Progressive Muscle Relaxation Therapy for Atopic Dermatitis: Objective Assessment of Efficacy

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ABSTRACT

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Psychological stress has been reported to play an important role in atopic dermatitis (AD). Psychological interventions have been reported to be effective in managing patients with AD. However, objective assessments of the efficacy of these interventions are lacking.

The goal of our study was to validate the efficacy of relaxation therapy (RT) in patients with AD and to evaluate the serologic parameters that can serve as objective measures of the efficacy of RT.

Twenty-five patients with AD were randomly assigned to either an RT group (n=15) or a control group (n=10). The RT group received one month of treatment consisting of progressive muscle relaxation (PMR) together with conventional treatments, while the control group was treated with only conventional treatments. We measured

psychological stress, including depression, anxiety, interaction anxiousness, and private body consciousness, and clinical severity, including the eczema area and severity index (EASI), pruritus, and loss of sleep (LOS) at baseline and after 1 month in both the RT and control groups. In addition, we evaluated serum levels of nerve growth factor (NGF), neuropeptide Y (NPY), and Th2 cytokines (IL-4, IL-5, and IL-13) at baseline and after 1 month in both the RT and control groups.

At baseline, among the psychological parameters, only anxiety was positively correlated with the pruritus score (state anxiety (SA): R=0.496, p=0.014; trait anxiety (TA): R=0.423, p=0.04). Additionally, serum levels of NPY were inversely related to the state-trait anxiety inventory (STAI) (SA: R=-0.475, p=0.019; TA: R=-0.418, p=0.042) and pruritus scores (R=-0.451, p=0.035) at baseline.

After one month of PMR therapy, the degree of pruritus and loss of sleep (LOS) were significantly decreased only in RT group (p<0.001 for both). SA scores showed significant improvement after treatment only in RT group (p=0.005). There were no significant changes in serologic parameters, including NGF, NPY, and Th2 cytokines in both groups, after treatment.

Although there were no significant changes in serologic parameters after treatment, NPY might be closely related with high levels of anxiety in AD at baseline. PMR might effectively reduce pruritus and LOS in AD patients through reducing anxiety. Thus PMR could be a useful adjunctive modality for the management of AD.

Key words: anxiety, atopic dermatitis, neuropeptide Y, nerve growth factor, relaxation therapy

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I. INTRODUCTION

Historically, many clinicians have considered allergic diseases to be psychosomatic[1]. Furthermore, recent epidemiological studies have demonstrated the detrimental effects of several psychosocial stressors, such as caregiver stress, certain personality types, poor family relationships and negative life events, on the symptoms of allergic disease[2,3]. Among psychological profiles, anxiety, assessed by the state-trait anxiety inventory (STAI), is strongly related to atopic dermatitis (AD)[4-6]. In a previous study, we also found that anxiety was higher in patients with AD than in healthy controls[7].

As clinical evidence regarding the association between AD and

psychological parameters has accumulated, psychological approaches to the management of AD are being implemented. Psychological interventions and programs, including cognitive-behavioral therapy, dynamic psychotherapy, autogenic training, relaxation therapy, and structured educational programs, have a more additive effect compared with conventional treatments alone in terms of severity of eczema, subjective severity, itching intensity, and scratching after intervention[8]. According to a recent review of the use of psychological interventions for AD, relaxation therapy (RT) is one of the most effective psychological interventions for AD[8]. Although there have been many studies of the effects of psychological interventions on the management of AD, there remains a need for well-designed studies that utilize objective assessments of psychological parameters[9]. Therefore, the purpose of this study was to validate the efficacy of RT in patients with AD and to evaluate the relevant serologic parameters among T helper type 2 (Th2) cytokines, neuropeptides, and neurotrophins which could correlate with changes in AD symptoms and psychological parameters after RT[6].

II. PATIENTS AND METHODS

1. Patients

Twenty-five patients (14 men, 11 women; mean age 23.5 years, range 12-40), with confirmed diagnoses of AD according to the criteria of Hanifin and Rajka[10] were enrolled in this study. None of the subjects had any other concomitant dermatological, medical, or psychological disorders. This study was approved by the institutional review board, and informed consent was obtained from each patient and from parents in the cases of pediatric patients. Enrolled patients were randomly assigned into two groups: (1) the RT group, which received RT together with conventional treatments including topical glucocorticoids, topical calcineurin inhibitors, topical emollients, and anti-histamines and (2) the control group, which received conventional treatment without RT. In both groups, systemic immunosuppressant and immunomodulating drugs were prohibited. This study was carried out from September 2009 to October 2009 for the purpose of excluding seasonal differences in the skin condition. Patients who experienced stressful life events during the study period, such as severe disease, death of a family member, conflicts in personal or parental relationships, or self-reported severe stressful life events, were excluded from this study. One patient

assigned to the RT group was excluded due to a self-reported stressful event.

