2008. Vol.29. No.5. 41-51
The Journal of Korean Oriental Medicine

Original Article

Non-comparative Study for the Observation of Clinical Efficacy and Safety of *CheungYeolYiSeup-tang* and *Hwangbaek* External dressings on Dampness-Heat Pattern Atopic Dermatitis

In-Hwa Choi

Department of Dermatology, Kyung Hee University, East-West Neo Medical Center, Seoul, Korea

Objective : To observe the efficacy and safety of *CheungYeolYiSeup-tang* and *Hwangbaek* external dressings on dampness-heat pattern atopic dermatitis(AD) in a non-comparative study.
Methods : 10 patients with AD were included for 4 weeks of treatment. Efficacy and safety assessment included the scoring atopic dermatitis index(SCORAD), typical signs and symptoms of AD, results of some laboratory tests related to toxicity, and the incidence of adverse events.
Results : Improvements in efficacy parameters were observed and produced no significant changes in laboratory tests related to toxicity in these patients. Their SCORAD results significantly decreased after 4weeks(P value<.01, according to the Wilcoxon sum of ranks test). Similarly, significant reductions from baseline in subjective pruritus scores and (P value<.05 by the Wilcoxon sum of ranks test) and the mean average of individual signs and symptoms of AD were reported after 4 weeks(P value<.05, P<0.01 by the Wilcoxon sum of ranks test). There were no significant changes in eosinophil, neutrophil, lymphocyte, immunoglobulin E and ESR in blood serum by paired t-test.
Conclusion : *CheungYeolYiSeup-tang* administration and *Hwangbaek* external dressings are an effective and safe treatment for the management of dampness-heat pattern atopic dermatitis.

Key Words : atopic dermatitis, herb-medicine, *CheungYeolYiSeup-tang*, *Hwangbaek* external dressings, Dampness-Heat pattern

Introduction

Atopic dermatitis(AD) is a chronic inflammatory disorder of the skin characterized by three or more of the following features: pruritus, distribution of typical exanthema during any course of chronic recurrence, and atopic predisposition[1]. Nowadays AD shows increasing prevalence[2-4] and has contributed to rising healthcare costs in many countries[5].

Although AD is a common condition, there are no entirely satisfactory treatments. Conservative treatments are frequently insufficient or impractical. Corticosteroids, although frequently effective, cannot be used continuously because of significant adverse effects. Newer modalities, such as oral cyclosporine, topical calcineurin inhibitors, are effective but likewise limited by adverse effects[6,7]. Also, the number of patients requiring other therapeutic methods has increased.

In Korea, some AD patients and their families who want release from this disease without side effects and complications, or who are unsatisfied with

· Received : 2 June 2008 · Revised : 3 November 2008 · Accepted : 12 November 2008
· Correspondence to : In-Hwa Choi
Department of Dermatology, Kyung Hee University, East-West Neo Medical Center, Seoul, 134-090, Korea
Tel : +82-2-440-6235, Fax : +82-2-440-7143, E-mail : inhwajun@hanmail.net

other treatments, often visit Korean Oriental Medicine hospitals or clinics, usually after trying conventional treatment.

I think that we, as Oriental Medicine doctors, should have had more success - in spite of many difficulties involved - in establishing our approach as a definitive second-line alternative to treat AD patients. However, as this approach has developed over a long period of time with much trial and error, we cannot provide evidence for its efficacy and safety within the framework of standard schemes such as randomized controlled trials[8].

There have been several reports on the efficacy of some herb-medicine or natural products on AD, but most of them lack an understanding of Oriental Medicine[9-11].

Therefore I developed this study as a pilot study on diagnosed dampness-heat pattern AD in Oriental Medicine. I observed the changes in clinical manifestations and test results, and will plan another randomized controlled, placebo or active controlled study in the future.

