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Effect of a new cryotherapy device on an itchy sensation in patients with mild atopic dermatitis

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Abstract

Background: The existence of an itchy sensation is a common complaint in patients with atopic dermatitis. More therapeutic modalities to address the itchy sensation in atopic dermatitis are still required.

Objective: We sought to assess the effect of a new cryotherapy device on the itchy sensation experienced by patients with atopic dermatitis.

Methods: A total of 28 patients with mild to moderate atopic dermatitis participated in this study. A split-body clinical trial was conducted for 2 months, where one side of each participant was treated with the novel cryotherapy device, and the other side of each participant was observed as a control. The cryotherapy device was set to −5°C and applied for five seconds. We evaluated the visual analog scale (VAS) score for itch at 10, 30, and 60 minutes and at 1, 2 and 8 weeks after cryotherapy application. In addition, the level of patient satisfaction and adverse events were evaluated every visit.

Results: On the day immediately after treatment, the VAS score for itch in the treated-side group was lower following cryotherapy application than as compared within the control-side group. Further, the VAS score for itch in the treated-side group at baseline (before treatment) was higher than at 1, 2 and 8 weeks after treatment. The proportion of patients reporting good or excellent satisfaction was 14.3%. No serious adverse events were recorded.

Conclusions: The novel cryotherapy tested herein may be a valuable antipruritic therapeutic remedy in patients with atopic dermatitis.

KEYWORDS

atopic dermatitis, cryotherapy, itch

1 | INTRODUCTION

Atopic dermatitis is a chronic complex and multifactorial eczematous disorder.[1] Due to its increasing prevalence, atopic dermatitis has grown to become a significant health issue in Korea and across the world.[1,2] Patients with atopic dermatitis seem to show both objective signs and subjective symptoms.[2] Meeting the therapeutic goals of atopic dermatitis requires a multistep approach, focusing on reducing the itchy sensation, and establishing disease control.[2] A variety of therapeutic modalities can be considered to control atopic dermatitis.[2-6] Nevertheless, the treatment of atopic dermatitis remains challenging, especially in patients with a moderate to severe condition.

An itchy sensation is a common complaint in individuals affected by atopic dermatitis.[7] Various mediators are implicated in the

appearance of chronic itch associated with atopic dermatitis,[8] with prior research reporting transient receptor potential ion channels (TRPA1 and TRPV1), protease-activated receptor 2 (PAR2), gastrin-releasing peptide receptor, and Mas-related G protein receptor to all be involved in the pathogenesis of this phenomenon.[8,9] A variety of cytokines and chemokines, such as thymic stromal lymphopoietin, interleukin (IL)-2, IL-4, IL-13, and IL-31, are correlated with chronic pruritus.[8,10] In addition, the interplay of epidermal barrier dysfunction, immune dysregulation, and activation of the central nervous system leads to the itch sensation in atopic dermatitis.[8] Therapeutic modalities for the itchy sensation in atopic dermatitis include moisturizers, topical and systemic immunomodulators, and neural desensitizers.[8,11,12] Localized warming and cooling therapies are also therapeutic modalities to address the itchy sensation in patients with atopic dermatitis.[13] Among other examples of this treatment approach, a 24°C plate has been used to cool down the skin.[14] In the present study, we used a new cryotherapy device to freely set the temperature from −20°C to 10°C for cooling the skin of patients with atopic dermatitis.

2 | MATERIALS AND METHODS

2.1 | Participants

Eligible subjects were enrolled according to the study inclusion and exclusion criteria. Specifically, we included subjects with mild-to-moderate atopic dermatitis suggested by an Eczema Area Severity Index score of less than 13 points. On the other hand, we excluded individuals who were pregnant, nursing, or hypersensitive to cold temperatures. We also excluded those who had been treated with systemic steroids or antihistamines within the previous 4 weeks or with topical steroids or antibiotics within the previous 2 weeks. The concurrent usage of other drugs within the study period was prohibited. A total of 28 participants (22 males and 6 females) aged 19-62 years (mean age: 29.0 ± 9.0 years) participated in this study.