2. Treatment protocol

Participants in the RT group received one month of treatment with progressive muscle relaxation (PMR), which was developed by the American physician Edmund Jacobson[11]. PMR comprises a physical and mental component. The physical component involves tensing and relaxing muscle groups over the arms, legs, face, abdomen and chest. With eyes closed, the target muscle group is intentionally tensed for about 10 seconds and is then relaxed for 20 seconds. The mental component involves concentrating on the sensation of tension and relaxation. In this study, the whole procedure was supervised by a psychologist using video and audio programs, which were modified for patients with AD by a psychologist. The patients were asked to perform PMR using video and audio programs at home twice a day for four weeks under controlled room temperature and light conditions without eating or drinking (only water was allowed). In addition, abstaining from drinking alcohol and caffeine-containing beverages was recommended during the study period. Patient compliance was assessed via checklists regarding their performance of PMR that were completed during the study and returned. In addition, we called the patients once a

week to see if they followed the instructions and to address any issues regarding RT.

3. Assessment of psychological parameters

The psychological parameters were evaluated using various types of questionnaires that assessed the patients for levels of depression, anxiety, interaction anxiousness, and private body consciousness.

The Beck Depression Inventory (BDI) is a 21-item test presented in multiple choice format that measures the presence and degree of depression in adolescents and adults[12]. The Korean version of the BDI demonstrated good psychometric properties[13]. Each item is evaluated using scores 0 to 3. The severity of depression increases with the overall score, which ranges from 0 to 63.

The STAI consists of 40 questions divided into 20 questions regarding state anxiety (SA) and 20 questions regarding trait anxiety (TA)[14]. SA refers to the level of anxiety felt at the time that the subject completes the questionnaires. Trait anxiety refers to anxiety felt in general. The Korean version of the STAI was previously shown to exhibit excellent psychometric properties[15]. Each question is evaluated using scores 1 to 4. Both of the total scores for SA and TA range from 20 to 80.

The interaction anxiousness scale (IAS) was constructed to measure the tendency to feel nervous in social encounters independent of patterns of inhibited, reticent, or avoidant behavior[16]. It consists of 15 items that span a broad range of anxiety-evoking situations, including interactions with strangers, parties, dealing with authority figures, cross-sexed encounters, and casual conversation. Each item is evaluated using scores 0 to 4. The total score ranges from 0 to 60.

The private body consciousness subscale is one of three subscales of the body consciousness questionnaire[17]. Its five questions assess attention to internal physical sensations, such as dry mouth, hunger, and body temperature. Questions are rated on a 6-point scale, with 0 representing an "extremely uncharacteristic" quality and 5 representing an "extremely characteristic" quality.

4. Assessment of clinical severity

Clinical severity was quantified using the eczema area and severity index (EASI)[18]. The EASI is a composite score, including an assessment of disease extent and percentage of area involved, which is assigned a proportional score from 0 to 6 (0=no eruption, 1=<10%, 2=10%-<30%, 3=30%-<50%, 4=50-<70%, 5=70%-<90% and 6=90%-100%). The body was divided into

four regions: head/neck (H), upper extremities (U), trunk (T), and lower extremities (L). The proportionate body surface areas were 10% (H), 20% (U), 30% (T), and 40% (L). In young children, the body regions were assigned proportionate body surface areas of 20% (H), 20% (U), 30% (T), and 30% (L). Each of the four body regions was assessed separately for signs of erythema, infiltration and/or papulation, excoriations, and lichenification, each on a scale from 0 to 3 (0=none, 1=mild, 2=moderate, 3=severe). The EASI score ranges from 0 to 72.

Two horizontal visual analogue scales (VASs) were used for the subjective assessment of pruritus and loss of sleep (LOS) with the anchors of no pruritus/no LOS at 0 and the most severe symptoms at 10.

5. Assay of serum NGF, NPY, IL-4, IL-5, and IL-13 levels

All blood samples were drawn in the morning, between 8:00 AM and 10:00 AM, to control for diurnal variation. Serum levels of nerve growth factor (NGF), neuropeptide Y (NPY), and Th2 cytokines (IL-4, IL-5, and IL-13) were evaluated at baseline and after 1 month of treatment. Peripheral venous blood samples were drawn into vacutainer SST tubes (Becton Dickinson, Mountain View, CA, USA) and allowed to clot at room temperature (20 to 24°C) for 30 minutes. The tubes were centrifuged at 1000 x g for 10 minutes.

The serum was aliquoted and stored at -70°C until they were tested. NGF was measured using NGF ELISA kit (R&D Systems, Minneapolis, MN, USA). NPY was measured using NPY ELISA kit (RayBiotech, Norcross, GA, USA). IL-4, 5, 13 were measured using IL-4 ELISA kit (eBioscience, San Diego, CA, USA), IL-5 ELISA kit (eBioscience), and IL-13 ELISA kit (R&D Systems). All parameters were measured according to the instructions of the manufacturer. All serum samples were assayed in duplicate at the same time.

6. Statistical analysis

Statistical analyses were performed using SPSS (SPSS Inc, Chicago, IL, USA) for Windows (version 12). Results were described as mean ± SD. At baseline, the differences in the EASI score, pruritus, LOS, the degree of stress, and the serum levels of NPY, NGF, IL-4, IL-5 and IL-13 between the RT and control groups were analyzed with the Mann-Whitney U-test. Differences in clinical parameters and the serologic parameters between baseline and 1 month after treatment in both groups were analyzed with paired t-tests. Additionally, the degree of difference, which was calculated by subtracting the value at the one-month follow-up from the baseline value for the EASI score, pruritus, and LOS, was compared between the RT and

control groups using the Mann-Whitney U-test. Pearson's correlation analysis of these parameters was performed to elucidate how the psychological and serologic parameters related to the severity of AD symptoms and clinical improvement. A p-value <0.05 was considered statistically significant.

