〈論文〉

The effects of cold compresses on itching in patients with atopic dermatitis: A cross-over controlled pilot trial

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Abstract - This cross-over controlled trial aimed to evaluate the effectiveness and safety of two types of cold compresses (towels and ice packs) in alleviating itching among patients with atopic dermatitis. The study recruited 19 participants diagnosed with atopic dermatitis and suffering from chronic itching for over 6 months. Each participant received both types of cold compress interventions. Itching sensations were assessed repeatedly using a visual analogue scale before and after the application of the cold compress. The mean and standard deviation of itching scores for the towel intervention were 16.9 ± 19.1 (baseline) and 11.4 ± 16.1 (post-application). For the ice pack intervention, the scores were 13.6 ± 14.7 (baseline) and 6.2 ± 9.8 (post-application). Although there was a reduction in mean itching scores following the application of cold compresses, the differences were not statistically significant for either intervention. Despite the lack of statistical significance, this study suggests that cold compresses, which are user-friendly and inexpensive, may safely reduce subjective itching in patients with atopic dermatitis without causing pain or discomfort. However, further research with a larger sample size is needed to confirm these findings.

Keywords: Atopic Dermatitis, Pruritus, Cryotherapy, Quality of Life, Skin Temperature

1. Introduction

The prevalence of atopic dermatitis (AD) has been estimated at around 10% of the world population [1] with the incidence and prevalence of AD increasing over the past several decades [2, 3]. AD is the 15th most common non-fatal disease, the skin disease that requires the greatest utilization of medical care, and the skin disease with the highest disease burden in terms of disability-adjusted life years [3]. Although AD itself is not considered a serious, life-threatening disease, the persistent itching brought on by AD can significantly impair patients' quality of life by causing difficulty concentrating, disturbing sleep, and in some cases making it difficult to build interpersonal relationships [4]. Scratching usually reduces the itching sensation in the short term but induces an even stronger itching in AD patients, known as an itch-scratch cycle [5]. To break this itch-scratch cycle, control of the itching is essential for the treatment of AD [6].

Currently, it is generally accepted that sensory stimulation, such as thermal stimulation and pain, relieves itching by inhibiting either primary afferents or second-order neurons [7]. Several previous studies have reported that alternate hot-cold stimulation and pain relieve itching [7-9]. Cold compresses are relatively inexpensive, safe, and easy to implement; thus, this intervention is widely used in self-care and home care for sprains and as comfort for fevers. Skin pain and frostbite are possible but not life-threatening adverse side effects of cold compresses. Applying cold stimuli may require additive attention to AD patient per their vulnerable skin abrased by constant scratch [10]. Hot and painful stimuli could also theoretically reduce itching, but are considered ineffective because these would exacerbate inflammation post-stimulation [11, 12].

Most previous studies on itching reduction, such as one by Bromm et al [13], artificially induced itching with histamine and subsequently tested the effectiveness of cooling in healthy population. Only few studies have examined if cooling alleviate itching in patients with AD. Therefore, this pilot study aims to test if cold compresses can safely relieve itching in people with AD.

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2. Materials and Methods

This study employed convenience sampling by recruiting through poster displays in hospitals, universities, and referrals from university faculty. The inclusion criteria were as follows: (1) physician-diagnosed atopic dermatitis; (2) self-reported chronic itching persisting for > 6 months, (3) absence of severe comorbidities; and (4) age ≥ 18 years. Participant recruitment occurred between July 10 to October 1, 2018.

For estimation of the effect size based on the Cohen formula, the researcher used the VAS score for a normal itching, which was measured in an interview survey for students with AD conducted by the author in 2017 as a preliminary experiment [14]. The mean value and standard deviation of normal itching scores were obtained, and it was estimated that the scores would be at least be halved by the interventions used in this study. As a result, the calculated effect size was 1.0. The required number of participants was estimated from an effect size of 1.0, a power of 80%, and a significance level of 5%. As a result of inputting these values into G* power [15], the required number of samples was 17.

