency TCSs than pediatricians and internists.

Table 2. Prescription Patterns of TCSs in AD patients compared with psoriasis patients

Characteristic	All age group			Child and adolescent group (age <20)			Adult group (age ≥20)		
	AD	Psoriasis	*p*-value*	AD	Psoriasis	*p*-value*	AD	Psoriasis	*p*-value*
Sex									
Male	3,439 (50.0)	1,234 (41.1)	<0.001	2,716 (48.6)	41 (46.1)	0.726	734 (53.8)	1,204 (40.9)	<0.001
Female	3,440 (50.0)	1,767 (58.9)	<0.001	2,867 (51.4)	48 (53.9)	<0.001	631 (46.2)	1,737 (59.1)	<0.001
Mean age (yr)	4	52		2	15		47	53	
Topical potency									
Class 1	253 (3.7)	1,370 (45.7)	<0.001	79 (1.4)	21 (23.6)	<0.001	174 (12.7)	1,349 (45.9)	<0.001
Class 2	124 (1.8)	799 (26.6)	<0.001	51 (0.9)	10 (11.2)	<0.001	73 (5.3)	789 (26.8)	<0.001
Class 3	514 (7.5)	843 (28.1)	<0.001	314 (5.6)	16 (18.0)	<0.001	200 (14.7)	827 (28.1)	<0.001
Class 4	1,009 (14.7)	470 (15.7)	0.214	634 (11.4)	19 (21.3)	0.006	375 (27.5)	451 (15.3)	<0.001
Class 5	3,364 (48.9)	473 (15.8)	<0.001	3,003 (53.8)	26 (29.2)	<0.001	361 (26.4)	447 (15.2)	<0.001
Class 6	1,091 (15.9)	187 (6.2)	<0.001	963 (17.2)	8 (9.0)	0.056	128 (9.4)	179 (6.1)	<0.001
Class 7	1,781 (25.9)	181 (6.0)	<0.001	1,623 (29.1)	7 (7.9)	<0.001	158 (11.6)	174 (5.9)	<0.001
Total (n)	6,879	3,001		5,585	89		1,365	2,941	

Values are presented as number (%). AD: atopic dermatitis, TCSs: topical corticosteroids. *Chi-squared test was used for categorical data and Wilcoxon rank-sum test for continuous data. Statistical significance was set at $p<0.05$.

TCSs prescription pattern by prescriber specialty

Non-mid-strength potency TCSs (Classes 1, 2, 6, and 7) were commonly prescribed by dermatologists (42.5%), pediatricians (41.5%), and internists (32.5%). In particular dermatologists prescribed more various potency of TCSs than pediatricians and internists (Fig. 4B).

Prescription patterns of TCSs in AD patients compared with psoriasis

High potency TCSs (Classes 1~3) are more often used in patients with psoriasis than in those with AD. In contrast, moderate-to-low potency TCSs (Classes 4~7) are often used in patients with AD (Table 2).

DISCUSSION

AD is a chronic, relapsing, inflammatory skin disease characterized by severe pruritus[1]. According to a study based on the data from the Korean National Health Insurance, the prevalence of AD in Korea is 9.5% in children under 10 years of age and 1.2% in those over 10 years of age, with an overall prevalence of 1.9% among the Korean population[6]. Therefore, appropriate topical medication is crucial to ensure effective treatment outcomes.

For the past 70 years, TCSs have been one of the most commonly used topical medications for the treatment of various dermatologic diseases, including AD[3]. They are considered first-line anti-inflammatory treatment for acute AD flares[7], with advantages of the availability in varying potencies and formulations. However, the long-term use of TCSs can lead to local adverse effects, such as skin atrophy, striae, rosacea, perioral dermatitis, acne, and purpura[8]. And also, severe systemic side effects, including the suppression of the hypothalamic-pituitary adrenal axis, hyperglycemia, diabetes, and glaucoma, can occur. Awareness and concerns for these side effects leads to the so-called, TCS phobia, which affects treatment compliance and leads to poor outcomes[9,10]. Therefore, it is recommended to apply appropriate potency of TCS; if the skin lesions improve, a less potent TCSs can be prescribed instead. Also, frequency of application can be reduced after sufficient disease control to minimize side effects[8].

TCIs, including tacrolimus and pimecrolimus, inhibit the activation of pro-inflammatory cells, such as T lymphocytes and mast cells. Since TCIs exert targeted anti-inflammatory effects without local or systemic side effects, they are regarded as an appropriate alternative treatment for TCSs in AD patients[5,11]. Furthermore, their safety has been widely recognized in long-term trials worldwide[12]. The most common adverse effects include mild-to-moderate application site reactions, including skin burning, stinging, and pruritus[13]. And these

adverse effects are usually temporary and gradually diminish after a few days with continued treatment. Thus, TCIs have become a safe alternative to short- and long-term maintenance treatment options for pro-active therapy in AD patients[1].