Abbreviations used:

AD: atopic dermatitis
SCORAD: the scoring atopic dermatitis index
ALT: alanine transaminase
AST: aspartate transaminase
BUN: blood urea nitrogen
CBC: complete blood count
WBC: white blood cell
D/C: different cont in white blood cell
ESR: erythrocyte sedimentation rate

Materials and Method

1. Patients

Through a recruit announcement, the 11 patients recruited were those diagnosed according to Hanifin & Rajka's criteria[1]. The age range was 4 - 26 years old. This study was approved by the Institutional Review Board , KyungHee University, East-West Neo Medical Center. Informed consent was obtained from the patients or their parents after a thorough explanation of the procedure.

1) Inclusion criteria

Recent 1-2 weeks of an acute state

Suspected tolerance on systemic or topical steroids, antihistamines, and immune suppressant treatment patients or their families didn't want to continue taking those medicines.

Patients had been diagnosed with Dampness-Heat pattern AD[12,13] by Korean Oriental Medicine Dermatology specialists.

2) Exclusion criteria

(1) Any patients who have taken any antihistamines, steroids and immune suppressant treatment in the last prior 4 weeks
(2) Epileptic
(3) Pregnancy or lactation
(4) Patients who need prompt treatment for serious infection in other organs - except dermatoses.
(5) Even though initially cleared with inclusion criteria, later abnormal results in ALT, AST, BUN, Creatinine in blood test at first visit.

2. Study design

Treatment, Non-randomized, Open label, Uncontrolled, Single group assignment, Safety & efficacy, Non-comparative study

3. Procedure

1) Record of medical history: sex, age, onset, the state of lesions, family and past history

2) Management: teaching about diet, environmental factors, moisturize

(1) Diet

A. Recommendation: stew, bland and not greasy or salty, soy milk, unpolished rice, grains which counteract any poisonous effects (soy bean, mung-bean, job's tears), SOD(superoxide dismutase) substances (vegetable, fruits, liver oil,

vegetable oil)

B. Contraindication: roast and fried food (over 100℃), spicy and salty food, food which add a chemical seasoning or antiseptic substance (precooked food), food which add milk products, butter, cheese (ice cream, chocolate, snack), polished rice, allergy induced material (strawberry, peach)

(2) Environmental Management: Hospitalization to separate the patient from environment allergens. Identification and elimination of triggering factors such as: irritants, allergens, emotional stressors, infectious agents (antibiotics as indicated for infection)

(3) Shower: Use warm water, only 15-20min, after taking shower in 3min, moisturize with lotions, emollient, and ointment without steroids and immune suppressant.

4. Materials

1) Prescription and Decoction

(1) Internal Medicine

The herbal formula, *CheungYeolYiSeup-tang* can help to clear heat, purge fire and resolve dampness. Especially, it could be expected to reduce erythma, itching, exudation signs in atopic dermatitis[14].

One package of pre-decocted herbs was composed as Table 1, herbs total 37g. I prescribed this treatment twice over 4 weeks 2 packs as a daily dose for the patients. The two-week course of herb-medicine, made from 28 packages, was boiled with purified water: 6,000cc for 90 minutes in a large, open pot, and then vacuum packed, 42 packs of 120cc each. The children whose weight was less than 20kg were prescribed 9 packages of the pre-herb mixture, to which 2,700cc purified water was added. After boiling, we had 42 packs of 50cc each. Patients weighing over 20kg, but less than 50kg were given 18 packages of pre-herbs, to which 4,000cc purified water was added. After boiling, we had 42 packs of 80cc each(Table 2).

Table 1. Components of *CheungYeolYiSeup-tang*(Korean; QingReLiShiTang in Chinese)[14]

Korean/Chinese	Scientific name	Dose (grams)
Chajeunja/Cheqianzi	*Semen Plantaginis*	3
Moktong/Mutong	*Akebia caulis*	3
Nabokja/Laifuzi	*Semen Rapani*	3
Hwalseok/Huashi	*Talcum*	5
Gamcho/Gancao	*Glycyrrhiza Radix*	5
Yongdamcho/longdancao	*Gentiana Radix*	3
Sengjihwang/Shengdihuang	*Radix Rehmanninae*	3
Hwangguem/Huangqin	*Radix Scutellariaei*	3
Taeksa/Zexie	*Rhizomz Alismatis*	3
Tobokreung/Tufuling	*Rhizoma Slimax Glabra*	3
Sasam/Shashen	*Radix Glehniae*	3
Total		37

