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아토피성 피부염의 한약치료 효과에 관한 고찰

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ABSTRACT

An overview of herbal medicine for atopic dermatitis

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목 적 : 한약 또는 한약제제의 아토피성 피부염에 대한 치료효과를 조사하고 향후 연구방향을 제시하기 위하여 고찰연구를 시행하였다.

방 법 : PubMed에 한약과 아토피성 피부염과 관련된 검색어의 조합을 넣어 포함기준에 맞는 무작위배정 대조군 임상연구만 포함하였다. 연구설계, 치료방법, 대조군, 평가지표, 결과, 부작용 관련 정보를 미리 정해놓은 자료 추출 형식에 맞추어 추출하고 방법론적 질 평가는 옥스포드 질 평가 척도와 그룹 할당 은닉(allocation concealment) 여부를 평가하였다. 연구들이 임상적 및 통계적으로 상이하여 메타분석은 이루어지지 않고 기술적 고찰만 실시하였다.

결 과 : 모두 8편의 연구가 고찰기준을 만족시켰다. 다양한 복합한약제제와 한약이 포함된 외용제가 평가되었는데 8편 가운데 5편에서 아토피성 피부염의 증상을 호전시키는 것으로 나타났다. 방법론적 질은 대체로 양호한 것으로 나타났으며 일부 효과적인 것으로 나타난 한약복합제제에서 간손상 등의 부작용도 보고되었다.

결 론 : 한약 또는 한약제제를 이용한 치료는 아토피성 피부염의 증상개선에 도움이 되는 것

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으로 보이나 현재 근거는 부족하다. 우리나라에서 많이 쓰이는 한약제제들 역시 엄정한 임상연구를 거쳐 그 효과를 평가하고 근거를 구축해야 할 것이다.

Key word : Herbal medicine, atopic dermatitis, herbal ointment, randomised controlled trial, cross-over study

Ⅰ. Introduction

Atopic dermatitis (AD) or atopic eczema is an intensely itchy and erythematous (red) inflammatory skin disease, usually involving the skin creases[1]. It has been reported that around 70% of AD patients are infants or children under 5[2] and they are often accompanied by other allergic diseases such as asthma or allergic rhinitis[3]. As there is no cure for this distressing disease, a range of interventions are to control symptoms. Standardised treatment usually consists of topical emollients and corticosteroid cream, which are often effective in mild-to-moderate AD. For more severe and wide forms of AD, however, current available treatments often fail in some patients and other interventions such as systemic steroid, azathioprine, and cyclosporine A are all associated with severe adverse events[4,5]. Due to the relapsing nature of AD, its chronicity, and its lack of response to steroids, there have been increasing efforts to develop better and safer complementary or alternative therapies including herbal medicine. Although herbal medicine has long been used to treat or relieve symptoms of AD in Korea and China, evidence supporting its use is not convincing; in the most recent systematic review on oral Chinese herbal medicine for atopic eczema, the authors reported that herbal medicine may be effective but small number of poorly reported trials of the same product precluded any firm conclusions[6]. Evaluating the efficacy of herbal medicines or mixtures has a range of difficulties as their particular distinguishing features do not fit exactly into the conventional drug testing framework. Previous studies have been judged as not ideally rigorous; no appropriate sample size calculation leading to small study effects, lacking details of allocation concealment, questionable blinding, no intention-to-treat analysis and high drop-out rate.

In Korea, more and more patients with AD are seeking treatments of Korean medicine including herbs[7] as it is probably conceived that treatments of Korean medicine are safe and may eradicate the origin of this refractory disease. In a recent survey asking "are treatments of Korean medicine or complementary alternative medicine for AD more effective than those of Western medicine?", however, 91% of responders answered 'no' or 'don't know'[7]. Taking all these into account, clear evidence and rigorous research are urgently needed. Therefore, an overview of the

current evidence on herbal medicine for AD was conducted to summarise and critically assess the evidence.

Ⅱ. Materials & Methods

1. Literature search

Electronic literature search in PubMed was performed from its inception to January 2009. The search terms used were "atopic dermatitis", "atopic eczema", "neurodermatitis", "Besnier's prurigo", "Chinese herbal medicine", "complementary medicine", and "complementary therapy" with limits of humans and randomised controlled trial. Reference lists of original articles and relevant reviews were examined for additional studies.