III. RESULTS

1. Characteristics of the enrolled atopic dermatitis patients

Twenty-five patients with AD were divided into two groups, the RT group (male: n=8, female: n=7; mean age ± SD: 24.2 ± 9.1) and the control group (male: n=6, female: n=4; mean age ± SD: 22.5 ± 7.7). There were no significant differences in gender or age between the groups. For the RT group (n=15), the mean EASI score was 16.5 ± 5.6 (range: 9-27.3) and the mean pruritus and LOS scores were 7 ± 1.2 (5-9) and 6.4 ± 2.4 (2-10), respectively. For the control group (n=10), the mean EASI score was 13.3 ± 4.1 (10.1-22.9) and the mean pruritus and LOS scores were 5.9 ± 1.1 (5-8) and 3.4 ± 0.7 (2-7), respectively. There were no significant differences in AD symptoms between the groups as assessed by EASI, pruritus, and LOS scores. The baseline scores for the psychological parameters and the baseline values of Th2 cytokines and neuropeptides, including NGF and NPY, are described in Table 1. With the exception of IL-13, there were no significant differences between the groups in these scores and values. Additionally, specific IgE levels were measured by the Pharmacia CAP system (Phadia, Uppsala, Sweden) for the following eight allergens, house dust mite, egg, wheat, peanut, soybean, pork, chub mackerel and staphylococcal enterotoxin.

A specific IgE measurement was considered positive if ≥ 0.35 kU_A/l (Table 2).

Table 1. Demographics and characteristics of subjects

	RT group (n=15)	Control group (n=10)	*p-value
Sex			
Male	8	6	
Female	7	4	
Age (yr)	24.2±9.1 (12-40)	22.5±7.7 (16-37)	0.57
EASI score	16.5±5.6 (9-27.3)	13.3±4.1 (10.1-22.9)	0.18
Degree of pruritus (0-10)	7±1.2 (5-9)	5.9±1.1 (5-8)	0.1
Loss of sleep (0-10)	6.4±2.7 (2-10)	5.0±1.3 (2-7)	0.1
Peripheral blood eosinophil count (number/μl)	498.7 ± 347.8	548±364.3	0.89
Total serum IgE level (IU/ml)	1592.8±1862.3	2685.4±2108.4	0.16
IL-4 (pg/ml)	152.8±457.6 (5.7-1800)	121.4±266.7 (8.3-124.8)	0.48
IL-5 (pg/ml)	738.4±268 (306.1-1369.9)	676.9±323.6 (259.2-1116.8)	0.18
IL-13 (pg/ml)	102.4±44.4 (39.3-157.5)	79.5±69.2 (3.8-252.1)	0.04
NGF (pg/ml)	376.1±143.6 (201.2-714.7)	445.5±290.7 (256.6-1199.4)	0.36
NPY (pg/ml)	47.1±11.6 (27.0-71.9)	45.3±9.2 (31.6-61.3)	0.83

	RT group (n=15)	Control group (n=10)	*p-value
Psychological parameters			
Depression (0-63)	13.2±6.2 (0-26)	9±4 (4-15)	0.07
State anxiety (20-80)	45.8±12.2 (21-61)	45.3±12 (24-60)	1
Trait anxiety (20-80)	52.9±11.4 (21-61)	49.3±10.2 (31-64)	0.32
Interaction anxiousness scale (0-60)	26.3±9.5 (15-48)	27.3±7.7 (9-35)	0.32
Private body consciousness subscale (0-25)	11.5±3.7 (8-19)	10.1±2.7 (6-14)	0.48

*Mann-Whitney U-test

Table 2. Sensitization rates to each allergen in subjects at baseline

	RT group (n=15)	Control group (n=10)
Mite allergen		
Dermatophagoides farinae	11 (73.3)	9 (90)
Food allergens		
Hens egg	3 (20)	3 (30)
Milk protein	0 (0)	2 (20)
Wheat	6 (40)	4 (40)
Peanut	5 (33.3)	4 (40)
Soybean	6 (40)	3 (30)
Pork	3 (20)	1 (10)
Chub mackerel	4 (26.7)	2 (20)
Bacterial allergen		
Staphylococcal enterotoxin B	4 (26.7)	3 (30)

The values expressed are n (%).

2. Baseline psychological parameters and their associations with atopic dermatitis symptoms and serum parameters

Before randomization, the STAI was the only psychological parameter that was positively correlated with pruritus (SA: R=0.496, p=0.014; TA: R=0.423, p=0.04), but not with the EASI or LOS scores (Figure. 1). Both pruritus and LOS were not significantly correlated with total serum IgE level, peripheral blood eosinophil count, or the EASI score.

