

SOUTH BAYLO UNIVERSITY

The Effectiveness of Acupuncture in the Treatment of Atopic Dermatitis:

A Literature Review

BY

Catherine Duong

**A RESEARCH PROJECT SUBMITTED
IN PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE**

Doctor of Acupuncture and Oriental Medicine

ANAHEIM, CALIFORNIA

JUNE 2018

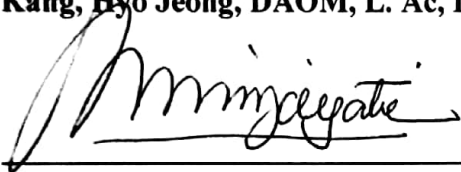
**THE RESEARCH PROJECT OF CATHERINE DUONG
APPROVED BY DOCTORAL RESEARCH COMMITTEE**



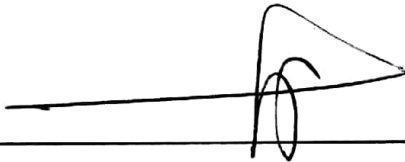
Melen, Pia, O.M.D, L.Ac, Academic Dean



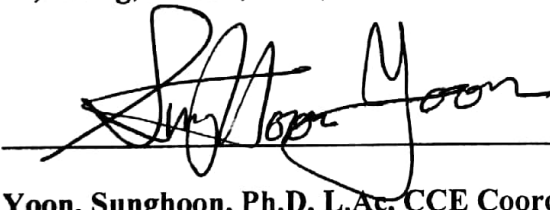
Kang, Hyo Jeong, DAOM, L. Ac, Director of SBU Clinic/Faculty



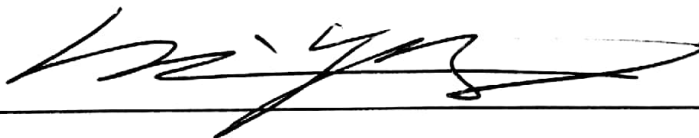
Sandjaya Tri, M.D., DAOM, L.Ac, Clinic Supervisor/Faculty



Li, Sheng, O.M.D, L.Ac, DAOM Clerkship Coordinator/Faculty



Yoon, Sunghoon, Ph.D, L.Ac, CCE Coordinator/Faculty



Suh, Joseph, Ph.D, L.Ac, Doctoral Research Coordinator/Faculty

SOUTH BAYLO UNIVERSITY

ANAHEIM, CALIFORNIA

JUNE 22, 2018

Copyright

by

Catherine Duong

2018

ACKNOWLEDGMENTS

I would like to express my appreciation to my advisor Dr. Yuri Ovchinnikov who guided me and helped me in completion of my literature review. I also would like to thank Dr. Wayne Cheng, Dr. Sheng Li, Dr. Sung-Hoon Yoon, Dr. Tri Sandjaya for their help and feedback. Lastly, I would also like to express sincere gratitude to my friends and family for the support and encouragement throughout this doctoral research project.

**The Effectiveness of Acupuncture in the Treatment of Atopic Dermatitis:
A Literature Review**

Catherine Duong

SOUTH BAYLO UNIVERISTY AT ANAHEIM, 2018

Research Advisor: Dr. Yuri Ovchinnikov, DAOM, L.Ac.

ABSTRACT

Atopic Dermatitis (AD) has a high negative impact on the quality of life. The costs associated with AD are difficult for patients and their family members to manage. AD incidents are increasing each year and there is no definitive cure for AD. Thus, patients often seek acupuncture as a complementary therapeutic option.

The main purpose and objective of this research is to evaluate evidence for the effectiveness of acupuncture in the treatment of atopic dermatitis. The research rational is to establish evidence on acupuncture effectiveness in treating atopic dermatitis or itchiness.

The research adopted a systematic search to identify clinical trials and reviews secondary data from publications. The research inclusion criteria included; (1) acupuncture-specific; (2) limited to atopic dermatitis or itching; (3) published in English; (3) clear objectives and outcome measures (5) Outcome measures must include itch. While the exclusion criteria included; (1) all the databases other than English language; (2) studies with outcome assessments that cannot be used to make a comparison with other studies, (3) studies with no data.

Acupuncture was used to treat atopic dermatitis, atopic eczema, urticaria, and pruritus. In the 3 RCTs show that acupuncture is effective to ameliorate itch intensity of itch-related disease compared with placebo acupuncture and no intervention. In 6 of 11 case studies show the significant acupoints LI11, LI4, SP10, ST36, GB31, Baichongwo (extra point) in reducing itching. In the 4 vivo studies show that there is a decreased in serum IgE levels and expression of pro inflammatory cytokines.

Acupuncture is effective in treating atopic dermatitis and only combination of certain acupoints are effective in treating itchiness. However; caution is warranted as acupuncture needling of a single acupoint in clinical research may not be equivalent to acupuncture treatment in clinical practice.

Keywords: Acupuncture and Atopic dermatitis

TABLE OF CONTENTS

| | |
|---------------------------|----|
| I. INTRODUCTION | 1 |
| II. LITERATURE REVIEW | 3 |
| III. MATERIAL AND METHODS | 9 |
| IV. RESULTS & DISCUSSION | 14 |
| V. CONCLUSION | 23 |
| VI. REFERENCES | 24 |
| APPENDIX | 29 |

ABBREVIATIONS

| | |
|--------|---|
| AD | Atopic dermatitis |
| VAS | Visual analogue scale |
| SCORAD | Severity Scoring of Atopic Dermatitis index |
| EASI | Eczema Area and Severity index |
| POEM | Patient-Oriented Eczema Measure |
| DNCN | 1-chloro-2,4-dinitrobenzene |
| VA | Verum acupuncture |

VA refers to traditional acupuncture, which is the technique of inserting thin needles through the skin to certain depths and at certain points on the body. The term verum acupuncture is used when comparing traditional acupuncture to sham (placebo) acupuncture. In sham acupuncture, needles do not go as deep and are not used at the same points on the body

| | |
|-----|--------------------------------|
| PA | Placebo acupuncture |
| NI | No intervention control |
| VAp | preventive verum acupuncture |
| Pap | preventive placebo acupuncture |
| VAA | abortive verum acupuncture |
| PAa | abortive placebo acupuncture |
| VC | Verum Cetirizine |
| PC | Placebo Cetirizine |
| GFD | Gluten-free diet |

I. INTRODUCTION

Atopic dermatitis (AD) overall has a high negative impact on quality of life. The burden of AD is difficult and costly. The direct and indirect costs are usually shared by the families and caregivers of patients with AD. Itching is an aspect of AD and is the most distressing for many patients and has been associated with mental stress and sleep disturbance [33]. Itchiness have shown limited efficacy and/or has significant side effects with conventional systemic approaches to reduce AD. The local and systemic side effects of topical steroids are well recognized. Local effects include skin atrophy, striae, telangiectasias, hypopigmentation, rosacea, perioral dermatitis and acne. Systemic side effects include adrenal suppression, cataracts, glaucoma and growth retardation in children.