2.2 | Methods

2.2.1 | A new cryotherapy device

A cryotherapy device was made to precisely control the refrigerant gas temperature from −20°C to 10°C with liquid CO_2.

2.2.2 | Study design for the clinical trial of the cryotherapy device

A split-body clinical trial was conducted for 2 months. One side of each participant was treated with the cryotherapy device and the other side of each participant was observed as the control. The cryotherapy device was set to −5°C for application for five seconds once a week for a total of 8 weeks. This study was performed after approval was gained from the Institutional Review Board of Kyungpook National University Hospital (IRB no. KNUH 2020-09-019). A written informed consent form was signed by participants before their inclusion into this study.

2.2.3 | Measurement

We recorded visual analog scale (VAS) scores for itch at 10, 30, and 60 minutes and at 1, 2 and 8 weeks after cryotherapy. In addition, the degree of patient satisfaction and the occurrence of any adverse events were evaluated at each visit.

2.2.4 | Patient satisfaction

Patient satisfaction was assessed with a five-point questionnaire, where the potential answers included worse, poor, moderate, good, and excellent.

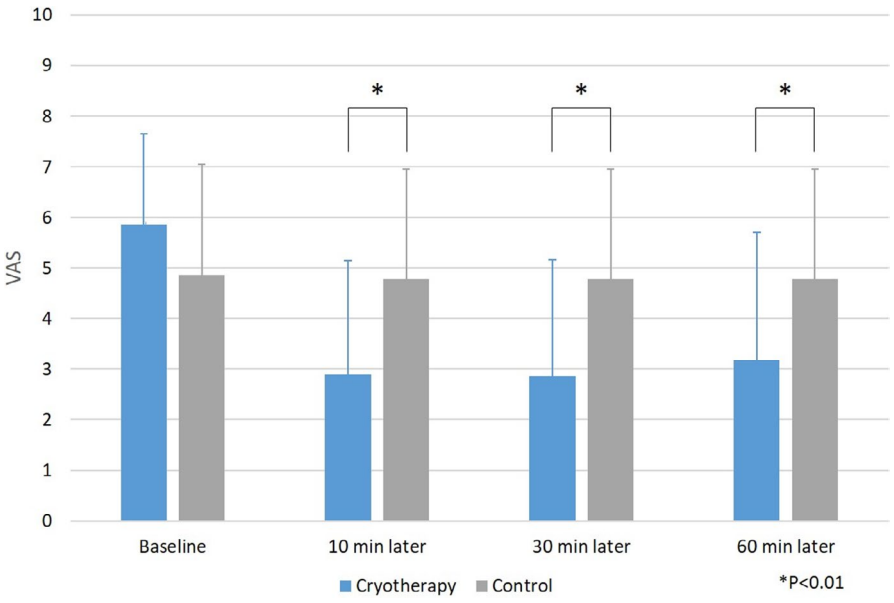

FIGURE 1 VAS scores for itch in the treated-side group were lower following treatment with the cryotherapy device than in the control-side group without treatment. VAS score comparisons for the treated-side group vs the control-side group are as follows: 5.86 ± 1.80 vs 4.86 ± 2.19 points at baseline, 2.89 ± 2.25 vs 4.79 ± 2.17 points at 10 min, 2.86 ± 2.31 vs 4.79 ± 2.17 points at 30 min, and 3.18 ± 2.53 vs 4.79 ± 2.17 points at 60 min. Data are presented as mean ± standard deviation (*$P < .01$)

2.2.5 | Adverse events

Adverse events were assessed using an open-ended questionnaire sheet and by an investigator review. Participants commented on subjective adverse events, and the investigator evaluated their objective signs.