The serum level of NGF was not correlated with the four psychological parameters at baseline. Clinical parameters were not significantly correlated with the level of NGF. Among Th2 cytokines, only IL-13 was positively correlated with NGF (R=0.414, p=0.04) (Figure. 2). In particular, the serum level of NPY was inversely related to the anxiety score (SA: R=-0.475, p=0.019; TA: R=-0.418, p=0.042) and pruritus scores (R=-0.451, p=0.035) at baseline (Figure. 3). However, the levels of NPY did not show any significant correlation with psychological parameters other than the STAI, clinical symptoms except for pruritus, and the levels of Th2 cytokines. Additionally, serum levels of IL-4, IL-5, and IL-13 were not correlated with any of the psychological or clinical parameters.

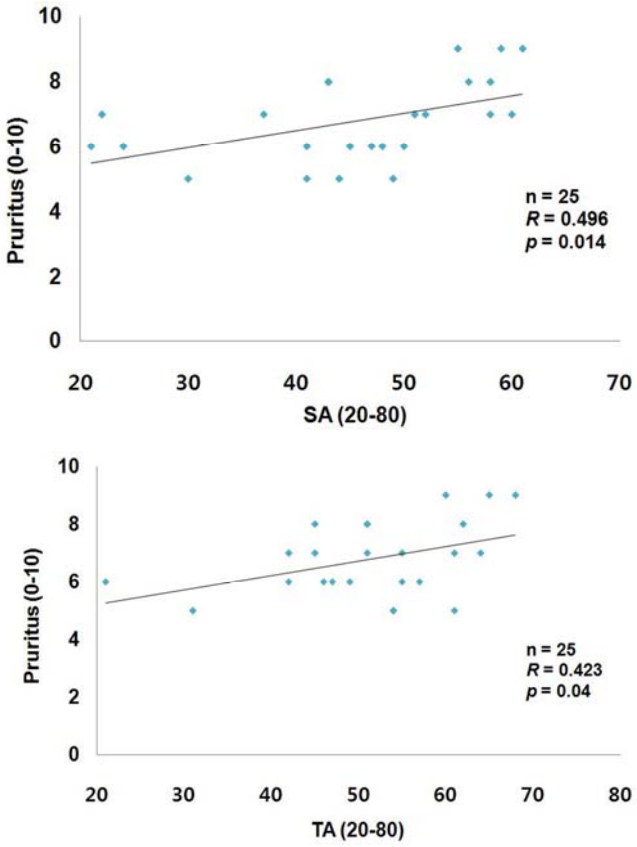


Figure 1. Relationship between psychological parameters and clinical parameters in atopic dermatitis patients at baseline. Among the four psychological parameters, only anxiety, as assessed by the STAI, was positively correlated with pruritus in all 25 participants at baseline (state anxiety (SA): R=0.496, p=0.014; trait anxiety (TA): R=0.423, p=0.04).

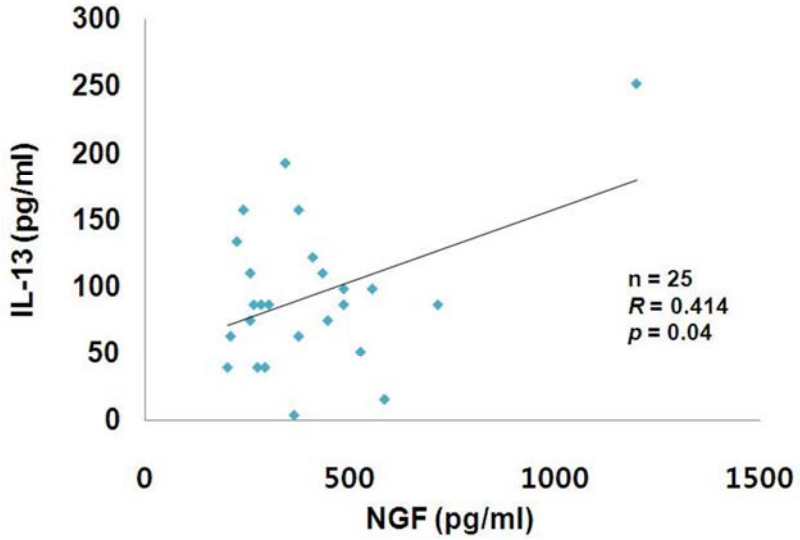
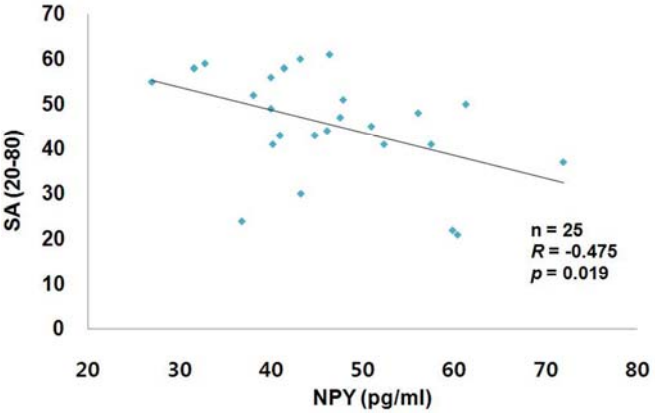


Figure 2. Relationship between serum level of nerve growth factor and Th2 cytokines in atopic dermatitis patients at baseline. Serum levels of NGF were positively correlated with IL-13, but not with IL-4 or IL-5 in all 25 participants (R=0.414, p=0.04).