A total of 19 participants met the inclusion criteria (n = 10 via direct recruitment, n = 9 via referrals). The participants comprised 14 females and 5 males, with a mean age of 28.3 years (range: 19-75 years).

Consent was obtained by oral and written forms from all participants. This study was approved by the Department of Nursing Ethic Committee of Okayama University Graduate School of Health Sciences (D18-01) and registered to the University Hospital Medical Information Network intervention study in October, 2023 (UMIN000052653).

Design and protocols. The primary outcomes, itching sensations and skin temperature, were repeatedly measured using a cross-over controlled design. We used two types of cold compresses towels and ice packs (the intervention using towels will henceforth be referred to as intervention A and the intervention using ice packs as intervention B). All subjects underwent two cold compress interventions. The material used as the initial cold compress was randomly assigned in order to limit any influence based on the order of use.

The experiment consisted of 5 phases (see Figure 1): the phase 1 measured participant baseline data. In phase 2, a room-tempered compress was placed on the participant arm for five minutes. After a 5-minute interval (phase 3), one of the cold compresses was placed for five minutes (phase 4). The participants remained on the bed for the next 15 minutes while their vital signs were monitored (phase 5). Between the two interventions, an interval time of at least three hours was allocated to avoid any layover effects.

Interventions. In intervention A, a 35×80 cm 100% cotton face towel soaked to a weight of 200 grams was used as the cold compress. The towel for phase 2 was kept at the room temperature ranged 24 and 26 ℃, while the one for phase 4 maintained at between 0 and 1 ℃. The towel was folded into a 140×80 mm size, the same dimensions as the ice pack (see Figure 2A and 2A').

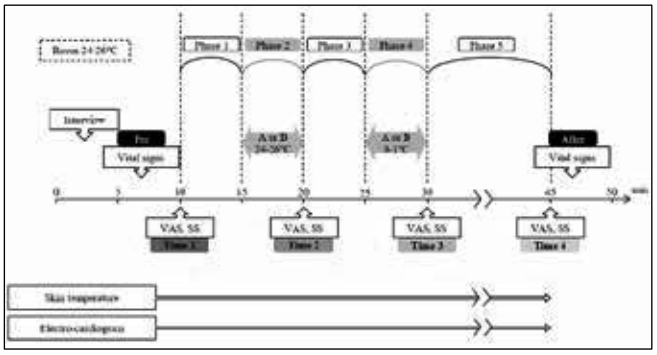

Figure 1: The protocol of intervention. Before the experiment, the researcher interviewed participants and measured baseline data. Phase 1 measured the baseline electrocardiogram and skin temperatures for five minutes. In phase 2, a room-tempered compress was placed on the participants for five minutes. After a five minutes interval (phase 3), a cold compress was set for five minutes as phase 4. The participants stayed on the bed for the next 15 minutes, and vital signs were measured. The room temperature was maintained between 24 and 26 ℃ by air conditioning. VAS: visual analogue scale; SS: subjective sensations; Time1 = baseline; Time2 = immediately after phase 2; Time3 = immediately after phase 4; Time4 = immediately after phase 5.

