

Therapeutic potential of traditional Korean music, Daegeum Sanjo in atopic dermatitis-like murine model

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ABSTRACT

Atopic dermatitis (AD) is an allergic and inflammatory skin. Recently, the limitations and side effects of drug therapy, and possibility of alternative therapies, such as music therapy are emerging in the treatment of AD. Thus, the present study determined whether traditional Korean music, Daegeum Sanjo, regulates AD symptoms by comparing the rhythm, Jinyangjo-jangdan and Jungmori-jangdan in an AD-like murine model. Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo reduced the duration of scratching behavior increased by DNFB challenge. Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo attenuated clinical symptoms. However, Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo did not inhibit IgE, histamine, interleukin (IL)-4, IL-6, or thymic stromal lymphopoietin levels in serum or AD-like skin lesions. In conclusion, the present study suggests that it is possible for Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo to ameliorate AD symptoms. However, further study is needed to clarify significant mechanisms of Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo therapy for AD symptoms.

Keywords Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo, atopic dermatitis, scratching

INTRODUCTION

Atopic dermatitis (AD) which is characterized by a complex pathophysiology (Bieber et al., 2017) is an inflammatory skin disease that accompanies skin itching (Chan et al., 2001). Chronic skin itching has an important impact on quality of life (Pavlis and Yosipovitch, 2018). AD drugs for the treatment of AD have been developed, but many patients still suffer from AD. Recently, limitations and side effects of drug therapy are emerging in the treatment of AD (Megna et al., 2016). New and evolving therapies can be an alternative to the treatment of this complex disease, AD.

Music has often been used to control and improve health conditions (Biasutti and Concina, 2013). Music therapy has been studied to manage psychological conditions such as stress, and there are strong significant evidences to support therapeutic effects (Degli Stefani and Biasutti, 2016). Kim (2014) reported that traditional Korean music therapy can be used to improve cognitive function, stimulate physical function, help to the emotional function, and enhance social skills. In addition, Kim et al. (2017) reported that Daegeum playing of Arirang might be considered a potential therapeutic intervention for the treatment of depression. The Sound of a Buk (Korean Traditional Drum) attenuated anaphylactic reactions (Kim et al., 2015).

Daegeum has the largest range of notes in wind instruments of traditional Korean music (Ko, 2018). Sanjo music is marked by

the diversity of melodic lines and has diversity of melodic lines, subtlety, and sophisticated rhythmic configurations (Song, 2000). Sanjo consists of a series of rhythmic cycles called jangdan, each of which is based on a slow, moderate, or fast tempo (Kim, 2016). Jangdan which is an essential element of rhythm in Korean music is the most prominent features of Sanjo (Ko, 2018). Jinyangjo-jangdan (4 sets of slow 6 beats) is the slowest rhythm in traditional Korean music. Jungmori-jangdan (12/4) makes the melody feel comfortable with a moderate tempo, but the rhythm can feel like a heartbeat (Ko, 2018). Daegeum Sanjo is a representative traditional forms of Sanjo.

Herein, we investigated a regulatory effect of Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo on AD symptoms in a 2,4-dinitrofluorobenzene (DNFB)-challenged murine model of AD.

MATERIALS AND METHODS

AD model

Acetone (100 µl) was applied to shaved abdominal skins of mice (eight-week-old). A week later, acetone (50 µl) was applied to shaved back skin as a vehicle group four times every three days. For DNFB (Sigma-Aldrich, Inc., St. Louis, MO, USA) sensitization, DNFB (100 µl of 0.15%) in acetone was applied to shaved abdominal skins of mice. A week later, AD-like skin lesions were induced by the repeated application of DNFB (50 µl of 0.15%) in acetone to shaved back skin four times every three days. Simultaneously, mice were exposed to Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo (n = 5 per group). Clinical features were photographed after the last DNFB challenge.

Cytokines assay

Levels of IgE (BD Pharmingen, San Diego, CA, USA), IL-4 (BD

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Pharmingen), IL-6 (BD Pharmingen), or TSLP (R&D Systems, Minneapolis, MN, USA) in serum or skin lesions of AD mice were examined with a sandwich enzyme-linked immunosorbent assay (ELISA) method according to manufacturer's instructions.

Histamine assay

Histamine levels were examined in serum of AD mice with *o*-phthalaldehyde spectrofluorometric procedure.

Statistical analysis

Results are shown as mean ± S.D. Results were analyzed by an independent t-test and ANOVA with Tukey post hoc test (IBM, Armonk, NY, USA). The *p* value < 0.05 was considered statistically significant.