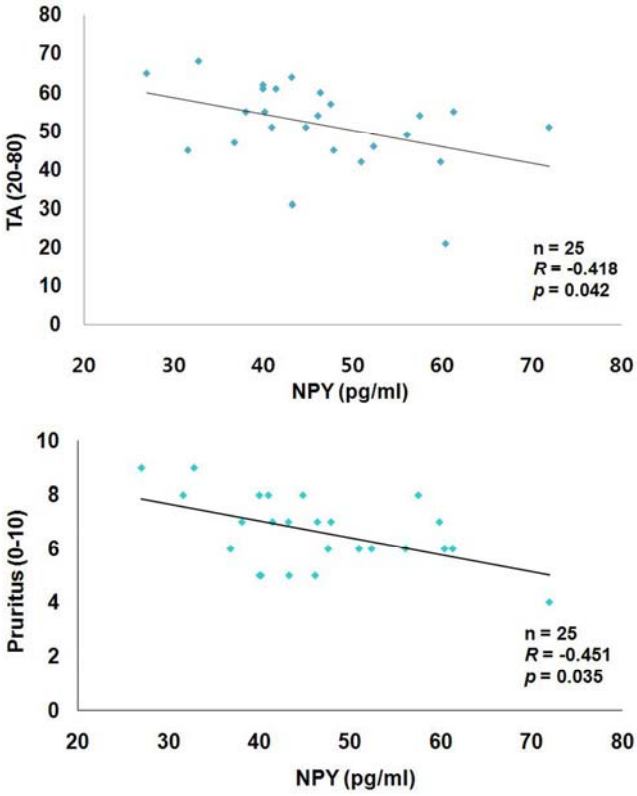


Figure 3. Relationship between serum level of neuropeptide Y and psychological parameters, clinical parameters in atopic dermatitis patients at baseline. Serum levels of NPY were negatively correlated with anxiety, both SA and TA, and pruritus in all 25 participants (SA: R=-0.475, p=0.019; TA: R=-0.418, p=0.042; pruritus: R=-0.451, p=0.035).

3. Effect of relaxation therapy on clinical symptoms, psychological and serologic parameters

At the one-month follow-up after PMR therapy, although AD patients in

both groups showed significant improvement in their EASI scores (p=0.001 and p<0.001, respectively), the degree of pruritus and LOS were significantly decreased in the RT group (p<0.001 in both), but not in the control group (Figure. 4). In terms of degree of improvement, which was calculated by subtracting the scores for the EASI, pruritus, and LOS at the one-month follow-up from the scores at baseline, the AD patients in the RT group showed considerable improvement in pruritus scores compared with the control group (p=0.04).

Among the psychological parameters, the BDI and SA scores showed significant improvement after treatment only in the RT group (p=0.003 and 0.005, respectively) (Figure. 5). However, the score of TA did not show a significant change after treatment even in the RT group. In the control group, there were no significant changes in the psychological parameters compared to baseline scores. None of the serologic parameters, including NGF, NPY and Th2 cytokines, showed correlation with BDI or SA scores, which decreased in the RT group after treatment.

Compared to baseline, post-treatment serum levels of NGF and NPY did not show significant changes in either the RT or control group. There were also no significant changes in IL-4, IL-5, and IL-13 after treatment in either the RT or control group.