There has been mixed findings on acupuncture use as an alternative modality in treating dermatitis. Studies have shown that the prevalence of CAM use in the general U.S. population to be around 38%. The national prevalence is estimated to be around 0.6% and 1.4% [2]. In one study, 51 percent of patients with AD reported use of acupuncture because patients reported high levels of dissatisfaction with prior treatment and frustration with the chronic nature of the disease reported [19].

With the increasing use of acupuncture as an alternative modality, there is a need to access the effectiveness of acupuncture in AD treatments as AD and health burden continue to rise, new approaches in AD management are imminent. Secondly, the most distressing aspect of AD is itchiness which needs to be emphasized as part of treatment management yet studies have shown that acupuncture has antipruritic actions and can assist in the treatment of AD.

Thus the study explores to evaluate the evidence of acupuncture's effectiveness for treatment of AD. It will focus on establishing evidence on acupuncture effectiveness in treating atopic dermatitis or itchiness. The invaluable information in understanding the evidence on acupuncture for the treatment of skin diseases can provide guidance for clinician to finding alternative managements when other modalities failed, as well as guidance for future research. Further, the significant evidence in acupuncture in treatment of AD can overall improve patients' quality of life and to reduce the burden of the disease and long terms med used that would lead to complication.

II. LITERATURE REVIEW

Dermatitis is an inflammatory condition of the skin characterized by itchy, red, swollen, and cracked skin. There are several types such as contact dermatitis, seborrheic dermatitis, nummular dermatitis, and stasis dermatitis. What makes atopic dermatitis different from other dermatitis is that AD exists with asthma and hay fever (allergic rhinitis). A person with atopic dermatitis often has a genetic mutation in a protein in their skin called filaggrin and usually occurs in children five years of age or younger. The age of a person and the present of allergies are important distinction of AD from other dermatitis.

Atopic dermatitis (AD) is categorized into the extrinsic and intrinsic types. Extrinsic or allergic AD shows high total serum IgE levels and the presence of specific IgE for environmental and food allergens. Intrinsic or non-allergic AD exhibits normal total IgE values and the absence of specific IgE.

Atopic dermatitis is seen in approximately 10% to 30% of children and 2% to 10% of adults in developed countries. This prevalence has increased two to three-fold in recent decades. Atopic dermatitis has a higher incidence at higher latitudes, which may be related to decreased sun exposure and lower humidity levels [12]. The prevalence of AD has increased greatly and its tendency to occur most frequently among infants aged one year or less and to reduce with increasing age has been maintained [33].

Many genetic and epidemiologic studies have concluded that AD is caused by multiple environmental triggers in susceptible individuals. The cause of AD is unknown, both genetic and environmental factors play a role. These factors include immune dysfunction, food allergens,

aeroallergens, air pollutions, and skin environment. The most common trigger is *S. aureus* colonization. More than 90% of patients with atopic dermatitis have *S. aureus* colonization of lesional skin, and more than 75% have colonization of uninvolved skin. [12]. Many other factors can also exacerbate or trigger atopic dermatitis, including stress, anxiety, systemic illness, and xerosis. The primary risk factor for atopic dermatitis is having a personal or family history of eczema.

The aetiology and pathogenesis of AD remain unclear, but there is involvement of genetic, immunological and environmental factors along with inflammation [20]. The pathogenesis is mostly multifactorial and involves a complex immunologic cascade, including disruption of the epidermal barrier, IgE dysregulation, defects in the cutaneous cell-mediated immune response, and genetic factors. The pathophysiology may also involve a mixture of type 1 and type IV-like hypersensitivity.

The diagnosis of atopic dermatitis is based on the findings of the history and physical examination. The clinical manifestation of AD is itchy, red, swollen, and cracked skin. Itch is the hallmark of the disease affecting the folds of the arms, the back of the knees, wrist, face, and neck. Asthma and allergic rhinitis are the accompanied clinical manifestation with AD that is considered in the diagnosis. Exposure to possible exacerbating factors, such as aeroallergens, irritating chemicals, foods and emotional stress are evaluated.

There are no specific laboratory findings or histologic features define atopic dermatitis. Although elevated IgE levels are found in up to 80 percent of affected patients, IgE levels are also elevated in patients with other atopic diseases [32].

Treatment and management of atopic dermatitis should start with education of the patient about chronic nature of the disease and importance of maintenance therapy. Treatment should be directed at limiting itching, repairing the skin and decreasing inflammation when necessary. Lubricants, antihistamines and topical corticosteroids are the mainstays of therapy. When required, oral corticosteroids are used for the early-intervention management of inflammation.

When atopic dermatitis is not controlled with topical agents, systemic agents include phototherapy (ultraviolet (UV) A, UVB, and narrow-band UVB), cyclosporine, azathioprine, mycophenolate mofetil, and methotrexate. The local and systemic side effects of topical steroids are well recognized. Local effects include skin atrophy, striae, telangiectasias, hypopigmentation, rosacea, perioral dermatitis and acne. Systemic side effects include adrenal suppression, cataracts, glaucoma and growth retardation in children.

The complications of atopic dermatitis may include asthma, hay fever, neurodermatitis, skin infections, allergic contact dermatitis, insomnia, and psychological effects. The prognosis is good for mild AD and most patients do improve.

As there is no definitive cure for atopic dermatitis, patients often seek acupuncture as other complementary therapeutic options [8].

