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Is acupuncture effective in reducing itch intensity and wheal size in patients with dermatologic conditions?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

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ABSTRACT

OBJECTIVE: The objective of this selective EBM review is to determine whether acupuncture is effective in reducing itch intensity and wheal size in patients with dermatologic conditions.

STUDY DESIGN: Review of all English language primary randomized controlled trials published after 1984

DATA SOURCES: Three randomized controlled trials were found using Pubmed database.

OUTCOMES MEASURED: The three trials measured various outcomes: Visual Analog Scale (VAS); Eppendorf Itch Questionnaire; Cumulative Itch Index; Perimeter of wheal and flare size before, during, & after acupuncture; Psoriasis Area and Severity Index (PASI)

RESULTS: Belgrade et al. found statistically significant improvement in itch intensity and flare size of patients with histamine-induced itch after active acupuncture compared to pseudo acupuncture and no acupuncture. In the study by Pfab et al., the direct and preventive effect of acupuncture on atopic eczema showed significant decrease in itch intensity, wheal, and flare size compared to placebo acupuncture and no acupuncture. Jerner et al. found slightly considerable yet statistically significant improvement in skin symptoms of plaque psoriasis after placebo acupuncture compared to active acupuncture.

CONCLUSIONS: Acupuncture, as an adjunct treatment to standard atopic dermatitis care, is an effective inhibitor of histamine-induced and atopic dermatitis itch and wheal/flare size.

KEY WORDS: Atopic dermatitis; acupuncture; skin diseases

INTRODUCTION

Atopic dermatitis (AD) and plaque psoriasis are two common chronic dermatologic conditions. AD is a chronically relapsing inherited skin disease that is associated with abnormalities in skin barrier function and allergen sensitization. AD is the atopic cutaneous manifestation included in the atopic triad with asthma and allergic rhinitis.¹ Psoriasis is a benign, chronic inflammatory skin disease with both a genetic basis and environmental triggers of trauma, infection, or medication.¹ The diagnosis of psoriasis has multiple presentations between plaque, guttate, pustular, and inverse psoriasis; the majority of patients have plaque psoriasis. AD affects over 30 million Americans with an increasing prevalence worldwide.² Recent estimates indicate that 65% of patients develop symptoms in the first year of life and 85% experience it by age five.³ Onset of AD after age 30 is less common.³ Psoriasis currently affects 7.5 million Americans and 125 million people worldwide, with the highest reported prevalence in Europe.⁴ Onset can appear at any age but often is diagnosed between ages 15 and 25.⁴ Both AD and psoriasis can lead to serious impairment of quality of life in affected patients. Physician Assistants working in primary care settings can provide education about the disease and support for patients coping with both physically and psychologically stressful events.

Unfortunately, there is no cure for either AD or psoriasis. It is estimated that health care costs for AD and psoriasis are over \$3 billion and \$11.25 billion annually, respectively.^{3,4} There have been reports of an estimated 7.4 million AD and over 3 million psoriasis health care visits each year.^{3,4} AD is a very common chronic inflammatory skin disease, but the cause is only partially defined.⁵ The disease is a result from a combination of genetic and environmental factors. It displays a variety of immunoregulatory abnormalities in skin barrier function, increased IgE sensitization, and delayed-type hypersensitivity reactions.⁵ Typical distribution

and morphology of AD is pruritic, erythematous, lichenified plaques in the flexural surfaces of the antecubital and popliteal folds.⁵ The skin of a person with AD loses moisture from the epidermal layer causing the skin to become very dry thus reducing its protective abilities.³ Lack of a protective layer in combination with abnormal immune system sets the person up for higher risk of bacterial infections.

The exact cause of psoriasis is unknown as well. It has been found that there is an autoimmune component which involves infiltrates of activated T cells responsible for keratinocyte hyperproliferation.⁵ Typical morphology is characterized by sharply demarcated papulosquamous, erythematous plaques covered by a silvery scale.⁵ Common distribution includes extensor surfaces of the elbows, knees, gluteal cleft, and scalp.⁵ Plaque psoriasis runs an indolent course with slow, unchanged enlarging plaques.