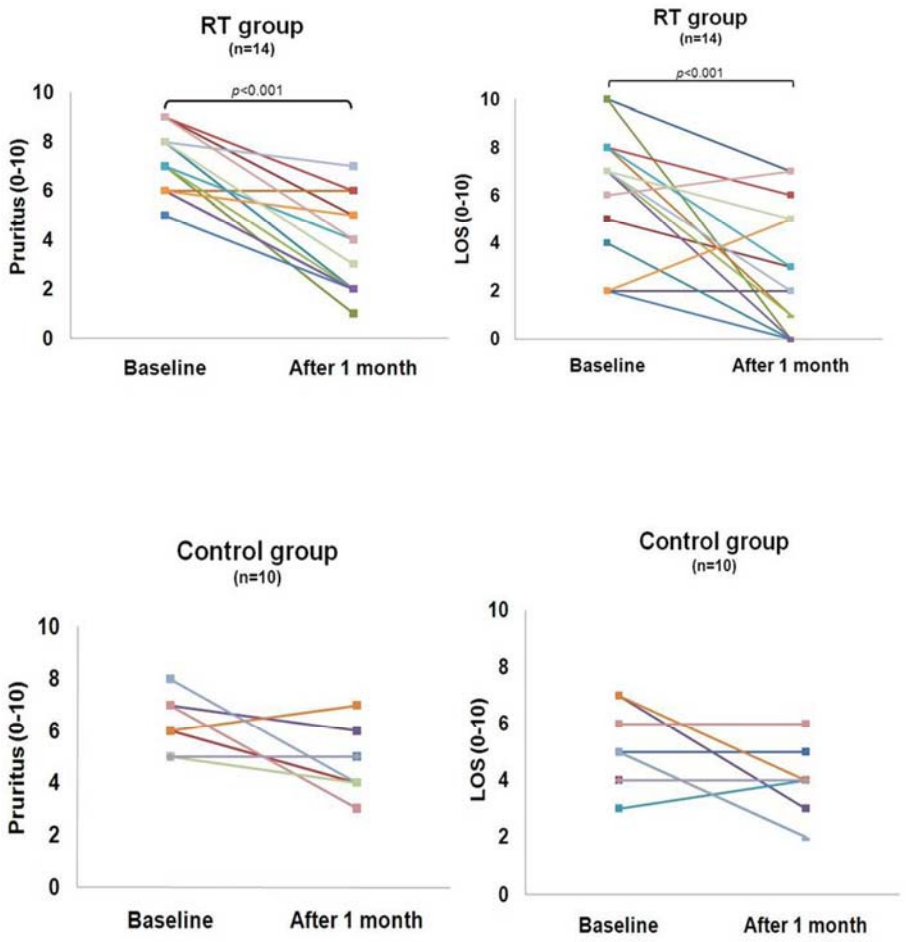


Figure 4. Effect of progressive muscle relaxation therapy on clinical parameters. The degree of pruritus and sleep disturbance was significantly decreased in the RT group, but not in the control group (pruritus: $p<0.001$; LOS: $p<0.001$).

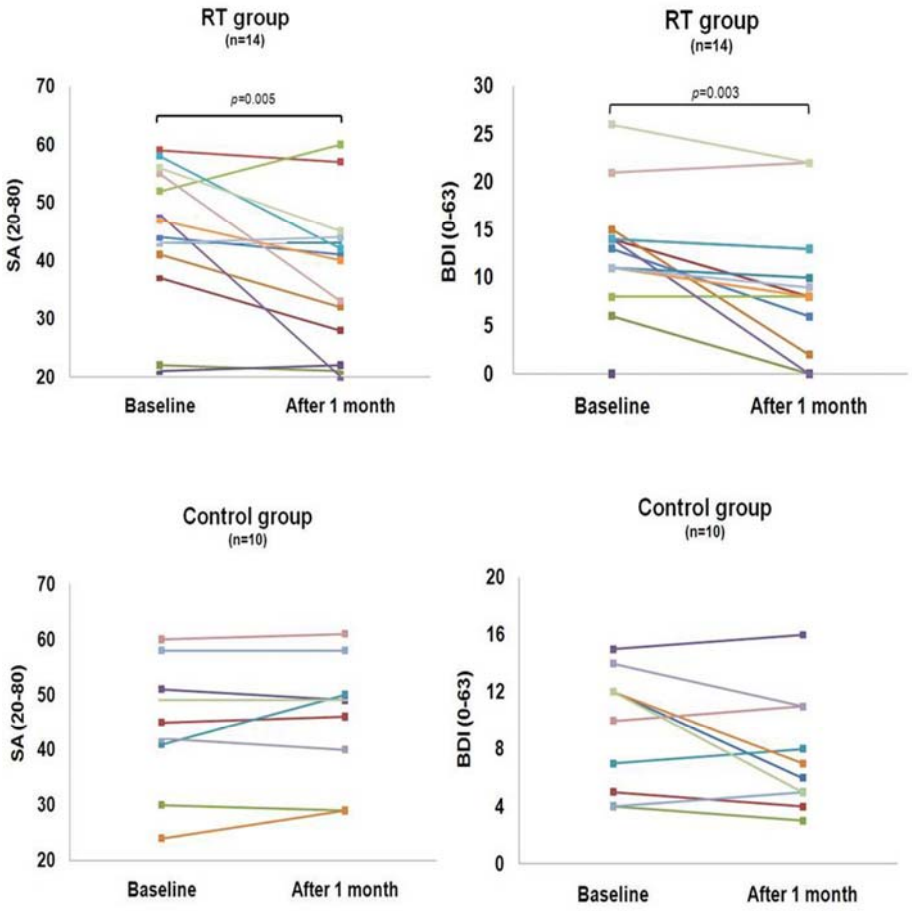


Figure 5. Effect of progressive muscle relaxation therapy on psychological parameters. Effect of PMR on psychological parameters. Among the four psychological parameters, depression, assessed by BDI, and SA were significantly decreased in the RT group, but not in the control group (BDI: p=0.003; SA: p=0.005).

IV. DISCUSSION

The formulation of effective psychological interventions would be helpful for ameliorating the psychological disturbances associated with AD, which could subsequently improve AD symptoms. In a previous study, we showed that anxiety, among various other psychological parameters, is positively correlated with the degree of pruritus in AD patients[7]. In addition, anxiety has been reported to be an important psychological factor that contributes to aggravation of AD[19]. Psychotherapy might be an important treatment option to improve both the psychological and dermatological condition of patients with AD, especially in patients with higher anxiety levels[20]. Tandospirone, a 5-hydroxytryptamine 1A receptor agonist with anxiolytic effects, has been reported to attenuate itching by controlling emotional response[21]. Therefore, we hypothesized that PMR might reduce anxiety in patients with AD and could be used as an adjunctive treatment to alleviate AD symptoms.