2. Selection of studies

Studies meeting the following criteria were included:

1) Randomised controlled trials, including cross-over designs;

2) Intervention should be Chinese herbal medicine for AD. Oral decoctions or ointment of Chinese herbs, either on their own or with other drugs, compared with placebo group or no treatment;

3) Patients should be diagnosed with AD or atopic eczema using diagnostic criteria such as Hanifin and Rajka definition[8] or its UK modification[1]. All other terms such as 'Besnier's prurigo' or 'neurodermatitis' should be supported with the evidence of atopic eczema in the flexures to be included;

4) Primary outcome measures should be patient-rated clinical responses, i.e. SCORing Atopic Dermatitis (SCORAD) score, proportion of patients with clinically significant changes in symptoms such as itching or sleep loss. Patient preference was also considered as primary outcome. Secondary outcome measures included global assessment by a doctor.

5) Only studies published in English were considered for review.

3. Methodological quality assessment

Assessment of methodological quality was performed using Oxford scale, i.e. Jadad scale[9]. In addition, allocation concealment was evaluated as 'adequate', if the group assignment could not be foreseen.

4. Data extraction

The following data were extracted using the pre-defined and -tested form: the first author's name, year of publication, trial design, allocation concealment as adequate, inadequate, not clear, or no allocation concealment, details of participants and diagnosis, number of patients, blinding, details of interventions, primary and secondary outcome measures available and withdrawals and dropouts. Corresponding authors were contacted via e-mail and asked to provide further information if necessary.

5. Data analysis

Heterogeneous reporting and small number of studies were expected, therefore, descriptive review instead of meta-analysis was performed. If there are more than one control group, efficacy in comparison with placebo was considered first.

Ⅲ. Results

Search results are shown in Fig. 1. From the searches, 8 relevant studies were located and their characteristics are tabulated in Table 1.