Acupuncture is one of the oldest forms of naturally healing dated back to early as the 4th or 3rd century BC [2]. There are many forms of acupuncture known, including filiform needling, dry needling, ear/auricular acupuncture, laser acupuncture and electroacupuncture [20]. It is the main component in Traditional Chinese Medicine and its technique involves inserting manually small thin needles on the skin superficially at specific anatomical points. Studies on the mechanism of

acupuncture suggest that the effects of acupuncture are due to physiological response and nervous activation by needle insertion [6].

TCM views the body as a constellation of dynamic forces called Qi, which flow through the body in a pattern of channels, or meridians, which form the basis of needle placement in acupuncture [2]. When the flow of energy becomes deranged by pathology, forces become congested in certain areas and deficient in others, and thus form the basis of illness in TCM. Acupuncture is considered a way of relieving this congestion. This method had originated in China and possibly dates as far back as 200 000–300 000 BC based on bone needles and bamboo shafts thought to be acupuncture tools [10]. With regards to Traditional Chinese Medicine, there are many possible TCM patterns that correspond to the western diagnosis of atopic dermatitis.

The TCM pattern of Damp Heat accounts for most cases of atopic dermatitis regardless of the age of the patient. Both Damp Heat and the deficiency of Spleen and Stomach are a possibility in subacute stages of atopic dermatitis. Lack of appetite is the most common spleen disharmony according to classical TCM pattern differentiation. The impairment of the spleen transformation and transportation function causes the various digestive symptoms which can give rise to the retention of dampness [14].

The TCM pattern of Heat in the Blood is also a possibility during the childhood phase of atopic dermatitis as well as the adolescent/adult phase. Though some Damp Heat may also be present, this pattern presents as the drier type of atopic dermatitis, with more redness and more intense itching than when there is only Damp Heat. Heart Heat is typically the underlying source of the Heat in the Blood. Heat in the Blood pattern can also occur in the acute or subacute stages of atopic dermatitis [13].

Most chronic stages of atopic dermatitis are seen in the adolescent/adult phase. The skin may exhibit lichenification where it is thicker, drier, rougher, and may have scaling. These cases are most often diagnosed in TCM as Blood Dryness Due to Damaged Yin with Accumulation of Dampness. This develops over a long period of time from Damp Heat. The Heat damages Yin. When the Damp accumulates in the skin and oozes out this exudation also damages Yin. This all eventually leads to dryness. There may also be Blood Stasis which is indicated if the lesions remain hyperpigmented after healing [13].

The most distressing aspect of AD is itchiness which needs to be emphasized as part of treatment management. The researchers noted that medical scientists “should pay more attention to evaluate the efficacy of acupuncture on itching [36].”

Studies show that there are specific acupoints that can significantly reduce itching. Lin, J. et al conducted a study showing that acupuncture can exert an antipruritic effect on pruritogen-induced scratching behavior in an animal model when acupuncture was performed on LI4 and LI11. Acupuncture can repress pruritogen-induced microglial activation [1]. Researches show that SP10, LI11, KI9 are acupoints that are beneficial in the treatment of atopic dermatitis by filiform needle [18].

Acupuncture may have a role in reducing itchiness or regulating IgE-mediated allergy in dermatitis. The antipruritic effects of acupuncture may be related to the induction of vasodilation or stimulation of inflammatory cell mediators by needle insertion, and depletion of neurotransmitters through the activation of C fibers [3].

Needling of acupuncture points activate the mechanoreceptors and sends afferent signals along the ventrolateral tracts, which activates the relevant brain nuclei that modulate pain or itch

sensation via descending inhibitory pathways [24]. Itch-mediating primary sensory neurons are equipped with distinct receptors and ion channels for itch transduction, including Mas-related G protein-coupled receptors (Mrgprs), protease-activated receptors, histamine receptors, bile acid receptor, toll-like receptors, and transient receptor potential subfamily V1/A1 (TRPV1/A1) [26].

A study conducted at the Department of Dermatology and Allergy in Germany in conjunction with Harvard researchers shows acupuncture as an effective complementary treatment for itchiness in atopic dermatitis. Previous neuroimaging studies have shown that acupuncture modulates some of the same brain structures known to process itch sensation in healthy adults [9].

The comparative validity and reliability of outcome measurements for accessing AD severity is unclear, however; studies show that only SCORAD, VAS, EASI, AND POEM have been tested sufficiently and performed adequately [20].

In this literature review, there was only three RCTs that involve using the SCORAD and VAS. Accurate and appropriate measurements of health outcome form the basis of good evidence-based practice and should be taken into consideration when investigating the effects of acupuncture in atopic dermatitis.

III. MATERIALS & METHODS

3.1 Research Design

The research adopted a mixed research approach to generate data by both quantitative and qualitative approach. This is necessary so as to gain great insight into acupuncture's effectiveness for treatment of AD. To validate the research instruments as well as the preciseness of the reliability, a combination of different types of data was used including RCT Analysis data, case studies analysis and animal studies analysis. For the secondary data sources, all searches were limited to clinical trials, controlled studies, case reports, and comparative studies.

3.2 Data sources

A systematic search was performed for English-language publications of clinical trials and reviews acupuncture relating to atopic dermatitis and itching. PubMed and EBSCO host online databases were performed with dates through September 2017. The search terms included: 'randomized controlled trial', 'acupuncture', 'acupuncture point', 'atopic dermatitis', 'acupuncture therapy', 'ear acupuncture', 'electroacupuncture', 'ear acupuncture', 'acupuncture and itching', 'acupuncture and pruritus', 'acupuncture and eczema', 'acupuncture and randomized controlled trial', 'acupuncture and skin diseases', 'acupuncture and dermatology'. Trials on all forms of classical acupuncture were included, and trials on non-acupuncture methods were excluded. Reviews that were not limited to acupuncture, not relating to atopic dermatitis or itching, no clear outcome measures were excluded.