RESULT AND DISCUSSION

Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo suppressed scratching behavior in AD-like murine model

Itching leads to deterioration and chronicity of AD (Yamaguchi et al., 2008). Thus, we evaluated a regulatory effect of Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo on scratching behavior in DNFB-challenged AD mice. DNFB increased the duration of scratching behavior, whereas Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo significantly reduced the

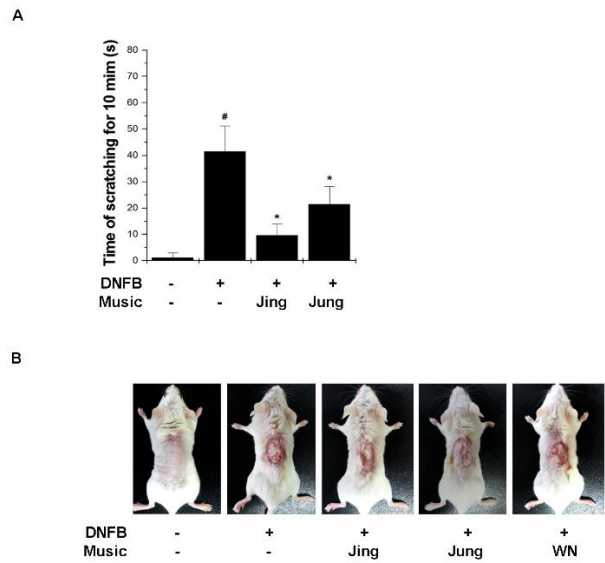


Fig. 1 Scratching behavior in AD mice. (A) The duration of scratching behavior was measured for 10 min. Data are expressed as mean ± S.D. [#]*p* < 0.05; significantly different from vehicle group. ^{*}*p* < 0.05; significantly different from DNFB-challenged group. (B) Each DNFB-challenged skin lesion was photographed. WN, white noise.