Table 2. Dose depending on patients' weight

Patients' weight(kg)	The packages of pre-herb mixture(packages)/total dose(grams)	Dose per liquid pack(cc)
over 50	28/1,036	120
20-50	18/666	80
less than 20	9/333	50

(2) External Medicine

Hwangbaek(Korean; Huangbai in Chinese scientific name Cortex Phellodendri) has the effect of eliminating heat and dampness, sedating fire, and also shows detoxifying and antibacterial effects[15].

It(dose;30g) was boiled with 1,000cc purified water in a large, open pot and vacuum packed, 20 packs of 120cc. I also applied these twice over 4 weeks.

2) Usage and taking medicine

(1) Internal Medicine:

taken 90 minutes after meals/3 times/day

(2) External Medicine:

wet dressing with gauze, more than twice a day, for 5-10 minutes each time

5. Parameters of Study

1) This study examined different combinations of medicine to treat AD- but excluded all anti-histamine, steroid, and immune suppressant treatment. I didn't give the patients any other Oriental Medicine treatment, for example, acupuncture treatment, negative therapy, and moxibustion. I only used *Cheung YeolYiSeup-tang* and *Hwangbaek* external dressings.

After counseling we could use emollient, lotions and ointment without steroids.

2) Contradiction:

antihistamines, steroids and immune suppressants.

6. Assessment schedule and evaluation

1) The patients were clinically examined at the beginning of the study, then regularly after 1 week, 2 weeks, and 4 weeks, which marked the end of the study. The evaluation of the efficacy was carried out by two methods. i) To observe the efficacy of each typical symptom of atopic dermatitis: erythema, exudation, itching, scale, scratch marks, dryness, and lichenification were grouped into the following five categories: 4: very severe, 3: severe, 2: moderate, 1: mild, 0: none. The efficacy was evaluated by the average value of each symptom. ii) Another method, The SCORAD, was adopted in order to evaluate the severity of atopic dermatitis as objectively as possible[16].

2) Taking photos:

Using a digital camera(IXUS 750, Canon, Japan), photos were taken at the beginning of the study, after 1 week, 2 weeks, and 4 weeks, which was the end of the study.

3) Patients were given blood tests, routine CBC, ESR, WBC D/C, serum Ig E, AST, ALT, BUN, and Creatinine at the beginning of the study and then after 4 weeks.

4) Safety evaluation

The safety of this study was assessed using adverse event reporting throughout the study, and with laboratory tests(e.g. AST, ALT. BUN, and Creatinine) at the first and final visits. Also, physical examinations were taken at the beginning of the study, after 1 week, 2 weeks, and 4 weeks.

7. Countermeasures to Adverse effect

All patients experiencing adverse events were monitored by clinical examination. Any adverse events were possibly or probably related to the sensitization and the severity of the symptoms.

8. Statistics

1) The Wilcoxon Sum of Ranks test was used to compare the SCORAD and clinical features.

2) The paired t-test was used to compare routine CBC, ESR, WBC D/C, serum Ig E, AST, ALT, BUN, and Creatinine tests at the beginning of the study and after 4 weeks.

Results

1. Patients

20 patients were recruited for the study; however,

9 patients were excluded for violation of the study protocol. Therefore, 11 patients participated in this study. Only 1 subject was excluded from the per protocol set due to an adverse event. So 10 patients were included in the per-protocol analysis. The patient who withdrew suffered from severe extremity edema 1 week after she had joined this study.

There were approximately equal numbers of male and female patients and all were between the ages 4 to 26 years. All patients had severe AD at the time of enrollment in this study(Table 3).