3.3 Study Selection criteria

Inclusion criteria:

The inclusion criteria are as follows: (1) randomized controlled trials (RCTs); (2) published in English; (3) diagnosis of AD which compared a common form of acupuncture with placebo interventions; (4) acupuncture-specific; (5) limited to clear objectives and outcome measures; (6) Outcome measures must include itch; (6) itch intensity using visual analog scale (VAS); (7) evaluated symptoms/sign severity using validated outcome measure instruments such as Visual Analog Scale (VAS), Eppendorf Itch Questionnaire, Cumulative Itch Index, Eczema Area and Severity Index (EASI), Patient-Oriented Eczema Measure (POEM).

Exclusion criteria

The exclusion criteria are as follows: (1) all the databases other than English language; (2) studies with outcome assessments that cannot be used to make a data analysis with other studies; (3) studies without integrated data; (4) duplicate studies; (5) literature review; (6) studies involving moxibustion, tuina, acupressure, plum-blossom needling, acupoint injection, blood-letting.

3.4. Data extraction

Articles that involve acupuncture in treatment of any diseases relating to itching, dermatitis, pruritus, eczema are automatically extracted for further review. Articles that involve acupuncture and indicator such as Visual Analog Scale (VAS), Eppendorf Itch Questionnaire, Cumulative Itch Index, Eczema Area and Severity Index (EASI), Patient-Oriented Eczema Measure (POEM) were also automatically extracted.

3.5 Data collection procedure

All searches were limited to clinical trials, controlled studies, case reports, and comparative studies. The abstracts and titles of the included articles were scanned for eligibility and irrelevant articles were excluded. Reference lists of the extracted studies were also manually searched for further relevant articles. An initial search identified a total of 134 articles related to atopic dermatitis. After screening for duplicates, title and abstracts, there was only 55 potentially relevant studies selected and retrieve for a full-text assesement. Of the remaining 55 articles, 5 studies were records review, 11 articles did not meet the inclusion criteria because the main therapy was not acupunture; 9 studies excluded because there were no data; 12 studies were not relevent. Finally after carefully examination of the contexts and contents in relation to Acupuncture, there were only 18 articles that had either met the inclusion criteria or had provided evidence of acupunture in the treatment of AD. The collections of articles consisted of 3 RCT's, 11 clincial studies, and 4 vivo animal studies. The process of study selection was shown in Figure 1.

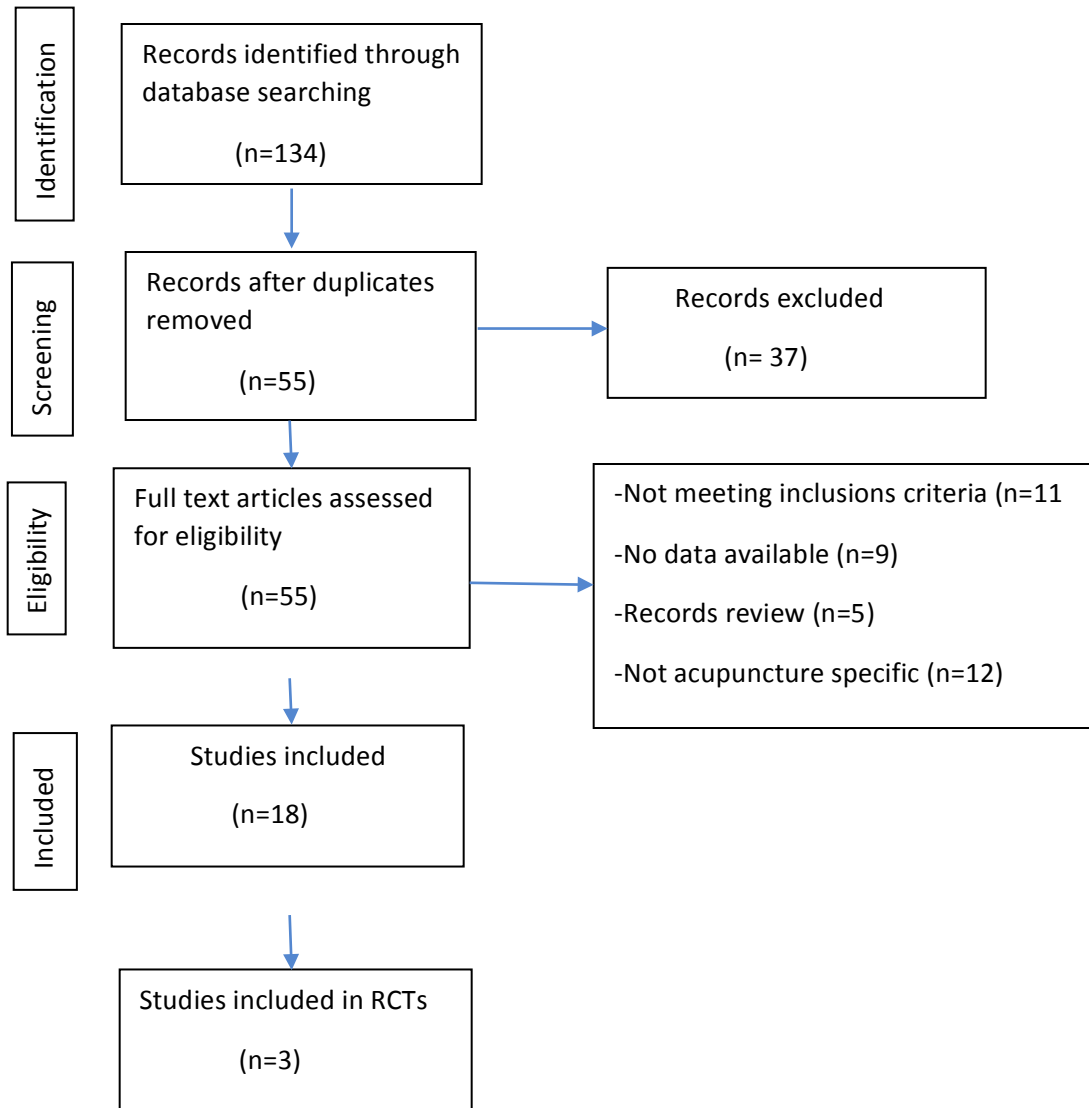


Figure 1. Literature search and study selection

3.6 Data Analysis

To analyze the data, data was first confirmed to ensure it contained all variables under study. It was further organized into table to compare cases. The data was further examined for differences in characteristic by use of statistical tools. For RCT's, the mean, standard deviation (SD), and 95% confidence intervals (CI) were calculated for VAS score measuring itch intensity. The VAS score was compared between the 3 RCT's experiment and among the control group. P

value and SD were compared among studies. Any $P < 0.005$ was regarded as significant. For 11 case studies, scores on VAS, EASI, DLQI, and any questionnaire relating to itching was used for supportive evidence to evaluate itching on different cases of various atopic dermatitis. For 4 vivo animal studies; serum IgE level, dermatitis score, pro-inflammatory cytokines and proteins, and scratching behavior were compared with the control.