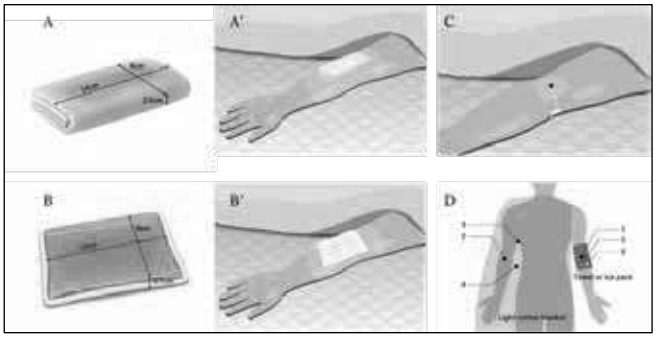

Figure 2: The two materials included in the cold compress and measurement probe fixation method and temperature measurement sites. (A) The face towels were sized 35×80 cm which were then folded into 140×80 mm, the same size as the ice pack. (B) The ice pack was filled with sodium carboxymethyl cellulose, water, glycerin, and sodium chloride. The ice pack was non-freezing. (A') Towel usage. The towel was placed and fitted by a net dressing (Pressnet®, ALCARE, Tokyo, Japan). (B') Ice pack usage. The ice pack was placed and fitted by a net dressing (Pressnet®, ALCARE, Tokyo, Japan). (C) The item that sensed temperature was a fixed film dressing with the probe fixed by surgical tape. (D) Six points of temperature monitoring: (1) cubital fossa on the cooling side, (2) cubital fossa on the control side, (3) axilla on the control side, (4) on the bed surface, (5) axillary side of the cooling material surface, and (6) distal side of the cooling material.

In intervention B, an ice pack filled with non-freezing material consisted with sodium carboxymethyl cellulose, water, glycerin, and sodium chloride weighing 100 grams was used as the cold compress. The ice pack temperature for phase 2 was kept at room temperature, and the one for phase 4 the temperature was maintained at 0 – 1 ℃. The ice pack was wrapped with cotton gauze to avoid creating any adverse skin effects (see Figure 2B and 2B').

Data collection. The Japanese Version of the Patient Oriented-Scoring of Atopic Dermatitis (PO-SCORAD) assessed severity of AD. The range of PO-SCORAD is 0 - 103.6 and higher value indicates poor condition. This self-evaluation tool for AD was proposed by the European Task Force on

Atopic Dermatitis in 2011 and a multicenter study has proven that the SCORAD score completed by doctors and patients are correlated [16].

The VAS measures itching, coldness, pain, and discomfort with each domain ranging from 0 as a complete absence to 100 as the strongest sensation. Although VAS has previously been recognized as a valid tool for assessing pain, Reich's study reported its applicability for itching [17]. The VAS was measured four times in total: before phase 1 and immediately after phases 2, 4, and 5. The primary endpoint of this study was to compare the VAS value for itching at Time 1 with those Time 3 and Time 4.

This study monitored temperatures at six locations: (1) cubital fossa on the cooling side, (2) cubital fossa on the control side, (3) axilla on the control side, (4) on the bed surface, 5) axillary side of cooling material surface, and 6) distal side of cooling material (see Figure 2C and 2D). An LT-8® thermometer (Gram Corporation, Saitama, Japan) was used to record the temperatures, and the mean score was used for analysis. Also, subjective sensations were measured four times in total: before phase 1 and immediately after phases 2, 4, and 5.

Data analysis. To compare the differences in the severity of AD among participants and experimental environments (e.g., room temperature and humidity), a Wilcoxon rank sum test was used. For the main outcome variable analysis, a Friedman's test and a Wilcoxon signed-rank test with Bonferroni correction test were used to test changes in the severity of the itching, coldness, pain, and discomfort. To detect the changes in vital signs (e.g., body temperature, blood pressure, and heart rate), a Wilcoxon singed rank test was used. The critical value was set at .05, and all analyses and mapping were conducted using R version 4.2.3 (R Project for Statistical Computing).

3. Results

Sixteen of the 19 participants (84.2%) reported AD onset prior to elementary school enrollment and a long history of itching. The Table1 reports characteristics of participants. Regarding disease severity, the majority of participants were categorized as having mild to moderate AD, with a minority classified as severe. There were no statistically significant differences in temperature and humidity between the two intervention environments.