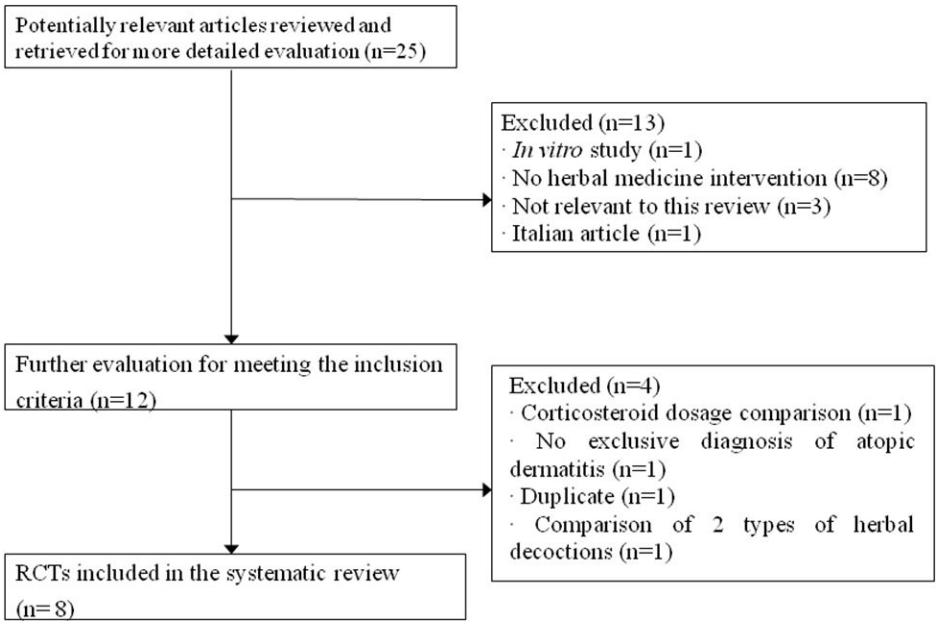

Fig. 1. Flowdiagram of Literature Search

Table 1. Characteristics of the included studies

Author (year)	Design	Allocation concealment	Methodological quality*	Participants & diagnosis	Intervention (no. of participants analysed / randomised)	Outcome measures
Klövekorn (2007)[10]	RCT, half-side comparison, double-blind, vehicle-controlled	No information	1+1+1+1+1 =5	• Patients aged 18-65 • By Hanifin and Rajka criteria / moderate to severe AD • 3-7 points by Rajka and Langeland grading criteria	• HM (87/88): herbal ointment containing alcohol-based plant extracts of *Mahonia aquifolium* (南天竹), *Viola Tricolor* (紫花地丁), and *Centella asiatica* (積雪草), 5g each per 100g ointment, twice/day to all affected areas in randomly allocated side for 4 wk • CON (87/88): DAC base formulation (vehicle), twice/day to all affected areas in randomly allocated side for 4 wk	• Change of summary score on a 4-point scale for erythema, oedema /papulation, oozing/crust, excoriation and lichenification of the target area between 1st and last day of treatment • 10 cm VAS for pruritis • Verbal assessment of global effectiveness on a 6-point scale
Hon (2007)[17]	RCT, 2 parallel groups,	Adequate	1+1+1+1+1 =5	• Children aged 5-21 • By Hanifin and	• HM (42/42): *Lonicerae flos* (金銀花)2g, *Menthae herba* (薄荷)1g, *Moutan cortex*	• SCORAD and CDLQI scores at the end of 12 wk treatment

	double-blind, placebo-controlled			Rajka criteria / moderate to severe AD (SCORAD score>15)	(牧丹皮)2g, *Atractylodis rhizoma* (蒼朮)2g, *Phellodendri cortex* (黃柏)2g in capsules, 3 capsules, twice/day for 12 wk • CON (43/43): matching placebo capsules	• CS and antihistamine use
Shapira (2005)[16]	RCT, 2 parallel groups, double-blind, placebo-controlled	No information	1+0+1+0+0 =2	• Patients aged over 1 • 3 out of following 4 criteria: 1) flexor surface involvement 2) asthma or hay fever or atopia in a 1st degree relative 3) dry skin, and 4) beginning signs of the disease before the age of 2	• HM (22/22): *Eleutherococcus* (五加皮), *Achillea millefolium* (一枝蒿), *Lamium album* (野芝麻) in hydro-ethanoic extract, 3 times/day for 2 wk • CON (22/22): placebo, no detailed information	• SCORAD at 2 wk
Schempp (2003)[12]	RCT, half-side comparison, double-blind, placebo-controlled	No information	1+0+1+1+1 =4	• Patients aged 12-59 • Subacute AD (SCORAD score<80)	• HM (18/21): St. John's wort (*Hypericum perforatum* L.) cream containing 1.5% hyperforin, twice daily for 28 days to the allocated side (Lt or Rt) • CON (18/21): Placebo cream, twice daily for 28 days to the allocated side (Lt or Rt)	• Modified SCORAD score • Bacterial colonisation of skin lesions
Patzelt-Wenczler (2000)[11]	RCT, double half-side comparison, hydro-cortisone-, placebo-controlled	No information	1+0+0+0+1 =2	• Mean age 45.5 • Moderate to severe AD (sum score of 3-7 for pruritis, erythema & desquama-tion (Max. 9))	• HM (69): Kamillosan cream®(2% ethanol extract from chamomile flowers), 50g, twice daily for 2 wk to the allocated side (Lt or Rt) • CON1 (36): 0.5% hydrocortisone cream, twice daily for 2 wk to the allocated side (Lt or Rt) • CON2 (33): Placebo cream, twice daily for 2 wk to the allocated side (Lt or Rt)	• Change of summary score on a 4-point scale for pruritis, erythema, & desquamation • Global assessment of each arm on a 4-point scale
Fung (1999)[13]	RCT, crossover, double-blind, placebo-controlled	No information	1+0+0+0+1 =2	• Patients aged 8-52 • By Hanifin and Rajka criteria / moderate to severe AD resistant to topical	• HM (37/40): Zemaphyte®† once daily for 4 wk and twice daily for next 4 wk followed by 4 wk wash-out and 8 wk placebo treatment • CON (37/40): Placebo treatment for 8 wk followed by 4 wk wash-out and then Zemaphyte® once daily for 4	• Standardised clinical score‡ at every 4 wk