IV. RESULTS & DISCUSSION

4.1. Literature Search Results:

Only 3 articles, which were RCTs that reported the itch intensity values (VAS) which is a valid key measurement in AD. There is only one study that evaluated the effects of acupuncture comparing intervention to a pharmacological agent. There are 11 clinical case studies that investigate itching on various problems such as AD, urticaria, uremic cutaneous pruritus, contact dermatitis, etc. [3,15,26,27,29,29,31,37,34,35,36]. The outcome measures are all different in these studies. Out of the 11 case studies, 1 article had investigate acupuncture in the treatment of AD with Chinese medicines. There was 2 articles that investigate in human model with intradermal injections of histamine to induce itch. There was 6 articles that shows the significant of LI 4, LI11, ST36, SP10, Gb31, Baichongwo (extra point) in reducing itching. There were 4 vivo animal studies that investigate the mechanism of acupuncture in itching by serum level. The studies reported either the decreased in total IgE serum level, scratching behavior, dermatitis score, or mrna expression of proinflammatory cytokines.

4.2. RCT Studies Analysis Results

The type of intervention in the included studies was active acupuncture to treat variety of itch sensations including histamine induced itch and grass pollen allergen stimulus. In each study has a fixed protocol of acupuncture points in the upper and lower extremities. LI11 is a significant acupoint used among three studies. The outcome of both itch intensity and wheal size were measured on VAS and Questionnaire scales at specific time intervals by the patient and investigator.

Pfab et al. (2012) study was the most comprehensive and assessed the matter in more than one criteria including wheal size, flare size and itch intensity. This study was the most significant comparing to the other two studies because it has the lowest standard deviation of 4.8 and was statistically closer to the 95% confidence level. This study has shown that acupuncture at the correct points has a significant reduction in type I hypersensitivity itch in patients with atopic eczema.

Pfab et al. (2011) study is also effective in reducing itching with SD of 7.54. This study is significant because it is the only study that compared acupuncture with a pharmaceutical drug, Cetirizine tablets. Both acupuncture and cetirizine significantly reduced type-I-hypersensitivity itch in AD patients, compared to both placebo and NI and showed similar effect sizes. Acupuncture that was commenced just prior to itch provocation (abortive acupuncture) was the only intervention to reduce itch perception below the clinically meaningful scratch threshold.

Chou et al. (2005) is the furthest away from the 95% confidence level comparing to other two studies. This study was conducted to validate an acupoint Quchi (LI11) to relieve itching, and was concluded acupuncture at LI11 was effective in reducing the pruritus score significantly, $P < 0.001$ immediately following treatment. Results show that the effect of the time of measurement on differences between pruritus scores was significant, $P < 0.001$.

All three RCT's studies indicated that acupuncture is effective to ameliorate itch intensity of itch-related disease with $P < 0.005$. Overall, significant reduction of itch was noted with use of acupuncture compared to when no interventions were made in the control process. The

effectiveness of acupuncture on itch intensity was summarized in Table 1. While the characteristic of each study was summarized in Table 2.

Table 1. Effectiveness of Acupuncture on Itch Intensity on 3 included studies

| Author | Acupuncture | | | Control | | | Weight | Mean Difference |
|-----------------------|-------------|-------|-----------|---------|-------|-----------|-------------|--------------------------|
| | Mean | SD | Total | Mean | SD | Total | | |
| Chou et al. (2005) | 24 | 25.87 | 20 | -29 | 25.04 | 20 | 9.70% | 19.7[16.67,22.7] |
| Pfab et al. (2011) | 16.55 | 4.8 | 10 | 38.2 | 4.8 | 10 | 41.60% | 53.00[21.44,84.56] |
| Pfab et al. (2012) | 32 | 7.54 | 20 | 46 | 0.8 | 20 | 48.70% | 10.3[3.12,17.48] |
| Total (95%) CI | | | 50 | | | 50 | 100% | 19.03[8.09,29.97] |

* All three RCT's show that acupuncture is effective in reducing itch intensity comparing to the control with p<0.005. Pfab et al. (2012) study is the closest to the 95% CI level.

Table 2. RCTs- Characteristics Data on 3 included studies

| Author/References | Study Design | Control Method | Population/ Sample Size | Intervention Acupuncture Points | Outcome Measures | Results |
|---------------------|--------------|---------------------------------------|---|---|---|--|
| Chou et al. (2005). | RCT | Placebo Acupuncture | Treatment Group: 20 mean age: 25.2 ± 4.5 Control: 20 | <i>Quchi</i> (LI 11), | Uremic pruritus VAS Pruritus score from questionnaire | Itching significantly reduced after treatment and 3 mts follow-up P<0.001 |
| Pfab et al, 2011 | RCT | Placebo Acupuncture + No Treatment | Treatment Group: 8 males, 2 females mean age: 25.2 ± 4.5 Control: 5 patients between 23 to 29 years old | <i>Quchi</i> (LI 11), <i>Hegu</i> (LI 4), <i>ZuSanLi</i> (St 36), <i>Xuehai</i> (Sp 10) | Atopic Dermatitis VAS Blood Serum – measure basophil activation | Reduction of itch intensity P < 0.001 |
| Pfab et al, 2012 | RCT | No Treatment | Treatment Group: 20 mean age: 18–50 Control: Each patient served as their own control | HT-3, ST-34, LiangQiu, SP10, LI-11, HT-3, | Atopic Dermatitis VAS SCOREAD- measure wheal and flare size | Reduction in itch intensity and flare size p<0.003 |

*The VAS score on these three trials all show a reduction in itch intensity compared to the control group with P<0.005.