PMR is a complementary therapy that has been in use since its introduction in 1938[11]. It has been reported to be clinically effective in treating anxiety disorders including panic disorder and generalized anxiety disorder[22]. A modern theoretical rationale for PMR is that psychological distress elicits a

generalized stress activation response, which comprises multiple central and peripheral physiological systems. Therefore, deactivation of a single subsystem, for example the muscular system, is thought to reduce activation in many other subsystems. PMR is often used for the treatment of AD and is regarded as one of the most effective psychological interventions for AD[18,19].

In our study, anxiety, especially SA, and depression were significantly decreased in the RT group after PMR therapy but not in the control group. Although there was significant improvement of EASI scores in both the RT and control groups after treatment, pruritus and sleep disturbance scores were significantly improved only in the RT group. In addition, only pruritus scores in the RT group showed significant improvement after PMR therapy when compared to control group. Therefore, our study suggested that PMR, through reducing anxiety, could be a useful treatment tool for managing pruritus and sleep disturbances associated with AD.

Most studies, which evaluated the usefulness of psychological interventions for AD have proven their effects through only clinical parameters[9]. The lack of effort to check of psychological interventions for AD using objective parameters is likely due to the unclear mechanism by which stress affects AD and the absence of objective parameters to verify association between stress and AD. However, previous studies suggest that stress stimulates the

hypothalamic-pituitary-adrenal (HPA) axis to induce a shift toward a Th2 cell phenotype; releases neuropeptide and neurotrophin, which influence the development and course of AD; induces epidermal barrier dysfunction; and lowers the itch threshold[19]. Therefore, in our study, objective parameters, such as Th2 cytokines, NGF, and NPY, were examined in addition to clinical and psychological parameters to elucidate which factors are associated with stress and respond to psychological interventions.

Among various neurotrophins and neuropeptides, NGF and NPY have been reported to be strongly associated with anxiety and are a possible link between anxiety and aggravation of AD[5,23-28]. NGF could be one of the psychological substrates in the response to anxiogenic stimuli[23]. Aside from its function as a trophic factor of neuropeptidergic and sympathetic neurons, NGF is now increasingly regarded as a potent immunomodulator, including mast cell activation, increases of vascular permeability, and cross-action between neuronal and immune cells[5,24]. NPY has an anxiolytic effect *via* the Y1 receptor in the amygdala and is induced by stress[25,26]. Mutant mice lacking NPY show increased anxiety-like behavior on various tests[27]. In addition, low levels of NPY in plasma and cerebrospinal fluid have been found in patients with anxiety disorders[28]. In addition to the protecting against anxiety, NPY, *in vitro*, activates mast cells and stimulates

angiogenesis[29.30]. Our previous study suggests that anxiety in patients with AD might be associated with the induction of pruritus through NPY and NGF[7].

In this study, serum levels of NGF in enrolled patients with AD were not correlated with EASI scores at baseline. After one month of treatment, there was no significant change in serum levels of NGF in either the control or RT group, though both groups had a considerable improvement in EASI scores. The relationship between AD severity and serum levels of NGF is still controversial[31]. Toyoda *et al*[32] reported that serum levels of NGF in patients with AD is positively related to the EASI score and could be a useful plasma marker of disease activity in AD. They postulated that the increased plasma concentration of NGF in patients with AD could derive from the enhancement, activation, and proliferation of Th2 cells and/or mast cells, which are able to synthesize, store, and release NGF. At baseline, we observed a positive correlation between serum levels of IL-13 and NGF. Sin *et al*[33] reported that NGF induces more IL-13 production from the basophils of allergic subjects than from the basophils of nonallergic subjects. Although our study provided evidence of a correlation between the Th2 immune response and NGF, neither of them were related to AD disease activity.

Even if anxiety is one of the important stimuli for the secretion of NGF,

NGF levels did not correlate with anxiety scores. Moreover, they did not show any correlation with changes in anxiety scores. However, it has been reported that there is a significant positive correlation between self-reported stress during pregnancy and maternal NGF levels[34]. The intrinsic type of AD could be more highly affected by neurotrophic mediators than the extrinsic type of AD[35]. Thus, the role of anxiety and NGF in the intrinsic type of AD might be more prominent. Since all of the participants in our study had the extrinsic type of AD, further studies regarding the influence of anxiety and NGF in patients with the intrinsic type of AD are required.

In our study, the serum level of NPY was inversely correlated with anxiety scores, both SA and TA, at baseline. To our knowledge, this is the first report to show an inverse correlation between NPY levels and anxiety scores in patients with AD. Previously, Zhou *et al*[36] reported that plasma levels of NPY are inversely correlated with trait anxiety in healthy individuals. Expression studies in rats indicate that acute stress down-regulates NPY mRNA expression, whereas prolonged stress induces the opposite effect (up-regulation of expression), which suggests a neuroadaptive response to cope with chronic stress[26]. Therefore, in our study, the inverse correlation between serum levels of NPY and anxiety scores in patients with AD observed in our study implies that low serum levels of NPY are responsible for high levels of

anxiety in patients with AD.

Regarding the protective role of NPY against anxiety, we expected levels of NPY to decrease if the anxiety of patients with AD resolved after PMR. However, we did not observe any significant changes in NPY levels in either group following PMR despite improvement in clinical parameters and anxiety scores. It is likely that the restoration of NPY levels following PMR may take a longer amount of time. Because many patients with AD are under conditions of chronic anxiety and stress, one month of PMR may not be enough to fully resolve their anxiety. This is supported by the observation that only SA, not TA, was reduced by PMR in our study. TA, which measures anxiety felt in general, might reflect chronic anxiety in patients with AD, whereas SA reflects anxiety felt at the time the questionnaires were completed.