				treatment	wk and twice daily for next 4 wk	
Sheehan (1992a)[14]	RCT, crossover, double-blind, placebo-controlled	No information	1+0+0+0+1 =2	• Children aged 1.5-18.1 • Extensive non-exudative AD resistant to standard topical treatment and to antihistamine	• HM (37/47): Zemaphyte®† once daily for 4 wk and twice daily for next 4 wk followed by 4 wk wash-out and 8 wk placebo treatment • CON (37/47): Placebo treatment for 8 wk followed by 4 wk wash-out and then Zemaphyte® once daily for 4 wk and twice daily for next 4 wk	• Standardised scoring system§ at every 4 wk
Sheehan (1992b)[15]	RCT, crossover, double-blind, placebo-controlled	No information	1+0+0+0+1 =2	• Patients aged 19-57 • By Hanifin and Rajka criteria	• HM (31/40): Zemaphyte®† once daily for 8 wk followed by 4 wk wash-out and 8 wk placebo treatment • CON (31/40): Placebo treatment for 8 wk followed by 4 wk wash-out and then Zemaphyte® once daily for 8 wk	• Standardised scoring system§ at every 4 wk

*, Methodological quality was assessed using the Oxford scale where two points are given for randomisation and appropriate randomisation method used, two points for double-blinding and appropriate blinding method used, and one point for description of withdrawals and dropouts; †, standardised formulation of plant materials consisting of *Ledebouriella seseloides* (防風), *Potentilla chinensis* (萎陵菜), *Clematis armandii* (木通), *Rehmannia glutinosa* (地黃), *Paeonia lactiflora* (白芍藥), *Lophatherum gracile* (淡竹葉), *Dictamnus dasycarpus* (白鮮皮), *Tribulus terrestris* (白蒺藜), *Glycyrrhiza uralensis* (甘草) and *Schizonepeta tenuifolia* (荊芥); ‡, according to the "rule of 9," the body was divided into 5.5 units, each treated as single units as each is equivalent to 18% of the total body surface area. The head was treated as a half unit. At each unit, two active signs (erythema and surface damage) and two chronic signs (lichenification and scaling) were assessed using a severity score of 0 (none) to 3 (severe). According to the area of involvement in each unit, an area score of 1 for <33%, 2 for 33-66% and 3 for >66% involvement was also made. An adjusted score for a clinical parameter was defined as the product of the severity score and the areas score in each unit. The sum of the adjusted scores in all units gave the clinical score for the assessed parameter. Clinical scores for erythema, surface damage, lichenification, and scaling were obtained for each patient; §, body surface was divided into 0 roughly equal areas and within each area, a score of 0 (none) to 3 (severe) for the degree of erythema and surface damage (i.e., population, vesiculation, scaling, excoriation, and lichenification) was made. For each of these clinical features and estimate of the percentage area within each zone affected by that particular feature was measured. A score of 1 where the area affected was <33%, 2 where the area was between 34 and 66%, and 3 where the area was >67%. The sum of the severity scores multiplied by the area scores provided a total body score for each feature, the Max. being 180; AD, atopic dermatitis; CDLQI, children's dermatology life quality index; CON, control group; CS, corticosteroid; DAC, Deutsche Arzneimittel-Codex; HM, herbal medicine; Lt, left; RCT, randomised controlled trial; Rt, Right; SCORAD, scoring atopic dermatitis; wk, week.