4.3. Case Studies Analysis Result

The collections of case studies consisted of different outcome measures evaluating the effects of acupuncture on itchiness for different atopic problems.

Certain acupoints such as LI11, LI4, SP10, ST36, Gb31, Baichongwo (extra point) can reduce itching based on the reviews of case studies for different atopic problems.

Acupuncture in conjunction with other modality can offer better results in treatment of itching. An example was indicated in Olsen et al. (2011) and Salameh et al. (2008).

Olsen et al (2011) used acupuncture and a gluten-free diet (GFD) for urticarial and severe eczema in a 48-year-old woman in a 4 months' duration for a total of 36 treatments [3]. Patient at the same time was also on a gluten-free diet to help relief the dermatitis symptoms.

The outcome parameter of Olsen et al (2011) was lesion pruritic intensity, on a 1 to 10 scale. The acupuncture point's needle was SP10, Baichongwo, LE-Extra Point 3), ST25, ST36, Du 20, Du14. The needles were retained for 45 minutes [3]. Results concluded that Acupuncture provided relief from the urticarial and eczema of dermatitis beyond by traditional treatment of GFD alone.

Salameh et al. (2008) is the most significant clinical study in AD because it is the only study that involves a comprehensive outcome measures involving VAS, EASI, DLQI. There was a significant reduction in EASI ($p=0.003$). DLQI ($p=0.0009$), VAS ($p=0.0008$). In this study, acupuncture and herbal medicine were both used as intervention and shown to have a significant effect in itching. The combination of acupuncture and Chinese herbal medicine have a beneficial

effect on patients with atopic dermatitis and may offer better results than Chinese herbal medicine alone [31,32].

Statistic data analysis was not obtainable from the included case studies. Outcome measurement for itch intensity are all different in the studies which had made the interpretation of patient outcome and comparison of results between different studies difficult to analyze and reflect the reliability of the clinical effects of the intervention.

The data from different case report studies was summarized in Table 4.

Table 4: Case Report Studies: - Evaluating Acupuncture in Treatment of Atopic Dermatitis.

| Author/References | Study Design | Population/Sample Size | Intervention Acupuncture Points | Comparison | Outcome Measures | Results |
|------------------------|-------------------|--------------------------------------|--|------------|---|--|
| Salameh et al. (2008) | Clinical Study | Treatment Group: 20 mean size: 20 | GB31, GB20, BL40, LI4 + herbal medicine | None | Atopic dermatitis VAS EASI DLQI | Significant reduction in EASI (p=0.003) DLQI (p=0.0009), VAS (p=0.0008). |
| Tao et al (2009) | Observation Study | Treatment Size: 31 mean age: 4-82 | Various location | None | Urticaria Clearance of Urticaria | Complete clearance of wheals without recurrence in 25.8%, clearance of >30%. |
| Ohlsen et al, (2011) | Case Report | Treatment Size: 1 mean age: 48 | SP10, Du 20, Du14, Baichongwo, LE-Extra Point 3), ST25, ST36 | None | Improvement in pruritus and erythema | Relief from pruritus |
| Napadow et al (2012) | Clinical Study | N=14 | LI11 to HT3 Various location | None | Atopic Dermatitis Itching rating | Diminished itching |
| Hongmei et al (2002) | Observation Study | 68 cases | LI 11 ST36 | None | Uremic pruritus Clearance of Urticaria | 9 cases had improvement 1 case was ineffective. |
| Lunderber et al (2008) | Clinical study | N=25 | (LI11, ST 36, SP10) | None | Reduction in Itch Intensity | Combination of (LI11, ST 36, SP10) greatly reduced itch |

| | | | | | | |
|----------------------|----------------|-------------------------------|----------------------------|---------|---|--|
| Liao et al (2008) | Case Report | 4 cases Mean age: 29 to 63 | Various location | None | Contact dermatitis | Mild case-itch subsided in few hrs., lesion healed in 2 days Severe case-itch subsided in 2 days, lesion heal after three sessions of treatment |
| Kesting et al (2006) | Clinical Study | N=32 | Electrical ear acupuncture | None | histamine-induced alopecia | Reduction in itching |
| Lee et al (2012) | Pilot Trial | N=12 | Acupressure at LI11 | Control | Atopic Dermatitis VAS EASI | Improvement in pruritus and lichenification |
| Gao et al (2006) | Clinical Study | 34 cases | LI 11, ST36 | None | Uremic Cutaneous Pruritus Clinical Observation | 24 cases complete alleviation of pruritus 9 cases with improvement 1 case ineffective |

*These collections of clinical studies [2,6,8,9,13,15,19,24,26,27,28,29,30,31] consisted of different outcome measures on various dermatitis problems. LI 11 was the most common acupoint used among the studies.

4.4. *Vivo Animal Studies Analysis*

These studies used either chemicals eliciting acute itch such as chloroquine, capsaicin, serotonin or the rodent models are induced by synthetic allergens such as 2,4-dinitrofluorobenzene (DNFB) oxazolone to provoke elicit acute itch with the purpose of investigating the mechanism of acupuncture on pruritus.

Serum IgE levels, expression of proinflammatory cytokine, inflammatory markers levels, and scratching behavior are the outcome measures compared with the control.

The collection of vivo animal studies show in common a decrease in total serum IgE and pro-inflammatory cytokines. Scratching behavior was an outcome measure evaluated only in Han et al. (2008) study and was unable to use for comparison among other study.

Characteristic data in the studies was summarized in Table 4. While significant findings in the studies was summarized in Table 5.