Table 3. Baseline characteristics of patients

Background Factors		No. of Cases	%
Sex	Male	4	40.0
	Female	6	60.0
Age	4-9 yrs	2	20.0
	10-19 yrs	6	60.0
	20-26 yrs	2	20.0
Length of clinical period	2-5 yrs	1	10.0
	5-10 yrs	5	50.0
	>10	4	40.0
Clinical severity	Severe	10	100.0
	Moderate	0	0.0
	Mild	0	0.0
Side of lesions	Face	8	80.0
	Scalp	1	10.0
	Neck	9	90.0
	Trunk & Back	6	60.0
	Groin	3	30.0
	Rump	4	40.0
	Popliteal region	10	100.0
	Antebrachial fossa	10	100.0
	Upper extreme	8	80.0
	Lower extreme	9	90.0
Clinical Features	Erythema	10	100.0
	Exudation	10	100.0
	Itching	10	100.0
	Scale	10	100.0
	Scratch marks	10	100.0
	Dryness	10	100.0
	Lichenification	10	100.0
Accompanied diseases	None	5	50.0
	Asthma	1	10.0
	Rhinitis	3	30.0
	Conjunctivitis	1	10.0
SCORAD at baseline	Mean±S.D.	57.40±11.51	
	Median	57.40	
	Min-Max	41.3-74.1	

2. Efficacy

Most patients experienced noticeable improvement in their AD within this study period. Their SCORAD results significantly decreased after 4weeks(P value <.01, according to the Wilcoxon sum of ranks test) (Table 4, Fig. 1).

Similarly, significant reductions from baseline in subjective pruritus scores and (P value<.05 by the Wilcoxon sum of ranks test)(Table 5) and the mean average of individual signs and symptoms of AD

Table 4. The change of the scoring atopic dermatitis index(SCORAD) (N=10)

	before	1 weeks	2 weeks	4 weeks
	Mean±S.D.	Mean±S.D. P value	Mean±S.D. P value	Mean±S.D. P value
SCORAD	57.40±11.52	47.76±12.30 0.005**	39.88±10.56 0.005**	35.30±11.47 0.008**

P<0.01**

Table 5. Change in subjective pruritus scores (N=10)

	Mean±S.D.	P value
baseline	7.90±2.33	0.017*
after treatment 4 weeks	5.40±2.87	

P<0.05*

Table 6. Scores for clinical signs and symptoms of atopic dermatitis (N=10)

	before	1 weeks	2 weeks	4 weeks
	Mean±S.D.	Mean±S.D. P value	Mean±S.D. P value	Mean±S.D. P value
erythema	2.80±0.42	2.3±0.67 0.025*	2.0±0.67 0.023*	1.8±0.79 0.015*
exudation	2.90±0.87	1.90±0.74 0.008**	1.10±0.99 0.007**	0.40±0.51 0.006**
itching	3.20±0.63	2.30±0.82 0.007**	2.20±0.79 0.020*	1.90±0.87 0.016*
scale	2.50±0.97	2.10±1.10 0.046*	1.50±0.71 0.014*	1.60±1.07 0.024*
scratch marks	3.30±0.94	2.50±0.71 0.005**	1.90±0.88 0.023*	1.60±0.96 0.011*
dryness	3.30±0.48	2.50±0.97 0.023*	2.10±0.87 0.006**	2.10±0.87 0.006**
lichenification	3.10±0.73	2.50±1.08 0.034*	2.50±1.08 0.034*	2.30±1.05 0.023*

P<0.05* P<0.01**

Table 7. The changes in laboratory test(efficacy items) (N=10)

	baseline	after treatment 4 weeks	*P* value
	Mean±S.D.	Mean±S.D.	
eosinophil(%)	7.21±4.3	6.96±3.76	0.708
neutrophil(%)	55.91±11.82	52.75±7.27	0.957
Ig E(IU/L)	2,855.12±4,470.30	3,370.05±4,525.20	0.367
ESR(mm/h)	8.80±6.59	10.10±7.96	0.581

Table 8. The Changes of laboratory test(safety items) (N=10)

	baseline	after treatment 4 weeks	P value
	Mean±S.D.	Mean±S.D.	
AST(IU/L)	25.20±5.76	24.70±5.47	0.485
ALT(IU/L)	14.10±4.33	15.30±5.10	0.470
BUN(mg/dL)	12.10±2.42	10.80±2.20	0.064
Creatinine(mg/dL)	0.60±0.16	0.64±0.15	0.037*

P<0.05*

were reported after 4 weeks(P value<.05, P<0.01 by the Wilcoxon sum of ranks test)(Table 6, Fig. 2).