In 2002 and 2004, tacrolimus and pimecrolimus were released in Korea, respectively. It was assumed that the prescription pattern for topical AD medication would change with the advent of TCIs; thus, the investigation was initiated using data from 2002. In Korea, to prevent an excessive burden on households due to expensive medical expenses, the government established a single mandatory NHIS[14]; data pertaining to prescription patterns could be reflected nationwide. Therefore, data from the NHIS were gathered and analyzed.

Upon analyzing the annual changes in prescription patterns, although TCIs were newly introduced, TCSs were still prescribed the most, followed by antibiotics and TCIs. Even though the prescription of TCSs slightly decreased while the use of TCIs slightly increased, the difference was not statistically significant. According to our experience, patients with AD tended to visit hospitals during an acute exacerbation but not commonly for pro-active treatment. In addition, the follow-up loss of patients was greater during the maintenance treatment period rather than during the acute treatment period. Overall, TCSs are relatively inexpensive and effective in managing acute flares[1] and hence, TCSs still remain as the most prescribed topical agents for AD.

When analyzing the prescription pattern according to the type of medical institution, tertiary hospitals exhibited the highest proportion of TCI and topical antibiotics prescriptions, followed by secondary and primary hospitals. In contrast, the proportion of TCS prescriptions showed the reverse trend. This may be due to the higher proportion of patients using TCIs as maintenance therapy in tertiary hospitals, since these institutions treat more chronic patients with severe conditions that are difficult to manage in primary and secondary hospitals. And higher proportion of severe AD patients with complications such as secondary skin infection in tertiary hospitals may account for higher topical antibiotics prescriptions.

In terms of prescription pattern according to the prescribing physician's specialty, dermatologists prescribed TCIs the most, followed by pediatricians and internists, while this trend was vice versa for TCSs. A higher prescription rate of topical antibiotics was observed among pediatricians, followed by dermatologists and internists. This may be because the prescription for TCIs is covered by insurance for AD and vitiligo in the exposed areas; thus, dermatologists who see a higher rate of chronic AD patients are far more likely to be familiar with TCIs. In addition, the higher frequency of antibiotic prescription in pediatric patients is probably because young patients easily scratch skin lesions, thus leading to infected eczema. However, according to recent reports, no evidence supports the concomitant use of topical antibiotics and TCSs[1,7]. Instead, a short course of systemic antibiotics was recommended for treating more extensive infections

When we analyzed the prescription pattern of TCS according to their potency, moderate-to-low-potency TCSs (Classes 5~7) were prescribed the most, whereas the prescription ratio of high potency TCSs (Classes 1~3) gradually decreased. Most physicians are aware of the side effects of TCSs, thus, TCSs of moderate-to-low potency were largely prescribed; this tendency was more pronounced annually.

According to the medical institution, the prescription of TCS potency showed that Class 5 TCSs were mainly used in primary and secondary hospitals, whereas Class 4 TCSs were used in tertiary hospitals. In the case of non-mid-strength potency TCSs (Classes 1~2 and 6~7), tertiary hospitals, in terms of institutions, and dermatologist, in terms of physician specialty, prescribed them the most. Also, dermatologists prescribed TCSs of varied potencies of TCSs. The overall results may be due to more severe and diverse patients in tertiary hospitals and dermatologists are more familiar with prescribing topical medications than other physicians as well as prescribing various potencies of TCSs according to the severity and area of skin lesions.

We also compared the prescription patterns of TCSs in AD patients with psoriasis, since it is a chronic inflammatory skin disorder caused by immunologic imbalance that requires topical medications for appropriate treatment[15]. Compared with psoriasis patients, moderate-to low-potency TCSs (Classes 4~7) were usually prescribed in AD patients. In contrast, high potency TCSs (Classes 1~3) were mostly prescribed to psoriasis patients. This is because psoriasis exhibits thicker, scalier skin lesions than AD. Thus, many topical treatments for psoriasis include Vitamin D analogs and topical keratolytics, which are helpful in blocking keratinocyte proliferation and thus alleviating hyperkeratotic lesions[16]. Furthermore, since typical AD also occurs in flexural areas[17] requiring low-potency TCS treatment, the overall potency may be relatively lower than

that of psoriasis.

Although TCSs are effective treatments for AD, many patients undergo TCS phobia, as described previously. A previous study revealed that 67.5% of parents of patients with AD showed TCS phobia and especially, parents of children with severe AD requiring long-term topical treatment showed higher TCS phobia[9]. TCIs do not exhibit the same side effects of TCS and thus can be good topical treatment alternatives. Currently, TCIs are mainly used by dermatologists and in tertiary hospitals. In the future, all types of medical institutions and physicians will need to promote the use of TCIs in these patients to efficiently and safely control AD.