2.3 | Statistical analysis

Statistical analysis was carried out using the Statistical Package for the Social Sciences (SPSS), version 18.0 (SPSS, Inc). The Student's *t* test was used to identify variations in the VAS score at each visit between the treated and control-side groups. In addition, repeated-measures analysis of variance was used to assess differences in the VAS score over time in each group. A probability value of <.05 was considered to be statistically significant.

3 | RESULTS

3.1 | VAS score for itch between the treated-side and control-side groups

On the first day of treatment, the VAS score for itch in the treated-side group was lower after treatment with the cryotherapy device than in the control-side group; specifically, the comparisons between the treated-side and control-side groups were as follows: 5.86 ± 1.80 vs 4.86 ± 2.19 points at baseline, 2.89 ± 2.25 vs 4.79 ± 2.17 points at 10 minutes, 2.86 ± 2.31 vs 4.79 ± 2.17 points at 30 minutes, and 3.18 ± 2.53 vs 4.79 ± 2.17 points at 60 minutes. Notably, statistically significant differences were apparent between the treated-side and control-side groups at all-time points except baseline (Figure 1).

3.2 | VAS score for itch during the day of cryotherapy in each group

On the first day of treatment, VAS scores for itch in the treated-side group included 5.86 ± 1.80 at baseline, 2.89 ± 2.25 points at 10 minutes, 2.86 ± 2.31 points at 30 minutes, and 3.18 ± 2.53 points at 60 minutes, revealing a decrease in the VAS score following cryotherapy application. Statistically significant differences were noted between the scores at 10 minutes and 30 minutes and that at baseline (Figure 2).

3.3 | VAS score for itch in the weeks following cryotherapy in each group

When considering the longer-term treatment outcomes, VAS scores for itch in the treated-side group were higher at baseline (5.25 ± 1.91 points) than at one (3.18 ± 1.88 points), two (3.50 ± 1.78 points), and eight (2.92 ± 1.51) weeks after treatment. This evaluation was performed using data of 12 patients who participated in the entire 2-month follow-up period. Statistically significant differences were noted between the scores at baseline and the respective weekly time points (Figure 3).

3.4 | Patient satisfaction

Patient satisfaction was assessed at 1 week in the treated-side group, with 53.2% reporting poor, 17.9% reporting mild, 14.3% reporting moderate, 10.7% reporting good, and 3.6% reporting excellent satisfaction, respectively. The combined proportion of patients reporting good or excellent satisfaction was 14.3% (Figure 4).