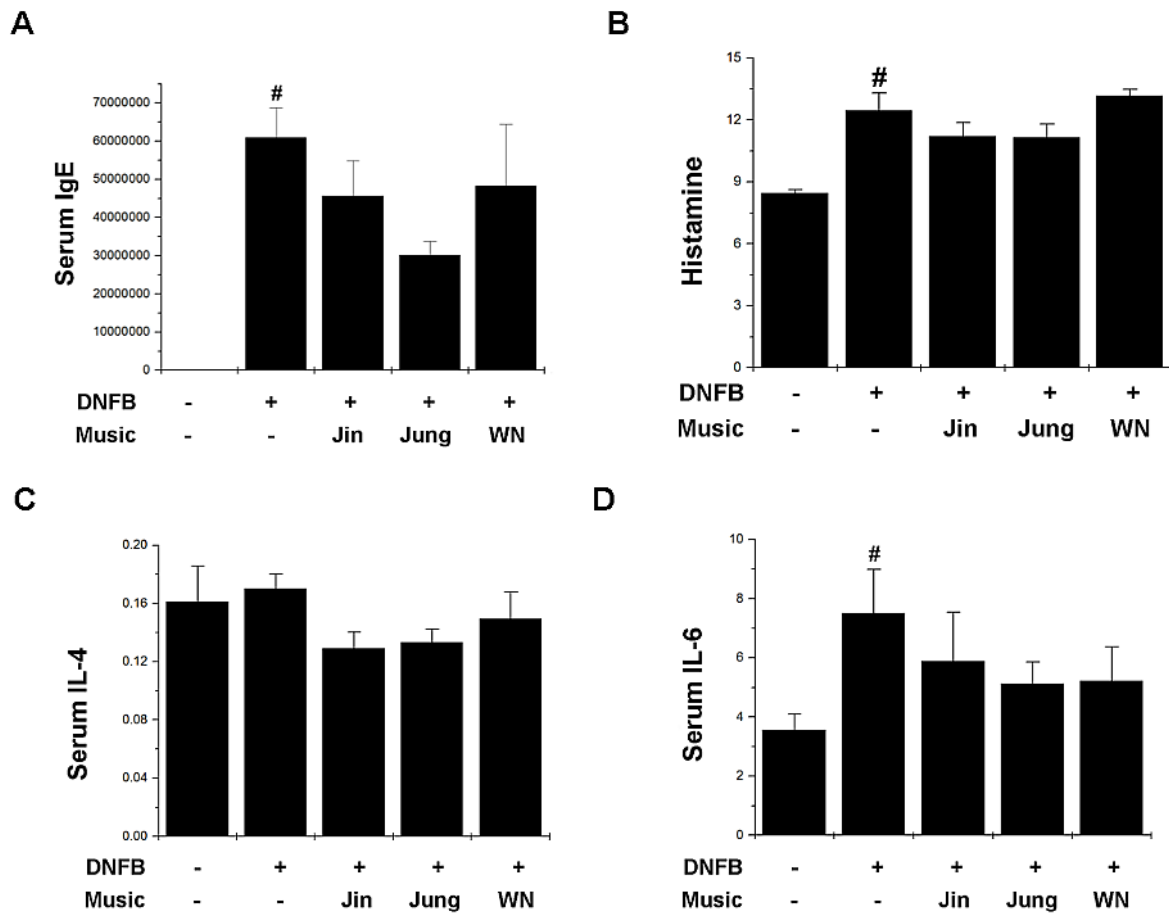


Fig. 2 Atopic inflammatory mediators in serum of AD mice. The levels of serum (A) IgE, (C) IL-4, and (D) IL-6 were measured with an ELISA analysis. (B) The levels of serum histamine were determined according to *o*-phthalaldehyde spectrofluorometric procedure. Data are expressed as mean ± S.D. [#]*p* < 0.05; significantly different from vehicle group. ^{*}*p* < 0.05; significantly different from DNFB-challenged group. WN, white noise.

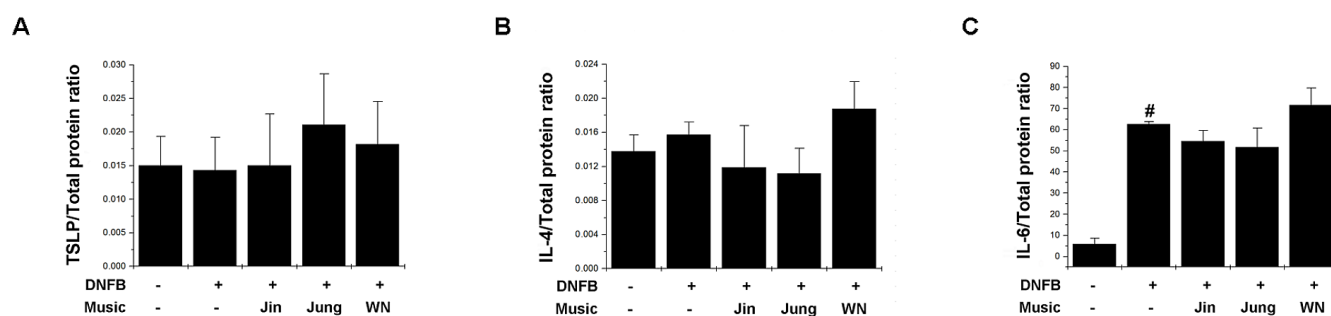


Fig.3 Atopic inflammatory mediators in skin lesions of AD mice. The levels (A) TSLP, (B) IL-4, and (C) IL-6 from AD-like skin lesions homogenates were determined with an ELISA analysis. The levels are expressed as a ratio to total protein levels. Data are expressed as mean \pm S.D. # $p < 0.05$; significantly different from vehicle group. * $p < 0.05$; significantly different from DNFB-challenged group. WN, white noise.

duration of scratching behavior (Figure 1A, $P < 0.05$). Next, we evaluated whether Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo would regulate clinical symptoms in skin lesions of DNFB-challenged AD mice. DNFB induced erythema and hemorrhage in AD-like skin lesions, whereas Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo alleviated the erythema and hemorrhage (Figure 1B). Burrai et al. (2014) reported that live saxophone music reduced pain and itching levels and improved clinical and quality-of-life in patients undergoing haemodialysis (Burrai et al., 2014). Thus, our findings suggest that Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo might be an alternative therapy of AD through down-regulating scratching behavior.

Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo did not suppress atopic inflammatory mediators in AD-like murine model

The pruritogenic factors exert itch responses by activating mast cells to release histamine (Ständer and Steinhoff, 2002). Histamine, IgE, TSLP, IL-4, and IL-6 evoked predominantly itching in mice (Carstens and Akiyama, 2014; Shimada and LaMotte, 2008; Weber et al., 2005; Wilson et al., 2013; Wong et al., 2017). Thus, we measured serum IgE, histamine, IL-4, and IL-6 levels. However, Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo did not show significant reductions in serum IgE, histamine, IL-4, and IL-6 levels increased by DNFB challenge (Figure 2). Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo did not reduce TSLP, IL-4, and IL-6 levels increased by DNFB challenge in skin lesions. (Figure 3). This is due to various factors, such as substance P, as well as these factors in controlling itching in AD (Liu and Ji, 2013). Thus, further research is needed to clarify the significant regulatory mechanisms of Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo on the itching of AD. However, in conclusion, the present study, at least in part, suggests that it is possible for Jinyangjo-jangdan and Jungmori-jangdan of Daegeum Sanjo to ameliorate AD symptoms.

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CONFLICT OF INTEREST

Author have no conflicting financial interests.

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