There were no significant changes in eosinophil, neutrophil, lymphocyte, immunoglibulin E and ESR in blood serum(by paired t-test)(Table 7).

3. Safety

There were no significant changes in AST, ALT and BUN. In Creatinine, there was a significant change within normal range, but no clinical meaning (Table 8).

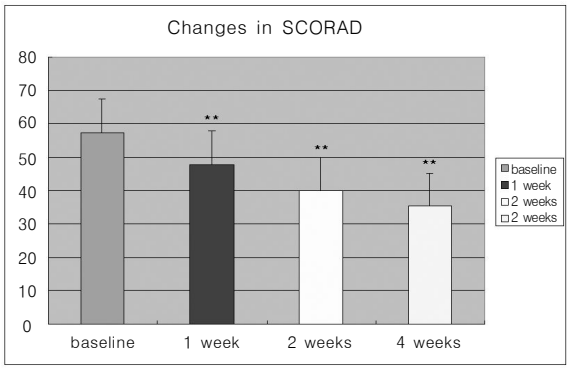


Fig. 1. Changes in SCORAD based on a scale of 0(absent) to 103(very severe). (**: P<0.01)

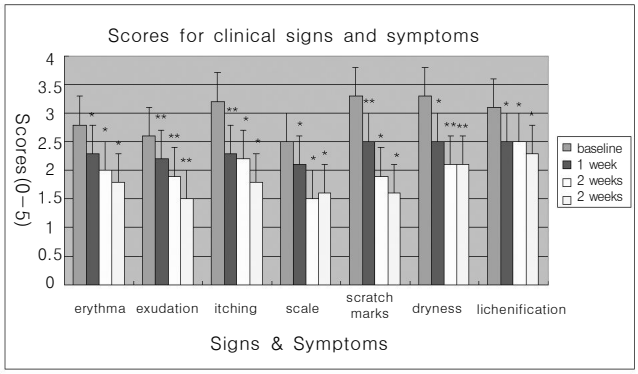
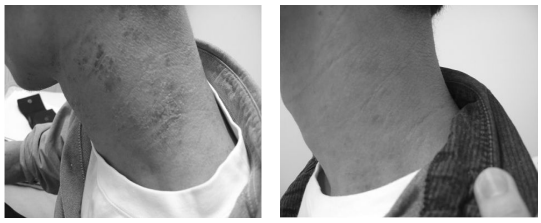
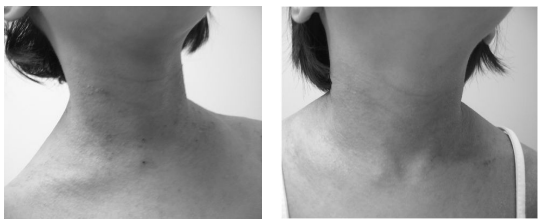


Fig. 2. Scores for clinical signs and symptoms in atopic dermatitis: for all time points compared with baseline. Scores based on a scale of 0(absent), 1(mild), 2(moderate), 3(severe), and 4(very severe) for each symptom. (*: P<0.05, **: P<0.01)



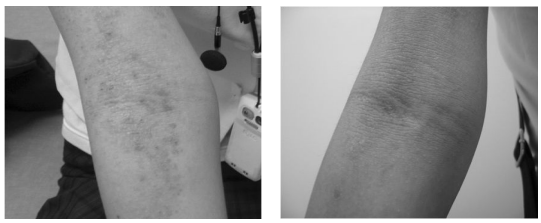
(A) baseline (B) after 4 weeks

Fig. 3. Neck, 26 year-old Korean male.