Table 2. Outcomes of the included studies

Author (year)	Outcomes	Tolerability or compliance / Adverse events	Comments
Klövekorn (2007)[10]	• NS in summary score • NS in pruritis severity • NS in global assessment of effectiveness	• Tolerability acceptable • No significant AE in HM group	• ITT analysis • HM superior to CON for summary score in a *post-hoc* subanalysis (n=64) considering the outside temperature (P=0.019) • CS, antihistamines, antipruritic agents, topical NSAIDs, antimicrobials, urea, coal tar, UV treatment, phototherapy, and immunosuppressive agents not allowed
Hon	• NS in total SCORAD score	• Tolerability acceptable	• ITT analysis

(2007)[17]	• HM superior to CON in CDLQI score (P=0.008) • NS in CS and antihistamine use	• No significant AE in HM group • NS in AE between groups	• Emollients, bath oil, soap substitutes, topical CS and oral systemic antihistamine allowed
Shapira (2005)[16]	• NS in total SCORAD score either at 2 wk or 8 wk • NS either in body surface area involvement or intensity score • NS either in sleep loss or pruritis at 2 wk	• Tolerability acceptable • No significant AE in HM group	• No description of withdrawals or dropouts • Changes in topical treatment, use of local immunomodulators not allowed
Schempp (2003)[12]	• HM superior to placebo in modified SCORAD score at all visits: day 7 (P=0.002), day 14 (P=0.016), day 28 (P=0.022), respectively • NS in bacterial colonization of skin lesions • HM superior to placebo in the no. of CFUs of *Staphylococcus aureus* (P=0.064)	• Tolerability acceptable • Cosmetic acceptability: good or excellent by over 65% patients • No serious AE	• ITT analysis • Concurrent use of topical agents or medicinal products containing CS not allowed
Patzelt-Wenczler (2000)[11]	• HM better than hydrocortisone and placebo in summary score for pruritis, erythema & desquamation • HM better than hydrocortisone and placebo in global assessment	• Tolerability acceptable	• No other treatment allowed • No proper statistical analysis performed or no corresponding information reported
Fung (1999)[13]	• NS in median changes in clinical scores for erythema (P=0.775), surface damage (P=0.822), and scaling (P=0.869) • HM superior to placebo in decrease in lichenification only (P=0.013)	• Few minor AEs including hair-loss, transient dizziness, GI upsets, and lichenoid eruption on the trunk • No serious AE	• Normal complete blood picture, renal and liver function throughout the study • No information on concurrent use of topical agents or medicinal products containing CS
Sheehan (1992a)[14]	• HM superior to placebo in median percentage decrease in erythema scores (HM 51.0, 95% CI [34.5, 72.6] vs. placebo 6.1, [-25.2, 30.7]) • HM superior to placebo in median percentage decrease in surface damage (HM 63.1, [34.5, 72.6] vs. placebo 6.2, [-25.2, 30.7])	• No information	• No proper sample size calculation • Different dosages for different ages • Concurrent use of CS not allowed • Normal haematological and biochemical profiles throughout the study
Sheehan (1992b)[15]	• HM superior to placebo in erythema (P<0.0005) and surface damage (P<0.0005)	• Minor AE: 2 patients having mild abdominal distension and headaches	• Normal haematological and biochemical profiles throughout the study • Normal blood pressure or weight

AE, adverse events; CDLQI, children's dermatology life quality index; CFUs, colony-forming units; CI, confidence interval; CON, control group; CS, corticosteroid; GI, gastrointestinal; HM, herbal medicine; ITT, intention-to-treat; NS, no significant difference; NSAID, non-steroidal anti-inflammatory drug; SCORAD, scoring atopic dermatitis; wk, week.

1. Description of studies

Three studies were conducted in Germany[10-12], two each in China[13] and UK[14,15], and one in Israel[16]. Number of patients involved in the studies was 474 and 445 were analysed. Two studies had children only[14,17], while the others had adults or mixed populations. Half of the included trials adopted Hanifin and Rajka criteria for diagnosis of AD[10,13,15,17]. In three trials, different herbal ointments were tested against vehicle[10], placebo cream[11,12], and hydrocortisone

cream[11]. The other trials investigated the effect of various oral extracts or decoctions. The treatment duration ranged from 2 weeks to 12 weeks.

2. Methodological quality

Two out of 8 studies were double-blind, placebo-controlled, two parallel group trials[16,17] and three were half-side comparison RCTs[10-12], while the other three were cross-over, double-blind, placebo-controlled studies[13-15]. Mean quality score was 3 points (SD 1.4, range 2 to 5); sequence generation method was considered inadequate or not described except two studies[10,17]; only three out of 8 trials were assessed to have used adequate double-blinding methods[10,12,17]. Information on adequate allocation concealment was not provided in any of the included trials except one where adequate sequence generation and allocation concealment was reported[17]. Only three trials reported intention-to-treat analyses[10,12,17].