There are multiple treatment options for both AD and psoriasis. Common topical methods for AD include various emollients such as Aquaphor, Eucerin, Petrolatum, and Vanicream, and low to midpotency glucocorticoids for flare ups.¹ Systemic medications include macrolide immunosuppressants such as Tacrolimus and Pimecrolimus.⁵ Common treatment methods for psoriasis include narrowband ultraviolet B (NB-UVB) phototherapy, oral or topical psoralen-ultraviolet-A (PUVA) photochemotherapy such as 8-methoxypsoralen (8-MOP) with UV-A exposure.⁵ Common systemic agents used include, oral retinoids such as acitretin, oral methotrexate, oral cyclosporine, and monoclonal antibodies such as etanercept, infliximab, adalimumab, and alefacept.⁵ Adjunctive therapies available for localized plaques include high potency topical glucocorticoids, vitamin D analogs, and coal tar.⁵

All of the treatment options mentioned for both AD and psoriasis play an effective role in treating aspects of each disease. However, each option has adverse effects and different rates of efficacy for individual patients. Based on the similar pathophysiology between itch and pain sensation along C fibers in the CNS, acupuncture has shown to have a well established pain relief effect thus similar relief from histamine-induced itch.⁶ Acupuncture is an alternative treatment option to diminish both the intensity and duration of itching produced by AD and psoriasis. This paper evaluates three randomized controlled trials (RCTs) comparing the efficacy of active acupuncture in reducing the itch intensity and wheal size in patients with histamine induced AD and plaque psoriasis.

OBJECTIVE

The objective of this selective EBM review is to determine whether or not acupuncture is effective in reducing itch intensity and wheal size in patients with dermatologic conditions such as atopic dermatitis and plaque psoriasis.

METHODS

Each of the three studies selected in this review were randomized controlled clinical trials and met the following criteria. The population included men and women between ages 18 and 75 with type I sensitivity to grass pollen, long standing plaque psoriasis, or healthy volunteers. The type of intervention in the studies was active acupuncture with electrical stimulation to treat a variety of itch sensations including histamine induced itch, grass pollen allergen stimulus, and plaque psoriasis. Each study had a fixed protocol of acupuncture points in the upper and lower extremities innervating specific viscera meridians, including Quchi, Xuehai, and Sanyinjiao (Belgrade), Quchi, Xuehai (Pfaff), and 20 classical Chinese points (Jerner). In the Jerner study

assessing treatment on plaque psoriasis, active acupuncture included the use of auricle acupuncture in addition to the classical Chinese points. The studies used either pseudo-acupuncture, placebo acupuncture, or no acupuncture as comparisons to the active acupuncture treatment. The pseudo/placebo acupuncture used in both the histamine and grass pollen stimulus studies was carried out in the exact fashion of the active treatment except the needles were inserted at sites near the classical points either within the same or adjacent dermatomes. The placebo acupuncture on plaque psoriasis involved inserting needles superficially subcutaneously 1cm outside the classic points without electrostimulation, only one medial auricle needle, and without achieving the numbness sensation known as 'deqi'. The outcomes of both itch intensity and wheal size in the studies were measured on various visual and questionnaire scales at specific timed intervals by the patient and the investigator.

The author performed searches of the PubMed database using the keywords atopic dermatitis, acupuncture, and skin diseases while setting the language as English. All articles were published in peer-reviewed journals and were selected based on relevance and importance of outcome to the patient. Inclusion criteria were as follows: randomized controlled trials (RCT) based on patient-oriented outcomes published after 1996, with the exception of one 1984 RCT. Exclusion criteria included patients under the age of 18 years, previous acupuncture treatment, or previous Cochrane or student published systematic reviews. Statistics used varied amongst each study. Belgrade et al. used mean change from baseline, p-values, and t-test. Similarly, Pfab et al. used mean change from baseline and p-values. Jerner et al. chose to present dichotomous data using relative benefit increase (RBI), absolute benefit increase (ABI), and numbers need to treat (NNT). In all studies, $p \leq 0.05$ was considered statistically significant.