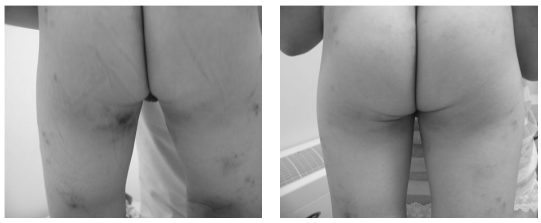
(A) baseline (B) after 4 weeks

Fig. 4. Neck, 7-year-old Korean girl.



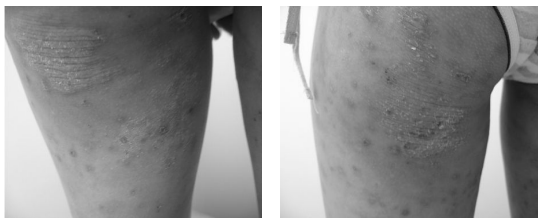
(A) baseline (B) after 4 weeks

Fig. 5. Forearms, 16-year-old Korean female.



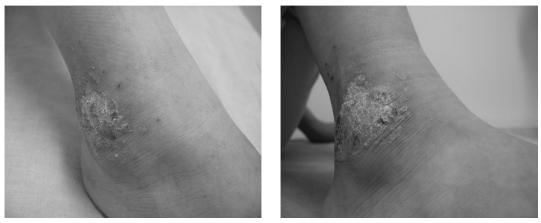
(A) baseline (B) after 4 weeks

Fig. 6. Rump, 4-year-old Korean boy.



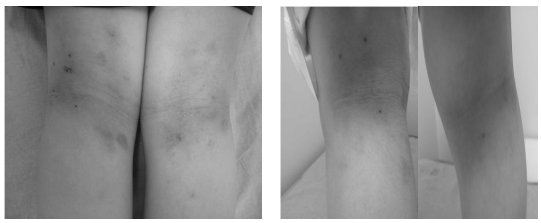
(A) baseline (B) after 4 weeks

Fig. 7. Rump, 11-year-old Korean girl.



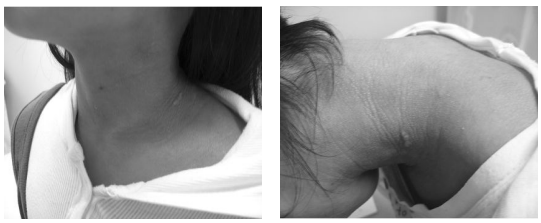
(A) baseline (B) after 4 weeks

Fig. 8. Right Ankle, 11-year-old Korean girl.



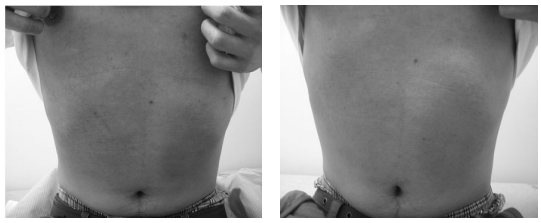
(A) baseline (B) after 4 weeks

Fig. 9. Popliteuses, 10-year-old Korean girl.



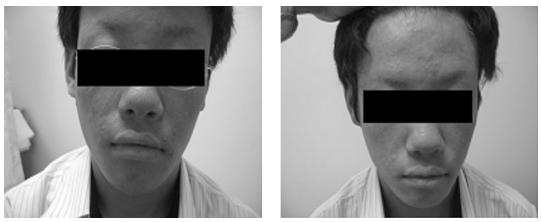
(A) baseline (B) after 4 weeks

Fig. 10. Neck, 12-year-old Korean girl.



(A) baseline (B) after 4 weeks

Fig. 11. Abdomen, 26-year-old Korean Male.



(A) baseline (B) after 4 weeks

Fig. 12. Face, 18-year-old Korean Male.

Discussion

AD is a complex, multifaceted disease for which definite guidelines of treatment have yet to be established. Treatments have been symptomatic, and include: topical or systemic use of steroids or immunosuppressive agents, external application of emollients, oral administration of antihistamines to solve pruritus, simultaneous investigation and elimination of allergens and aggravating factors, and appropriate selection of therapeutic methods for repair and prevention of functional disorders of the skin barrier[17,18].