To date, most studies have focused on the efficacy and side effects of topical agents in AD. However, we conducted this study to analyze the prescription patterns and trends of topical medications in order to establish treatment strategies and to provide directions to all physicians treating AD patients.

In conclusion, we confirmed that the prescription pattern of topical medications changed over time, which showed different trends according to institutional use and physician's specialty. Among these, TCSs were still the most prescribed topical agents, while tertiary hospitals and dermatologists had higher prescription rates of TCIs than other institutions and physicians. Since AD is a chronic, relapsing disease, physicians of all institutions and departments should be aware of the importance of using TCIs as pro-active and maintenance treatment for AD patients, as well as managing acute flares using TCSs. Currently, new topical agents, such as phosophodiesterase-4 and Janus kinase inhibitors, are emerging; thus, the prescription patterns of topical medications will become more complicated and diverse in the future[18]. Therefore, to provide effective and safe treatment options for AD patients, more constructed topical treatment prescription algorithms are needed.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

FUNDING SOURCE

This work was supported by the project program of the Korean Atopic Dermatitis Association in 2017.

DATA SHARING STATEMENT

The data that support the findings of this study are openly available in National Health Insurance Sharing Service (NHISS) at https://nhiss.nhis.or.kr

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REFERENCES

1. Kim JE, Kim HJ, Lew BL, Lee KH, Hong SP, Jang YH, et al. Consensus guidelines for the treatment of atopic dermatitis in Korea (Part I): general management and topical treatment. Ann Dermatol 2015;27:563-577.
2. Kang S, Lucky AW, Pariser D, Lawrence I, Hanifin JM. Long-term safety and efficacy of tacrolimus ointment for the treatment of atopic dermatitis in children. J Am Acad Dermatol 2001;44(1 Suppl):S58-S64.
3. Sulzberger MB, Witten VH. The effect of topically applied compound F in selected dermatoses. J Invest Dermatol 1952;19:101-102.
4. Harkins CP, McAleer MA, Bennett D, McHugh M, Fleury OM, Pettigrew KA, et al. The widespread use of topical antimicrobials enriches for resistance in Staphylococcus aureus isolated from patients with atopic dermatitis. Br J Dermatol 2018;179:951-958.
5. Simpson EL. Atopic dermatitis: a review of topical treatment options. Curr Med Res Opin 2010;26:633-640.
6. Kim BK, Kim JY, Kang MK, Yang MS, Park HW, Min KU, et al. Allergies are still on the rise? A 6-year nationwide population-based study in Korea. Allergol Int 2016;65:186-191.
7. Eichenfield LF, Tom WL, Berger TG, Krol A, Paller AS, Schwarzenberger K, et al. Guidelines of care for the management of atopic dermatitis: section 2. Management and treatment of atopic dermatitis with topical therapies. J Am Acad Dermatol 2014;71:116-132.
8. Coondoo A, Phiske M, Verma S, Lahiri K. Side-effects of topical steroids: a long overdue revisit. Indian Dermatol Online J 2014;5:416-425.

9. Li AW, Yin ES, Antaya RJ. Topical corticosteroid phobia in atopic dermatitis: a systematic review. JAMA Dermatol 2017;153:1036-1042.
10. Lee JY, Her Y, Kim CW, Kim SS. Topical corticosteroid phobia among parents of children with atopic eczema in Korea. Ann Dermatol 2015;27:499-506.
11. de Paulis A, Stellato C, Cirillo R, Ciccarelli A, Oriente A, Marone G. Anti-inflammatory effect of FK-506 on human skin mast cells. J Invest Dermatol 1992;99:723-728.
12. Munzenberger PJ, Montejo JM. Safety of topical calcineurin inhibitors for the treatment of atopic dermatitis. Pharmacotherapy 2007;27:1020-1028.
13. Lebwohl M, Gower T. A safety assessment of topical calcineurin inhibitors in the treatment of atopic dermatitis. MedGenMed 2006;8:8.
14. Jeong HS. Korea's National Health Insurance--lessons from the past three decades. Health Aff (Millwood) 2011;30:136-144.
15. Michalek IM, Loring B, John SM. A systematic review of worldwide epidemiology of psoriasis. J Eur Acad Dermatol Venereol 2017;31:205-212.
16. Armstrong AW, Read C. Pathophysiology, clinical presentation, and treatment of psoriasis: a review. JAMA 2020;323:1945-1960.
17. Hüppop F, Dähnhardt-Pfeiffer S, Fölster-Holst R. Characterization of classical flexural and nummular forms of atopic dermatitis in childhood with regard to anamnestic, clinical and epidermal barrier aspects. Acta Derm Venereol 2022;102:adv00664.
18. Nygaard U, Deleuran M, Vestergaard C. Emerging treatment options in atopic dermatitis: topical therapies. Dermatology 2017;233:333-343.