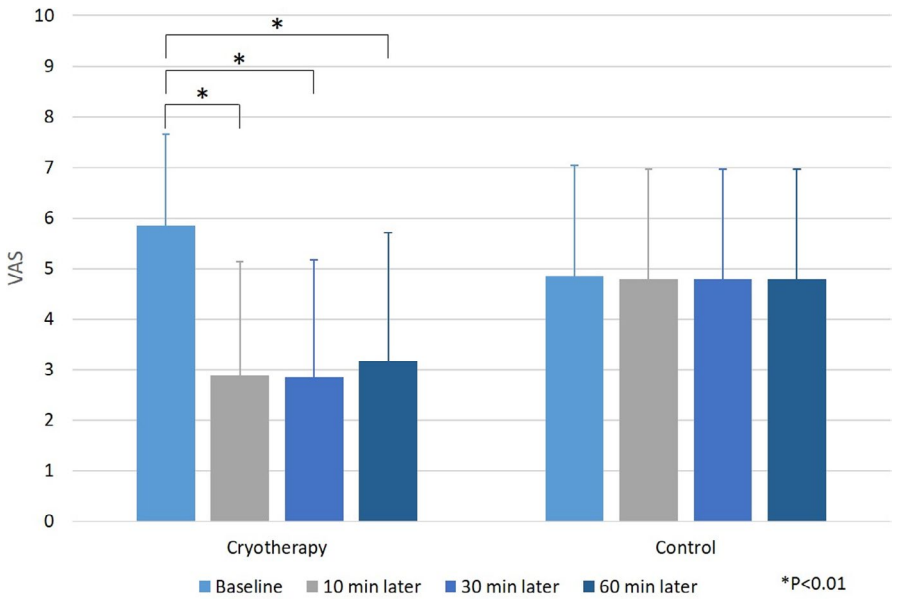

FIGURE 2 VAS scores for itch in the treated-side group was lower after treatment with the cryotherapy device relative to at baseline as follows: 5.86 ± 1.80 at baseline, 2.89 ± 2.25 points at 10 min, 2.86 ± 2.31 points at 30 min, and 3.18 ± 2.53 points at 60 min. Data are presented as mean ± standard deviation (*$P < .01$)

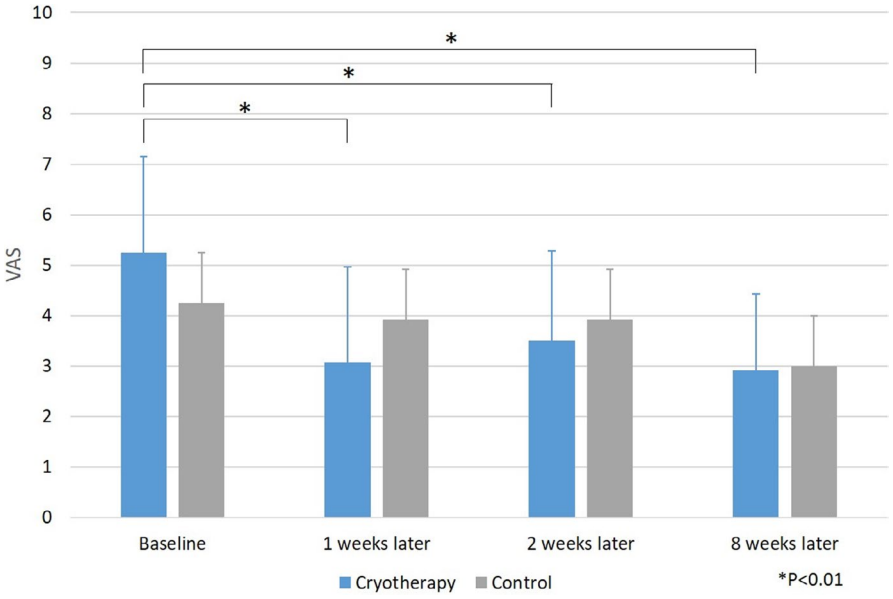

FIGURE 3 VAS scores for itch in the treated-side group at baseline (5.25 ± 1.91 points) were higher as compared with at one (3.18 ± 1.88 points), two (3.50 ± 1.78 points), and eight (2.92 ± 1.51) weeks after treatment. Data are presented as mean ± standard deviation (*$P < .01$)

3.5 | Adverse events

There were no serious adverse events recorded. A dry sensation was reported by two participants, and a tingling sensation was experienced by one participant.

4 | DISCUSSION

Treatments for pruritus in patients with atopic dermatitis include both nonpharmacologic and pharmacologic therapies.[15] Moisturizing lotions and creams have been used as frequent nonpharmacologic therapeutic options to improve the itchy sensation experienced by patients with atopic dermatitis.[16] If this therapy fails, pharmacological therapy including topical and systemic medications can be considered.[17] However, further investigations should be considered to determine how to relieve treatment-resistant pruritus in atopic dermatitis.

Cooling is an effective temporary therapeutic modality able to reduce itch in a variety of itchy dermatologic disorders including insect bites, poison ivy, and atopic dermatitis.[13] On the contrary, cooling can also be a causative factor of itch; it was shown to upregulate endothelial nitric-oxide production, and it has been reported that nitric-oxide mediates serotonin-evoked itch.[18,19] Therefore, cold-induced nitric-oxide production may contribute to the enhancement of serotonin-evoked itch.