The table 1 reports individual and summary scores of PO-SCORAD and changes of VAS of itching. In intervention A using towels, the mean and standard deviation of the itching in VAS was 16.9 ± 19.1 (Time 1), 11.6 ± 15.7 (Time 2), 11.4 ± 16.1 (Time 3), and 7.7 ± 9.2 (Time 4). In intervention B using ice packs, the mean and standard deviation of the itching in VAS was 13.6 ± 14.7 (Time 1), 12.4 ± 13.7 (Time 2), 6.2 ± 9.8 (Time 3), and 7.2 ± 8.5 (Time 4). Friedman's test revealed significant differences in itching for the towel ($p = 0.006$, effect size = 0.23) and ice pack interventions ($p = 0.005$, effect size = 0.23) over the four-time points. However, further analysis using the Wilcoxon signed-rank test with Bonferroni correction did not show a significant difference in efficacy between the four-time points in the two interventions, respectively. We then compared the effect of the cold compress between Time1 and Time 3 (intervention A: $p = 0.003$; intervention B: $p = 0.001$). The relation between the presence of itching at baseline and the effect of cold compress was analyzed using Fisher's exact test (see Figure 3). The VAS values for pain were low, although there was significant difference during cooling ($p = 0.023$, $p = 0.0383$, interventions A and B, respectively).

In both interventions, the heart rate was significantly lower after the experiments ($p = 0.004$, $p = 0.003$, in interventions A and B respectively). Skin temperature, in-bed climate, and temperature of the materials used were measured to note any differences in the respective temperatures in the two interventions (see Table 2).

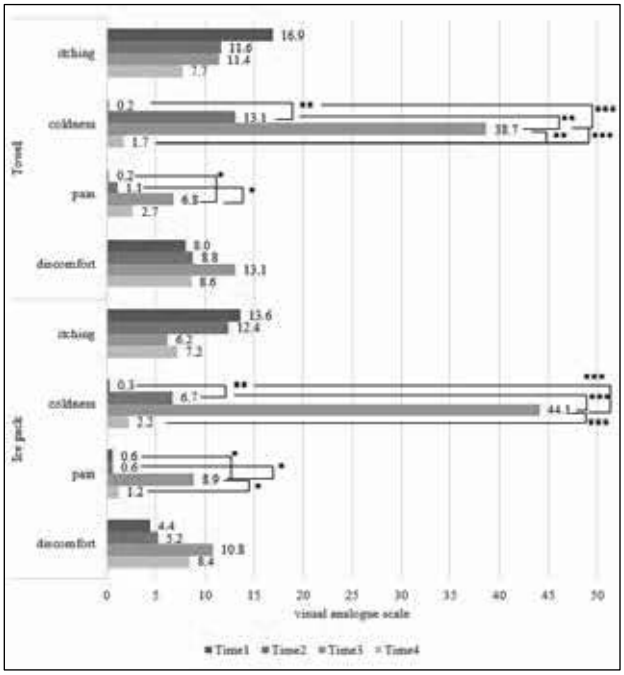

Figure 3: The changes in subjective sensations of atopic dermatitis patients during the interventions. The numbers next to the graph are mean. Time1= baseline; Time2 = just after control; Time3= just after cooling; Time4 = 15 minutes after cooling. A Friedman's test and a Wilcoxon signed rank test with Bonferroni correction test were used to test changes in the severity of the itching, coldness, pain, and discomfort. * $p < 0.05$: ** $p < 0.01$: *** $p < 0.001$.

4. Discussion

Contrary to our hypothesis that cold compresses would reduce itching in AD, this study indicated an insignificant reduction in itching. One possible reason is that many participants reported only a mild itching at Time 1 (Table 1). The itching at Time 1 was milder than anticipated, resulting in a smaller change in itching. This may have prevented the detection of a statistically significant difference with the number of subjects in this study. Both cold compress modalities (towels and ice packs) significantly reduced mean itching scores from baseline to the final measurement (Δ = -5.5 and -7.4, respectively; see Figure 3). These changes indicate that the subjective sensation of the itching was alleviated by the cold compress. Theoretically, the perception of itching starts when an itch-causing substance, or pruritogen, enters through the stratum corneum and binds to its receptors on sensory afferent nerves, or C-fibers,