OUTCOMES MEASURED

Belgrade et al. measured patient oriented outcomes as Cumulative Itch Index (CII) rating itch intensity on a six point scale over 60 minutes after itch onset, and max perimeter of flare size during active, pseudo, and no acupuncture. Pfab et al. used patient oriented outcomes in the study, including a Visual Analogue Scale (VAS) measuring itch intensity at 20 second intervals over 15 minutes with a 33% scratch threshold level, Eppendorf Itch Questionnaire (EIQ) of 80 questions rating itch intensity with descriptive items, wheal size, and flare size, all measured during active, placebo, and no acupuncture. Jerner et al. used a Psoriasis Area and Severity Index (PASI) measured by the investigator before, during, and 3 months after both active and placebo acupuncture to determine the severity of the skin lesions.

RESULTS

The demographics of the studies included in this review are outlined in **Table 1**. Each study included patients with a different dermatologic presentation, who had never received prior acupuncture treatment. All participants in the studies were asked to withhold from the use of all current systemic or topical medications prior to and during the study.

Table 1 - Demographics & Characteristics of included studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Belgrade, 1984 (1)	RCT	25	21-33	Healthy volunteers; age 21-33	Age over 50 or under 21; knowledge of acupuncture; regular use of antihistamines, sedatives, aspirin; lack of itch response to intradermal injection of histamine	0	Histamine injection with acupuncture & electrical stimulation (@ Quchi, Xuehai, Sanyinjiao) VS. histamine injection with pseudo-acupuncture without electrical stimulation (@ adjacent dermatomes) VS. no intervention

Pfab, 2009 (2)	RCT	30	18-50	Atopic eczema; age 18-50; type I sensitivity to grass pollen	Any systemic or topical tx w/ immunosuppressive agents on the non-dominant arm; knowledge of acupuncture	1	Applied grass pollen with either Verum-point acupuncture (@ Quchi, Xuehai) or placebo-acupuncture (same dermatomes) VS. no acupuncture
Jerner, 1997 (3)	RCT	56	18-75	Stable plaque psoriasis; age 18-75; no change in tx during previous 3 mos; no ongoing tx w/ oral anti-psoriatic drugs, UV therapy, or extensive use of topical corticosteroids	Previously tx w/ acupuncture; contraindications to electroacupuncture	2	Active acupuncture (classical IM points) + ear acupuncture, all attached to electrostimulation VS. placebo acupuncture (SC 1cm away from classical points) + ear acupuncture, without electrostimulation

The study conducted by Belgrade et al. compared the outcomes of itch intensity and flare size in active acupuncture, pseudo-acupuncture, and no acupuncture. Twenty-five healthy volunteers were injected intradermally with fresh histamine phosphate solution and blindly participated in all three experimental sessions by randomization. Pertinent personal data from the volunteers was identified with respect to any influence on the response to histamine. No participants dropped from the study. **Table 2** summarizes the results of the study by Belgrade et al. The mean value for CII while receiving active acupuncture showed a statistically significant decrease in itch compared to pseudo acupuncture ($p < 0.02$) and even more statistically significant decrease compared to no acupuncture ($p < 0.001$). The maximal flare size achieved during active acupuncture was significantly smaller than with pseudo acupuncture ($A = 2.28 \pm 0.19$, $P = 2.58 \pm 0.20$, $p < 0.04$) or no intervention ($\phi = 2.62 \pm 0.21$, $p = 0.003$). The student t-test showed a positive correlation with subject's last hot shower to CII in no intervention ($t = 0.6$, $p < 0.001$) and active acupuncture ($t = 0.4$, $p < 0.05$), but not in pseudo acupuncture ($t = 0.03$, $p = 0.4$). Subjects

with atopic history were significantly ($p < 0.05$) associated with greater itch intensity and smaller flare in the active acupuncture only. Note that the data was continuous and could not be converted to dichotomous data; thus, analysis of risk reduction, benefit increase, and numbers needed to harm or treat could not be performed.