The roles of transient receptor potential cation channel subfamily M (melastatin) member 8 (TRPM8) and TRPM8-expressing sensory neurons in the antipruritic effect inherent with cooling have been investigated.[14,20] One study found that cooling of the skin surface from 30°C to 20°C or lower essentially inhibited chloroquine- and histamine-induced itch sensations in mice.[20,21] However, the

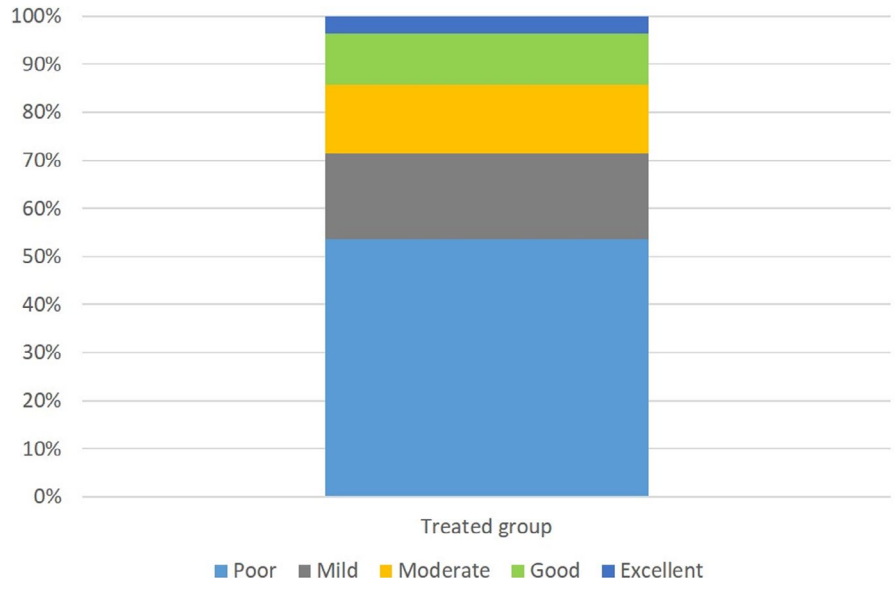

FIGURE 4 Regarding patient satisfaction, 53.2% of patients reported poor, 17.9% reported mild, 14.3% reported moderate, 10.7% reported good, and 3.6% reported excellent

antipruritic effect of cooling in these mice required continuous cold stimulation, which is consistent with findings in human studies.[21] TRPM8 and TRPM8-expressing sensory neurons are associated with the antipruritic effects of mild cooling of 20°C.[20] Cooling to much lower temperatures (≤17°C), which can induce pain, reduced the severity of itchy sensation in a manner independent of TRPM8 and TRPM8-expressing sensory neurons, indicating that a TRPM8-independent cold-sensitive pathway may contribute to thermal sensing at lower temperatures.[20] It has also been suggested that there are cold-sensitive channels other than TRPM8 that could potentially contribute to the cold-driven inhibition of itch.[22-24] Application of the very low temperature of −5°C, which was used for the modulation of pruritus in this study, can induce pain. Nevertheless, cooling to less than the temperature of −5°C blocked itchy sensation in patients with mild to moderate atopic dermatitis. It was reported previously that the effect of temperature modulation on pruritus was limited to appearance within the first 10 minutes after treatment.[13] In this study, however, the antipruritic effect of cooling was maintained for at least 60 minutes. In addition, a long-term effect for multiple weeks of application of the cooling device on the itchy sensation of patients with atopic dermatitis was observed and there were no serious adverse events recorded.

In conclusion, the novel device for cryotherapy assessed herein is a safe and effective antipruritic therapeutic remedy, although the mechanisms of its cooling effect on pruritus remain elusive.

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CONFLICT OF INTEREST

There are no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

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

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