Recently, we have debated how to treat those patients whose symptoms recur after basic treatment and also those who demonstrate higher – grade symptoms[19]. Because of the recurring nature of AD, its chronicity, and its lack of response to steroids, many researchers have sought alternative treatments[20]. Worm and Henz[21] reviewed controlled trials of AD treatment with herbal medicine, and concluded that any new type of unconventional therapy should thus be thoroughly evaluated, and shown to be equal or superior to conventional treatments with regard to both efficacy and tolerability, before it is recommended for use in clinical practice.

Korean Oriental Medicine(KOM) is a traditional medicine developed in Korea based on Chinese traditional medicine. The principle of KOM is elimination of exogenous factors of disease to control abnormal homeostasis of the body. Its prescription comprises natural drugs containing multiple components prescribed differently for each individual patient. Even for the same disorder, different drugs can be administered according to the condition of the patient.

This approach can make it difficult to develop a singular study methodology. However, it can and often does lead to varied and effective methods of treating diseases such as AD.

Therefore I developed this study as a pilot study on diagnosed dampness-heat pattern AD in Oriental Medicine. I observed the changes in clinical manifestations and test results, and will plan another randomized controlled, placebo or active controlled study in the future. We have already reported a experience about the effectiveness of *CheungYeolYi Seup-tang* administration and *Hwangbaek* external dressings on acute lesion of atopic dermatitis[22].

Most patients experienced noticeable improvement in their AD within this study period. Their SCORAD results significantly decreased after 4weeks. Similarly, significant reductions from baseline in subjective pruritus scores and the mean average of individual signs and symptoms of AD were reported after 4 weeks. The Dampness-Heat pattern symptoms, especially, such as erythma, exudation, and itching had shown improvement over other symptoms. There were no significant changes in eosinophil, neutrophil, lymphocyte, Immunoglobulin E and ESR in blood serum. The levels of serum total Ig E, peripheral eosinophils and eosinophil cationic protein (ECP) are known to be elevated in patients with atopic dermatitis. However, the relationship between these laboratory findings and the clinical severity of atopic dermatitis is controversial. There were no significant changes in AST, ALT and BUN. In creatinine, there was a significant change within the normal range, but of no clinical value. So this herbal formula can be considered efficacious and safe for AD treatment.

The patient who withdrew suffered from severe extremity edema 1 week after she had joined this study. This case appears to be unrelated to my study. I will consider more about the cause of side effects in the future.

There are several limitations in this study. First of all, unfortunately, we haven't achieved a standardization of herb-medicine treatment in Korea yet. My study is likely to be reproduced.

I suggest there should be future clinical trials in order to more efficiently assess and better standardize this method. Even though Oriental Medicine may be less effective for certain conservative AD treatments, such alternative treatments can help to reduce side effects and avoid recurrent symptoms without toxicity when treating AD. This is a strong reason

for us to continue working with this treatment. Furthermore, Oriental Medicine could be expected to be more helpful for the long-term management of AD and we should promote research on its effects continuously.

Acknowledgement

This research was supported by the Kyung Hee University Research fund in 2007.(KHU - 20070721)