Table 2: Summary of mean CII and max flare perimeter after active, pseudo, and no acupuncture⁶

Expt ^a	CII ^b	Max flare size (sq. in)
Φ	8.34±1.00	2.62±0.21
P	6.16±0.95	2.58±0.20
A	3.16±0.65	2.28±0.19
P < Φ	(p=0.005)	NS ^c
A < Φ	(p<0.001)	(p=0.003)
A < P	(p<0.02)	(p<0.04)

^aIntradermal injection of histamine with acupuncture (A), pseudo acupuncture (P), and no intervention(Φ)

^bCumulative Itch Index defined as the area under the function I(t) which gives the itch intensity at time t.

^cNS= not statistically significant. Comparisons made using Student t-test comparing independent sample means.

Pfab et al. compared the patient oriented outcomes of itch intensity and flare size in 30 atopic eczema type I sensitivity to grass pollen patients with verum acupuncture, placebo acupuncture, and no acupuncture. Patients received a skin prick of known sensitized allergen to induce itch, observed for 15 minutes, then randomized into one of the experimental groups. After a second 15 minute resting period, a second allergen stimulus was applied without acupuncture to measure the preventive effect. One patient showing no itch response was excluded from the study. **Table 3** summarizes the direct and preventive effect assessments of acupuncture via VAS, EIQ, wheal, and flare size. Mean VAS ratings regarding direct and preventive intervention on itch intensity included a statistically significant decrease between verum acupuncture (VA) and

no acupuncture (NA) (direct $p < 0.009$, preventive $p < 0.001$), as well as VA compared to placebo acupuncture (PA) (direct $p < 0.022$). The mean itch intensity of VA was below the 33% scratch threshold level after direct intervention compared to NA and PA. The preventive approach of VA was reduced to a 26% below scratch threshold compared to NA, and 10.9% compared to PA. Mean EIQ ratings were significantly lower in VA compared to NA ($p < 0.0001$) and PA ($p = 0.02$) in treatment approach; and significantly lower in VA ($p < 0.00001$) and PA ($p = 0.0004$) compared to NA in preventive approach. Direct effect of both wheal and flare size were significantly lower in VA compared to NA and PA (VA<NA wheal $p = 0.015$; VA<PA flare $p = 0.002$); and preventive approach of VA was also significantly lower compared to NA (wheal $p = 0.008$; flare $p = 0.001$).

Table 3: Summary of direct effect and preventive effect of VA, PA, and NA by VAS, EIQ, wheal and flare size⁷

	Expt	Mean VAS ^a	Mean EIQ ^b	Mean wheal size (mm ²)	Mean flare size (cm ²)
NA	Direct	45.8±7.8%	1.15±0.10	48±9	10.1±2.1
	Preventive	44.6±6.2%	1.17±0.10	73±28	15.1±4.1
PA	Direct	40.4±5.8%	1.06±0.09	45±7	10.4±1.8
	Preventive	37.8±5.6%	1.06±0.10	54±13	13.5±2.8
VA	Direct	35.7±6.4%	0.99±0.11	37±9	7.79±1.6
	Preventive	34.3±7.1%	1.01±0.10	38±12	8.1±2.0
VA<NA	Direct	$p = 0.009$	$p < 0.0001$	$p = 0.015$	
	Preventive	$p < 0.001$	$p < 0.00001$	$p = 0.008$	$p = 0.001$
VA<PA	Direct	$p = 0.022$	$p < 0.02$		$p = 0.002$
	Preventive				$p < 0.001$
PA<NA	Direct		$p < 0.01$		
	Preventive	$p = 0.002$	$p = 0.0004$		

*Direct and preventive values = mean values ± standard deviation

^aVisual Analogue Scale percentage measured at 20s intervals over 15min.

^bEppendorf Itch Questionnaire of 80 questions rating painful sensations from 0 to 4.