Table1 Characteristics of participants and status of interventions

Age	Sex	Treatment	Cold compress	PO-SCORAD	VAS of itch (0-100) Time 1	Time 2	Time 3	Time 4
22	F	TS	T	43.0	72	58	66	26
			IP	43.0	42	42	8	14
23	F	TS, AH	T	36.5	38	8	7	2
			IP	33.7	8	10	1	0
33	F		T	51.6	37	26	14	26
			IP	51.6	34	32	5	23
32	F	TS, CI,	T	36.1	32	19	15	0
		ciclosporin	IP	33.1	17	11	0	11
20	F		T	38.1	30	40	24	18
			IP	45.7	42	45	36	25
21	F	TS, M	T	38.2	27	23	27	20
			IP	35.3	32	13	12	0
20	F	TS, AH	T	29.0	22	5	4	3
			IP	28.6	13	18	3	5
20	M		T	43.8	20	11	8	15
			IP	39.2	27	16	7	12
20	F	TS, M	T	42.3	15	8	4	3
			IP	47.5	17	17	28	3
20	F	TS	T	26.4	11	12	3	5
			IP	23.0	4	5	0	4
34	F	TS	T	19.1	10	5	2	0
			IP	16.8	8	3	3	0
19	M	TS, M	T	29.4	5	3	2	1
			IP	32.9	0	0	0	0
21	M	TS, M	T	43.5	2	3	27	4
			IP	56.9	7	9	6	3
23	M	TS, M	T	31.0	0	0	0	11
			IP	31.0	4	6	5	7
61	F	TS, M	T	36.9	0	0	13	13
			IP	30.4	2	0	0	5
75	F	TS, M	T	36.9	0	0	0	0
			IP	36.9	2	1	2	1
19	F	TS, AH	T	19.2	0	0	0	0
			IP	25.5	0	0	0	0
19	F	TS, M	T	6.4	0	0	0	0
			IP	5.3	0	0	0	0
36	M	TS, HM	T	41.5	0	0	0	0
			IP	42.9	0	8	2	23
			Mean(T)	34.2	16.9	11.6	11.4	7.7
			Mean(IP)	34.7	13.6	12.4	6.2	7.2

The participants are displayed in the order which the itch at the start was strongest. PO-SCORAD = patient-oriented score of atopic dermatitis; VAS = visual analogue scale; time 1= baseline; time 2 = immediately after control; time 3 = just after cooling; time 4 =15 minutes after cooling; TS = topical steroid; AH= antihistamine; CI = calcineurin inhibitors; M = moisturizer; HM = herbal medicine; T = towel; IP = ice pack.

Table2 Comparison of temperature changes between the two types of cold compresses

Item	Cold compress	phase 1 (℃) (Mean ± SD)	p-value	phase 2 (℃) (Mean ± SD)	p-value	phase 4 (℃) (Mean ± SD)	p-value	phase 5 (℃) (Mean ± SD)	p-value
Skin Temperature									
Cubital fossa (cooling side)	Towel	34.4 ± 0.6	0.33	32.7 ± 0.8	0.001	24.6 ± 1.6	0.44	32.8 ± 0.7	0.81
	Ice pack	34.3 ± 0.6		33.3 ± 0.5		25.0 ± 2.0		32.7 ± 0.8	
Cubital fossa (control side)	Towel	34.6 ± 0.8	0.37	34.9 ± 0.7	0.84	35.0 ± 0.6	0.73	35.1 ± 0.5	0.37
	Ice pack	34.7 ± 0.7		34.8 ± 0.7		34.9 ± 0.7		34.9 ± 0.7	
Axilla (control side)	Towel	35.8 ± 0.4	0.83	36.0 ± 0.4	0.75	36.2 ± 0.4	0.47	36.3 ± 0.4	0.36
	Ice pack	35.9 ± 0.5		36.0 ± 0.4		36.2 ± 0.4		36.3 ± 0.4	
Temperature of bed (climate)									
	Towel	30.1 ± 0.9	0.46	31.2 ± 1.1	0.49	32.2 ± 1.2	0.73	32.6 ± 1.1	0.21
	Ice pack	30.2 ± 1.1		31.1 ± 1.2		32.0 ± 1.1		32.3 ± 1.2	
Temperatures of cooling materials									
Skin side	Towel			31.3 ± 0.7	0.015	19.8 ± 1.8	0.70		
	Ice pack			31.8 ± 0.6		19.9 ± 2.5			
Exterior	Towel			26.1 ± 0.6	< 0.001	9. 8± 1.4	0.19		
	Ice pack			27.5 ± 0.8		10.5 ± 3.7			