3. Outcomes

1) Efficacy/effectiveness

Five trials reported significant symptom improvements; Hon et al. reported twice-daily dosing of three capsules of herbal formula consisting of 5 herbs, i.e. *Lonicerae flos* (金銀花), *Menthae herba* (薄荷), *Moutan cortex* (牧丹皮), *Atractylodis rhizoma* (蒼朮), *Phellodendri cortex* (黃柏), for 12 weeks resulted in 30% improvement in Children's Dermatology Life Quality Index (CDLQI) score at the end of treatment (P=0.008). However, there was no significant intergroup difference either in SCORAD or corticosteroid/antihistamine use[17]. St. John's wort (*Hypericum perforatum* L.) cream containing 1.5% hyperforin, applied twice daily for 4 weeks, was superior to placebo cream in SCORAD score at 1, 2, and 4 week visits (P=0.002, 0.016, 0.022, respectively)[12]. When Kamillosan cream® made from 2% ethanol extract from chamomile flowers was applied twice daily for two weeks, a significant improvement in pruritis, erythema, desquamation, and patients' global assessment was achieved compared with placebo cream or 0.5% hydrocortisone cream[11]. This study, however, did not report values from proper statistical analysis thus validity of the results is questionable. Three studies tested the same product, Zemaphyte® in different doses. Zemaphyte® is a standardised formulation consisting of *Ledebouriella seseloides* (防風), *Potentilla chinensis* (萎陵菜), *Clematis armandii* (木通), *Rehmannia glutinosa* (地黃), *Paeonia lactiflora* (白芍藥), *Lophatherum gracile* (淡竹葉), *Dictamnus dasycarpus* (白鮮皮), *Tribulus terrestris* (白蒺藜), *Glycyrrhiza uralensis* (甘草) and *Schizonepeta tenuifolia* (荊芥), in sachets prepared by Phytopharm Plc, UK. Two London studies in 1992 showed benefit from Zemaphyte® in reducing erythema and surface damage[14,15], a Chinese study in 1999 did not find such benefit[13]. Concomitant treatments including corticosteroids were not allowed in 5 studies of which, three studies demonstrated positive results[11,12,14].

2) Tolerability/safety

Herbal medicine used in the included trials had all acceptable tolerability and also no serious adverse events were reported in any of the studies. In the Fung 1999 study, two patients complained of transient dizziness, 4 reported gastrointestinal upsets, and one developed lichenoid eruption on the trunk[13]. Mild abdominal distension

and headaches were reported in another Zemaphyte® study[15]. Only one trial missed such information[14]. Three studies reported normal haematological and biochemical profiles[13-15]. Later, however, Sheehan et al. reported their long-term follow-up results; fatal hepatic abnormalities were observed in two children in the following observational study but returned to normal after discontinuing the herbal therapy[18]. Gastrointestinal upsets were often reported after taking Zemaphyte® and a mild laxative effect was observed in about one-third of patients who continued with the treatment[18,19].

Ⅳ. Discussion

1. Summary of main findings

This overview of the current evidence on herbal medicine for AD found inconsistent results. Tested herbal medicine varied across trials and also was given in different form and dosage for different duration. A formulation of *Lonicerae flos* (金銀花), *Menthae herba* (薄荷), *Moutan cortex* (牧丹皮), *Atractylodis rhizoma* (蒼朮), *Phellodendri cortex* (黃柏) in capsules improved CDLQI score in children aged 5-21[17]. St. John's wort cream[12] and Kamillosan cream®[11] seem to alleviate symptoms compared with placebo. Although Zemaphyte® consisting of 10 herbs showed benefit for both adults and children[14,15], serious adverse events have been reported. Evidence is limited both in numbers and quality.

2. Applicability of evidence

As this review included only 8 heterogenous RCTs, a careful look at the individual studies is needed. The included studies adopted various forms of herbal medicine, from powder in capsule to herbal ointment. Although three out of 8 studies looked into the same product, no clear direction of outcome could be seen from the studies. Two studies had children only[14,17], while the others had adults or mixed populations. Control regimen and concomitant treatment greatly varied across studies. This high level of clinical heterogeneity needs caution in interpretation and application of the findings of this review.