Table 4. Vivo Animal Studies - Evaluating Acupuncture in Treatment of Atopic Dermatitis

| Author/References | Population & Sample Size | Intervention Method | Outcome Measures | Results |
|--------------------------|--|---|---|--|
| Wang et al. (2017) | N=8/ group Control = 8 8 weeks old male rats | Acupuncture St36 | Serum IgE Cytokines | Decreased in serum IgE, inflammatory cytokines |
| Jung et al. (2014) | N=12 Control =7 New born male rats | Acupuncture BL13 (bilateral), LI11, ST36, SP10, SP6. | Serum IgE Dynorphin release, Dermatitis score | Decreased in dermatitis score and dynorphin expression |
| Park et al (2013) | N=5/group Control=7 7 weeks old mice | Acupuncture LI11 | Serum IgE | Reduction in pro-inflammatory cytokines and proteins |
| Han et al, 2008 | N=9/ group Control=9 Male rates weighing 250-350 g | Acupuncture and EA LI II, LI4 | Scratching Behavior | Scratching behavior significantly reduced at high EA intensity and at correct dermatomes |

*Outcome measures was focus mainly on serum IgE levels, expression of proinflammatory cytokine, inflammatory markers levels, and scratching behavior.

Table 5: Vivo Animal Studies - Significant Findings in Treatment of AD

| Study | Significant Findings |
|--------------------|---|
| Wang et al.(2017) | ST 36 elicit a cellular and immune response in treatment of ACD. Secretion of interleukin (IL)-10 in the local acupoint tissue following EA stimulation was increased and showed suppressive function. This new finding can provide an alternative and promising therapy for atopic AD. |
| Jung et al. (2014) | BL13 (bilateral), LI11, ST36, SP10, SP6. – Only the dermatitis score and dynorphin expression were decreased in the EA group compared with the control non-EA group. This study suggested that high-frequency EA alleviates pruritus of atopic dermatitis-like lesions in rats induced by capsaicin injection, via the release of dynorphin. |
| Park et al (2013) | Acupuncture treatment effective in alleviating allergic contact dermatitis by reducing pro-inflammatory cytokines and proteins. |
| Han et al (2008) | The number of scratching bouts evoked by a high-frequency EA stimulation is decreased at least by 39% compared with plain acupuncture. This study suggests that the effectiveness of acupuncture as treatment for pruritus is enhanced when high-frequency EA stimulation is performed in the dermatones of affected sites or in adjacent dermatomes. |

* Outcome measures are serum IgE levels, expression of proinflammatory cytokine, inflammatory markers levels, and scratching behavior.

4.5 Summary of Evidence

Acupuncture is an effective treatment option in reducing itch intensity as demonstrated in the RCTs studies. Certain acupoints such as LI11, LI4, SP10, ST36, Gb31, Baichongwo (extra point) can reduce itching based on the reviews of case studies for different atopic problems. Acupuncture used in conjunction with other modality such as herbal medicine or a specialized healthy diet can help reduce itching. Vivo animal studies show a decrease in serum IgE and pro-inflammatory cytokines. Although vivo studies are involved, it does not mean that the article is poor-quality evidence. The study does provide indication of the current state of evidence of the efficacy of acupuncture in the management of AD.

4.6 Limitations

In AD, there remains lack of standardization of objective severity scales. There are too many published outcome measures for AE. Most have not been tested properly or perform adequately when tested. Valid and reliable outcome measurements are a prerequisite for evidence-based practice. There are not enough RCTs and large sample size to evaluate the effectiveness of acupuncture in atopic dermatitis. Clinical trials in atopic dermatitis (n= 50) represent only a small number of acupuncture research which puts a limitation on the validity of the results. Clinical case studies and vivo animal studies were used as supportive studies because of lack of RCTs.

4.7 Suggestion for Future Research

There needs to be a lot more gold standard studies before acupuncture maybe considered as independent therapeutic options that is accepted world-wide. Future studies on a larger patient population and more acupuncture points would be needed to stronger confirm the effectiveness of acupuncture in AD treatment. In order to provide a more valued evidence for evidence-based medicine of acupuncture treating itching, an international rating scale of itch and its evaluation standard is urgently required.

VI. CONCLUSION

Only certain combination of acupoints (LI11, LI4, SP10, ST36, Gb31, Baichongwo (extra point) is effective in reducing itching. Itching is significantly reduce if acupuncture is used in conjunction with other modality such as Chinese herbal medicine or a gluten-free diet. Based on statistics analysis of RCT's and supportive evidence from case studies and vivo animal studies, acupuncture is effective in reducing itchiness and is a useful adjunctive therapy for atopic patients.

VII. REFERENCES

1. Lin,J., Lee,Y., Tseng,C., et al. (2016). Electroacupuncture inhibits pruritogen-induced spinal microglial activation in mice. *Brain Research*. vol. 1649, no.part A, pp.23-29.
Doi.org/10.1016/J.brainres.2016.07.007.
2. Park,J., White,A.,Stevinson,C. (2002). Validating a new non-penetrating sham acupuncture device: two randomized controlled trials. *Acupuncture in Medicine*, 20(4): 168-174.
Doi.org/10.1136/aim.20.4.168
3. Ohlsen, Bahia. (2011). Acupuncture and gluten-free diet relieve urticaria and eczema in a case of undiagnosed dermatitis herpetiformis and atypical or extraintestinal celiac disease: a case report. *Journal of Chiropractic Medicine*, 10:294-300.
4. Choi,YY., Kim,M., Kim, S.,Park,J., Park, H., Yang,W. (2013). Affects of Acupuncture on 1-Chloro-2,4-dinitrochlorobenzene-Induced Atopic Dermatitis. *Evidence-Based Complementary and Alternative Medicine*, 8(1).
5. Pfab,F., Kirchner, M.T, Marp-Huss, J., Schuster, T., Schalock, P.C., et al. (2012). Acupuncture compared with oral antihistamine for type I hypersensitivity itch and skin response in adults with atopic dermatitis- a patient-and examiner-blinder, randomized, placebo-controlled, crossover trial. *European Journal of Allergy and Clinical Immunology*, 67(4): 566-573.
6. Lu,C., Wang, K., Wu,X. Xiang,Y. (2009-2014). An overview of acupuncture for psoriasis vulgaris. *Journal of Dermatological Treatment*, 8 (1).