This study monitored temperatures at six locations: (1) cubital fossa on the cooling side, (2) cubital fossa on the control side, (3) axilla on the control side, (4) on the bed surface, (5) axillary side of cooling material surface, and (6) distal side of cooling material. An LT-8® thermometer (Gram Corporation, Saitama, Japan) was used to record the temperatures, and the mean score was used for analysis. A Wilcoxon singed rank test was used to compare the differences in temperatures. SD = standard deviation.

which transmit the resulting signal to the central nervous system, where the brain interprets it as an itching sensation [18]. The cold stimulus may inhibit primary or secondary afferents, thereby reducing the itching [7]. Additionally, when applying the wet towel compress, we observed a swift reduction from 16.9 to 11.6 between Times 1 and 2 while the ice pack compress was reduced by only 1.1 as a mean score. It can be assumed then that a mild cold compress would produce ample effects in reducing the itching and avoiding possible adverse reactions, such as frostbite.

The optimal temperature range for itching alleviation in AD remains undetermined. Fruhstorfer et al. reported reduced itching when AD patients immersed their arms in 10 ℃ water; however, post-intervention skin temperatures were not documented [19]. Separate research has indicated that maintaining cutaneous temperatures below 25 ℃ decreases sensory transmission rates [20]. In our study, interventions reduced skin temperatures to approximately 25℃. These findings suggest that a 2 ℃ reduction in cutaneous temperature may be sufficient to mitigate itching in AD patients.

Temperatures outside the range of 15 – 45 ℃ are typically perceived as nociceptive stimuli, despite the rapid adaptation of thermoreceptors within this range [21]. In our study, mean skin temperatures during cold compress application were 24.6 ℃ and 25.0 ℃ for interventions A and B, respectively (Table 3), providing a tolerable thermal stimulus for participants. Transient mild pain was reported by 5 and 6 participants in interventions A and B, respectively, resolving within 15 minutes post-intervention. Subjective discomfort ratings were minimal and showed negligible change over time (Figure 3). These findings suggest that both wet towels and ice packs effectively mitigate itching without inducing significant pain or discomfort.

Clinical applications

While this study demonstrates the efficacy of wet towel cold compresses in itching mitigation, it further suggests that effective itching management in AD patients can be achieved without reliance on refrigeration or cryotherapy equipment. Given that AD is a chronic condition with substantial impact on quality of life, our findings indicate the potential utility of a self-administered cooling intervention for daily symptom management. This methodology demonstrates potential applicability in regions with limited access to advanced medical facilities or inconsistent power supply, suggesting its utility in resource-constrained environments.

Limitations of the study

This study has several limitations. Primarily, the absence of participants with severe itching at baseline precludes assessment of the intervention's efficacy in this demographic; further investigation is warranted to address this gap. Additionally, the limited sample size impeded analysis of potential age- or sex-related variations in intervention efficacy. Consequently, the generalizability of these findings may be constrained.

5. Conclusion

In subjects with moderate AD, application of cost-effective and user-friendly cold compresses resulted in a reduction of mean and subjective itching scores, albeit not reaching statistical significance. The interventions did not induce notable pain or discomfort, suggesting potential safety for self-administration in patients with moderate AD. While not a randomized controlled trial, this study represents the first interventional investigation of cold compress efficacy in AD patients.

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