In Korea, there are few RCTs of herbal medicine for AD; most of the studies are animal study, case report, or before-after comparison study when searched with the keyword 'atopic dermatitis' in Korean Oriental Medical Society's electronic database (Nov 2009 accessed). Moreover, randomised, double-blind, placebo-controlled trials are sparse. Frequently used Korean herbal decoctions should be tested in rigorously designed and well conducted RCTs to inform patients with this refractory disease of effective treatment options available. For Korean Medicine Doctors who are more familiar with oral administration of water extract of herbal medicine, herbal powder in capsule or ointment in this review provides new ideas on what approach should be sought or could be possible in the future.

3. Quality of studies

The Oxford scale or Jadad scale was used to assess methodological quality of the included studies[9]. The scale evaluates three important domains, i.e. randomisation, blinding, and handling withdrawals and dropouts. In addition to this, allocation concealment was assessed as in the Cochrane reviews. Mean quality score was generally high (mean±SD, 3±1.4). The highest risk of bias

in the included trials, however, may lie in allocation concealment. It has been reported that inadequate allocation concealment in trials where a subjective outcome was analysed overestimates intervention effect[20]. Outcomes used in the included trials, i.e. SCORAD, summary score for several symptoms, or CDLQI, are subjective and thus prone to bias. Only one study described adequate sequence generation and allocation concealment[17] and this should be taken into account when interpreting the results. Only three trials reported intention-to-treat analyses[10,12,17]. In all three cross-over trials of Zemaphyte®, carry-over effects were reported with no significance[13-15].

4. Potential biases

Bias can be introduced in every step of reviewing and this review is no exception. As this review looked at the publications enlisted in PubMed only, the potential of missing eligible trials, especially from Chinese databases, may be greater than expected. Empirical evidence tells us that including publications in languages other than English appears to have little impact on the conclusion of the review[21] and it remains unanswered whether this could be the case for this review. A recently published review on Chinese herbal medicine for AD looked into 29 Chinese articles and the treatment regimens were more diverse and at the same time, lacking appropriate testing[22]. Rigorous clinical trials in this field are warranted.

5. Implications for practice and research

Based on the findings of this review, it is not clear whether herbal medicine alleviates symptoms of AD, i.e. itching, or sleep loss. Due to heterogeneity of the studies, the findings in this review are difficult to interpret as a firm evidence against herbal medicine for AD. Some of herbal decoction or ointment tested in the trials included in this review appear to reduce symptoms of AD compared with placebo, but the evidence is limited. Little evidence emerged for any harm caused by herbal medicine except Zemaphyte®. The evidence presented in this review should be made available to both Korean Medicine Doctors and patients with AD to help them make informed decisions on whether or not to use herbal medicine for AD. A number of questions should be answered in future studies. This review found rigorous trials testing herbal decoctions that Korean Medicine Doctors frequently use for AD are few. These decoctions, i.e. Saeng-hyul-youn-boo-eum (生血潤膚飮), On-chung-eum (溫淸飮), Bang-poong-tong-sung-san (防風通聖散), Pyung-wee-san (平胃散) or Yang-wee-tang (養胃湯), once tested in a before-after comparison[23,24], should be tested in a well-designed and -conducted, double-blind, placebo-controlled RCTs. The trials should answer a range of research questions such as its efficacy, optimal dosage and treatment duration, best responders, i.e. children or adults, acute or chronic stage, or types of pattern (辯證型), safety, and mechanism whereby these decoctions work. If oral administration of water extract of herbal medicine is not preferred by the patients, especially children, different types of herbal medicine such as powder in tablets, or ointment should be developed and tested. We have no sound data on the costs associated with herbal medication for AD. Future studies should be planned and conducted to address all these

issues.

V. Conclusion

To conclude, current evidence seems to support the use of herbal medicine for AD but the results are inconsistent and rather limited. The heterogeneity of the studies available to date prevents making a firm conclusion. Further research seems to be warranted.

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