7. Pfab,F., Gatti, A., Fuqin, J., Huss-Marp, J ., Pfab,F., (2010). Influence of acupuncture on type I hypersensitivity itch and wheal and flare response in adults with atopic eczema blinded, randomized, placebo-controlled, crossover trial. *European Journal of Allergy and Clinical Immunology*; 65: 903-910
8. Schachter O, Perla D, Greenberger S, Barzilai A, Baum S. (2017). Traditional Chinese Medicine in Treatment of Atopic Dermatitis. *Dermatol Clin*. 2017 Jul;35(3):373-394.
9. Li,A., Kim,J., Schalock,P., Napadow,V., Kaptchuk,T. (2012). Brain circuitry subserving acupuncture relief of itch in atopic dermatitis: an fMRI study. *BMC Complement Alternative Med.*, 2(Suppl 1): O32.
10. Li, A., Kim, J., Schalock, P., Napadow, V., Kaptchuk, T. Literary review compilation on Traditional Chinese Medicine. PUBMED. Prickly Business
11. Pfab,F., Athanasiadis GI.,Huss-Marp., et al. (2011). Effect of Acupuncture on Allergen-Induced Basophil Activation in Patients with Atopic Eczema: A Pilot Study. *Journal of Alternative and Complementary Medicine*, 17(4): 309-314
12. Atopic Dermatitis. Retrieved 09/06/2017
<http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/dermatology/atopic-dermatitis/>
13. Yu,J. Anupama,K. (2012). Chinese Herbs for the Management of Atopic Dermatitis: A Case Report. *Topics in Integrative Health Care*,3(4): 3-4006
14. Integrative View of Atopic Dermatitis Part II: The TCM Basics. Retrieved 12/22/2017.
15. Napadow,A., Li,A., Loggia,M.m et al. OAO8.O4. (2012). Brain circuitry subserving acupuncture relief of itch in atopic dermatitis: am fMRI study. *BMC Complementary and Alternative Medicine*, 12(Suppl 1):032.

16. Kim, Yu., Yeim, M, Kang, S., et al. (2017). Antipruritic Effect of Acupuncture in Patients with Atopic Dermatitis: Feasibility Study Protocol for a Randomised, Sham-Controlled Trial. *Evidence-Based Complementary and Alternative Medicine*, 14(1).
17. Charman, C. & Hywel, W. (2000). Outcome Measures of Disease Severity in Atopic Eczema. *American Medical Association*, 136:763-769.
18. Chen, Chung-Jen & Yu, Hsin-Su. (2003). Acupuncture, Electrostimulation, and Reflex Therapy in Dermatology. *Dermatologic Therapy*, Vol. 16, 87-92.
19. Cantarutti, A., Dona, D., et al. (2015). Epidemiology of Frequently Occurring Skin Diseases in Italian Children from 2006 to 2012: A Retrospective, Population-Based Study. *Pediatric Dermatology* 32(5).
20. Lio, Peter. (2011). Alternative Therapies in Atopic Dermatitis Care, Part I. Practice Dermatology..
21. Schmitt J., Langan, S. William, HC, et al. (2007). What are the best outcome measurements for atopic eczema?. A systematic review. *J Allergy*, 20(6):1389-1398.
22. Chou, C. Wen, C., Tsung-Min, K., et al. (2005). Acupuncture in haemodialysis patients at the Quchi (LI11) acupoint for refractory uraemic pruritus. *Nephrol Dial Transplant*, Sep; 20(9): 1912-5.
23. Jung, D., Lee, S., Choi, I., et al. (2014). Effects of electroacupuncture on capsaicin-induced model of atopic dermatitis in rats. *Journal of Dermatological Science* 74, 23-30.
24. Nanna, G., Chen, M., Fujita, T. et al. (2010). Adenosine A1 receptors mediate local anti-nociceptive effects of acupuncture. *Nature Neuroscience*.
25. Han, J., Kim, C., Sun, B, et al. (2008). The Antipruritic Effect of Acupuncture on Serotonin-Evoked Itch in Rats. *Acupuncture & Electro-Therapeutics Res.* 33: 145-156.

26. Hongmei,G, Wanxiang,Z., Ying,W., et al. (2012). Acupuncture Treatment for 34 Cases of Uremic Cutaneous Pruritus. *Journal of Traditional Chinese Medicine* 22(1):29-30
27. Lunderbert,T., Bondesson, L., Thomas,M. (2008). Effect of acupuncture on experimentally induced itch. *British Journal of Dermatology*, 117,771-777.
28. Kesting, M., Thurmuller,P.,Holzle,f., et al. (2006). Electrical Ear Acupuncture Reduces histamine-induced Itch (Allknesis). *Acta Derm Venereol*;86;399-403.
29. Salameh,F, Soloman,M Perla,D., et al (2008). The effectiveness of combined Chinese herbal medicine and acupuncture in the treatment of atopic dermatitis. *J Altern Compliment Med*. Oct;14(8):1043-8.
30. Sang L, Kim,J., Han,Y et al. (2011). A proposal: Atopic Dermatitis Organizer (ADO) guideline for children. *Asia Pac Allergy*. Jul;1(2):53-63.
31. Liao, SJ. (1988). Acupuncture for Poison Ivy Contact Dermatitis. A clinical report. *Acupuncture electrother Re*. 13(1):31-9.
32. Wang,Z.,Yi,T.,Long,M.,et al. (2017). Electro-Acupuncture at Zusanli Acupoint (ST36) Suppresses Inflammation in Allergic Contact Dermatitis Via Triggering Local IL-10 Production and Inhibiting p38 MAPK Activation. *Inflammation*, 40(4).
33. Woods,Carmela. (2017). Overview of Atopic Dermatitis. *Am J Management Care*. 23-S0.
34. Lee KC, Keyes A., Hensley JR., et al. (2012). Effectiveness of acupressure on pruritus and lichenification association with atopic dermatitis: a pilot trial. *Acupunc Med* 30:8-11.
35. Gao H, Zhang W., Wang Y (2002). Acupunture treatment in 34 cases of uremic cutaneous pruritus. *J Traditional Chinese Medicine* 22:29-30.
36. Stellon A. (2005). The use of laser acupuncture for the treatment of neurogenic pruritus in a child-a case history. *Acupunct Med* 23;31-33.

37. Tao.S. (2005). Acupuncture Treatment for 35 cases of urticaria. J Traditional Chinese Medicine 2005;3.

APPENDIX

A. Incidence and prevalence estimates for atopic dermatitis, stratified according to sex, age, and geographic area, from 2006-2012 (Source: Pediatric Dermatology 32(5), April 2015).