After dividing RT group patients into 3 groups according to TA; low TA (20-39) (n=2), intermediate TA (40-59) (n=8), high TA (60-80) (n=4), the average degree of improvement in pruritus and LOS were larger in low or intermediate TA group than in high TA group (pruritus: 3.4 ± 2.1 *vs* 3.2 ± 2.0; LOS: 4 ± 3.8 *vs* 2.2 ± 2.1). These findings might support that high TA reflect chronic anxiety and could be a predictive factor of poor response to PMR.

Limitations of our study included small number of patients, short duration of PMR therapy, and short follow-up period. In addition, all of the enrolled patients had extrinsic type of AD and it was impossible to control all variables, such as individual daily activity or hours of sleep, which could influence anxiety. However, we did exclude patients who reported a stressful life event.

V. CONCLUSIONS

The results of our study indicate that, among various psychological parameters, anxiety may have the most prominent role in the chronicity and persistence of AD. Through reducing state anxiety, PMR could be a useful adjunctive modality for the management of pruritus and sleep disturbances in patients with AD. Although we observed an inverse correlation between NPY levels and anxiety scores and a significant improvement in BDI and SA scores following PMR treatment in the RT group, we could not find out the objective parameters such as serum levels of NGF and NPY, which are considered to be strongly associated with anxiety. Further studies are needed to elucidate the interaction between anxiety and AD symptoms and the key mediators that connect the two. Such studies will open up new possibilities to discover promising therapeutic targets and new therapeutic modalities for patients with AD who do not respond to conventional treatments.

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ABSTRACT (IN KOREAN)

아토피피부염에서 점진적 근육 이완요법: 효과에 대한 객관적 접근

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배병기

정신적인 스트레스가 아토피피부염에서 중요한 역할을 하고 아토피피부염의 치료에 정신과적 치료법이 효과적이라고 보고되었다. 그러나 이러한 정신과적 치료법이 아토피피부염의 임상적 지표와 정신과적 지표의 호전을 가져온다는 것으로 그 효과가 증명된 적은 있지만 그것 외의 객관적인 지표로 그 효과가 검증된 적은 없었다.

본 연구의 목적은 아토피피부염환자에서 정신과적인 치료법인 이완요법의 효과를 임상적으로 검증하고 그와 더불어 이완요법의 효과를 객관적으로 반영할 수 있는 혈청학적 지표를 찾는 것이었다.

총 25명의 아토피피부염 환자를 무작위적으로 이완요법을 받은 군 (n=15) 과 이완요법을 받지 않은 대조군 (n=10) 으로 나누었다. 이완요법을 받는 군은 1달 동안의 점진적 근육 이완요법을 고식적 치료와 함께 시행하였다. 대조군은 1달 동안 고식적 치료만을 시행하였다. 정신적 스트레스는 우울, 불안, 대인관계불안, 개인신체의식 4가지를 측정하였으며

아토피피부염의 임상적 지표로 eczema area and severity index (EASI), 가려움증, 수면장애를 측정하였다. 또한 환자의 혈청에서 nerve growth factor (NGF), neuropeptide Y (NPY), Th2 사이토카인 (IL-4, IL-5, IL-13) 을 측정하였으며 상기의 모든 측정은 치료전과 치료 한달 후의 시점에서 시행했다.

치료 전 기저상태에서는 정신과 지표중에서, 오직 불안만이 가려움증과 통계학적으로 유의한 양의 상관관계를 보였다 (상태불안: R=0.496, p=0.014, 특성불안: R=0.423, p=0.04). 혈청내 NPY 는 불안 및 가려움증 정도와 통계학적으로 유의한 음의 상관관계를 보였다 (상태불안: R=-0.475, p=0.019, 특성불안: R=-0.418, p=0.042, 가려움증: R=-0.451, p=0.035).

치료 한달 뒤 가려움증과 수면장애는 이완요법을 시행한 군에서만 통계학적으로 유의한 감소를 보였다 (p<0.001 for both). 정신과적 지표중에서는 상태불안이 이완요법을 시행한 군에서만 통계학적으로 유의하게 감소하였다 (p=0.005). NGF, NPY, Th2 사이토카인을 포함한 혈청학적 지표는 이완요법 후에 통계학적으로 유의한 변화를 보이지 않았다.

이완요법 후에 통계학적으로 유의하게 감소하는 혈청학적 지표를 찾지는 못했지만, NPY 는 아토피피부염환자의 불안과 밀접하게 관련되어 있을 것으로 생각된다. 이완요법은 정신과 지표중 특히 불안을 감소시켜 가려움증과 수면장애를 효과적으로 감소시키는 것으로 생각된다. 따라서 이완요법은 아토피피부염 환자에서 보조요법으로 유용하게 사용될 수 있을 것으로 생각된다.

핵심되는 말: 불안, 아토피피부염, neuropeptide Y, nerve growth factor, 이완요법