References

1. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. Acta Derm Venereol(Stockholm)suppl 1980;92:44-7.
2. Williams HC. Is the prevalence of atopic dermatitis increasing? Clin Exp Dermatol 1992;17: 385-91.
3. Kim HJ, Honig PJ. Atopic dermatitis. Curr Opin Pediatr 1998;10:387-92.
4. Willams H, Robertson G, Stewart A. Worldwide variations in the prevalence of symptoms of atopic dermatitis in the international study of asthma and allergies in childhood. J Allergy clin Immunol. 1999;103:125-38.
5. Su JC, Kemp AS, Varigos GA, Nolan TM. Atopic eczema: its impact on the family and financial costs. Arch Dis Child. 1997;76:169-72.
6. Sowden JM, Berth-Jones J, Ross JS. Double-blind, controlled, crossover study of cyclosporine in adults with severe refractory atopic dermatitis. Lancet 1991;338:137-40.
7. Salek MS, Finlay AY, Luscombe DK. Cyclosporine greatly improves the quality of life of adults with severe atopic dermatitis: a randomized, double-blind, placebo-controlled trial. Br J Dermatol 1993;129:422-30.
8. Hiromi K, Kuniaki T, Nobuyuki M, Haruo K, Masamitsu. An alternative approach to atopic dermatitis: Part Ⅰ-case series presentation eCAM 2004;1(1):49-62.
9. Noori S. Al-Waili. Topical Application of Natural Honey, Beeswax and Olive Oil Mixture for Atopic Dermatitis or Psoriasis: Partially Controlled, Single-Blinded Study. Complementary Therapies in Medicine 2003;11:226-34.
10. M.Y.Shapira, Y.Raphawlovich, L.Gilad, R. Or, A.J.Dumb, A. Ingber. Treatment of Atopic Dermatitis with Herbal Combination of Eleuyherococcus, Achillea millefolium, and Lamium Album has no Advantage over Placebo: A double blind, placebo-controlled, randomized trial. J Am Acad Dermatol 2005;52:651-3.
11. FM Keane, SE Munn, AWP du Vivier, NF Tayor and EM Higgins. Analysis of Chinese herbal creams prescribed for dermatological conditions. BMJ 1999;318;563-4.
12. Hwa-Jung Yoon, Woo-Shin Ko. Clinical Study of Atopic Dermatitis; the Classification of Oriental Medical Clinical Type and Treatment. J Korean Oriental Med 2001;22(2):10-21.
13. Hwa-Jung Yoon, Jung-Won Yoon, So-Won Yoon, Woo-Shin Ko. A Study the Severity Scoring Systems of Atopic Dermatitis; Comparison, Analysis and Establishment. J Korean Oriental Med 2002;23(4):15-26.
14. Li B J. Pikezhengzhigaiyao, Renminweisheugchubanshe, Beijing, 2001:222.
15. Soon-Il Kim, Young-Min Ahn, Se-Young Ahn, Ho-Kyung Doo, Byung-Chel Lee. The Effects of Phellodendri Cortex Treatment on Hematological and Cyto-pathological Alterations in Non-Bacterial Prostatitis Rat Model. J Korean Oriental Med 2006;27(3):51-62.
16. European task force on atopic dermatitis, severity scoring of atopic dermatitis: the SCORAD index (Consensus Report of the European Task Force on Atopic Dermatitis). Dermatology 1993;186: 22-31.

17. Furue M, Furukawa F, Hide M, Takehara K. Guidelines for therapy for atopic dermatitis 2003. Jpn J dermatol 2003;113:451-7.
18. Baron ED, Barzilai D, Johnston G, Kawashima M, Takigawa M, Nakagawa H, *et al*. Atopic dermatitis management: comparing the treatment patterns of dermatologists in Japan, U.S.A. and U.K. Br J Dermatol 2002;147:710-5.
19. Hiromi K, Kuniaki T, Nobuyuki M, Haruo K, Masamitsu. An alternative approach to atopic dermatitis: Part Ⅱ-case series presentation. eCAM 2004;1(2):145-55.
20. Michael Y Shapira, Yisrael Raphaelovich, Leon Gilad, Reuven Or, Avraham J. Dumb, Arieh Ingber. Treatment of atopic dermatitis with herbal combination of Eleutherococcus, Achillea millefolium, and Lamium album has no advantage over placebo: A double blind, placebo-controlled, randomized trial. J Am Acad Dermatol 2005; 52:691-93.
21. Worm M, Henz BM. Novel unconventional therapeutic approaches to atopic eczema. Dermatology 2000;201:191-5.
22. Byeong-Kook Son, In-Hwa Choi. 6 Cases of Acute Lesion of Atopic Dermatitis Diagnosed as Dampness-heat Type. The Journal of Korean Oriental Medical Ophthalmology, Otorhinolaryngology & Dermatology 2007;20(2):213-20.