In the Jerner et al. study, 56 plaque psoriasis patients were double-blinded, randomized to either active or placebo acupuncture during the autumn or spring season for 10 weeks then observed over 3 months. Two patients were excluded in the final evaluation. One patient did not show up at the last control, and another patient received oral corticosteroid therapy for bronchial

asthma at the end of the acupuncture phase. **Table 4** shows only slight improvement in skin symptoms based on PASI scores of both active and placebo acupuncture groups. Mean PASI scores decreased from 9.6 to 8.3 in the active group and from 9.2 to 6.9 in the placebo group ($p < 0.05$ for both), showing somewhat greater improvement with placebo. PASI scores slightly further reduced three months after therapy, although in the active group this was due to exclusion of two high values of patients receiving other treatment after completing acupuncture.

Table 4: Mean PASI scores in patients before and after receiving active or placebo acupuncture⁸

Treatment Group	Baseline	After 10 tx	After 20 tx	3mos after completion
Active	9.6±4.8 (35) ^a	8.6±3.9 (35)	8.2±4.5* (35)	7.3±3.2 (33) ^b
Placebo	9.2±2.7 (19)	7.9±2.7 (19)	6.9±3.1* (19)	6.6±2.0 (19)

* $p < 0.05$ compared to baseline value.

^aNumber of patients.

^bTwo patients with high PASI values had to start other treatment for their psoriasis after completing the acupuncture treatment.

Table 5 represents the patients' responses in whether they found improvement by the treatment rated on a worse to better scale. This data demonstrates a 21% RBI and 12% ABI in using acupuncture to improve psoriatic lesions, both correlating with somewhat beneficial treatment. The NNT determined that 9 plaque psoriasis patients need to be treated with acupuncture to prevent 1 additional patient with increased severity of psoriasis lesions compared to the control.

Table 5: Analysis of blinded opinions about the effects of completed acupuncture therapy⁸

Experimental Event Rate (EER)	Control Event Rate (CER)	Relative Benefit Increase (RBI)	Absolute Benefit Increase (ABI)	Number needed to treat (NNT)
Active (70%)	Placebo (58%)	21%	12%	9

There were no adverse events or complications reported in any of the clinical trials.

DISCUSSION

Active acupuncture has been shown to be an effective treatment option in reducing itch intensity and wheal/flare size in atopic dermatitis, as demonstrated in the Belgrade and Pfab studies. However, active acupuncture did not show impressive results in the treatment of plaque psoriasis, while the placebo treated effect was considerable. Patients with chronic dermatological disorders quite often turn to alternative medical approaches to treat irritative symptoms.⁸ Acupuncture treatment for atopic dermatitis is becoming increasingly influential amongst Chinese doctors, while the current attitude in China regarding application of acupuncture for psoriasis seems to be rather vague.⁸ It has been utilized to treat a variety of medical conditions including asthma, colitis, menstrual irregularities, vomiting, post-operative pain, headache, osteoarthritis, sleep disturbances, nicotine addiction, and many more.⁹ Acupuncture is an accepted and available Complementary and Alternative Medicine (CAM) option in the United States.⁹ Despite this, patients may encounter problems with insurance coverage. Many medical insurance companies do cover acupuncture treatment, but under specific conditions such as referral from PCP, limited number of treatments per year, and only for specific medical conditions. Contraindications for the use of acupuncture are pregnancy, coagulopathy, immunocompromised conditions, local infections, region of implanted electrical devices, or vertebral lesions.¹⁰

The effects of acupuncture on itch are most likely due to the effects on neurogenic inflammation.⁷ Some data indicates that acupuncture influences endogenous opioid peptides in the CNS mediating the analgesic effect and has a counter-irritative effect reducing prostaglandin E2 in both the brain and serum.⁷ The pseudo-acupuncture applied in opposite limbs to active acupuncture accounted for both the control for placebo effect and to control the effect of counter-

irritation inhibition of itching.⁶ Further experiments show acupuncture locally inhibits activation and proliferation of mucous mast cells, substance P, and vasoactive intestinal peptide in the colon of rats.⁷

Although the data presented supports the use of acupuncture for atopic dermatitis, the small study size in these trials puts a limit on the validity of the results. Participants with atopic dermatitis only add up to a total of 55 patients in the two trials and 54 patients in the plaque psoriasis trial.

CONCLUSION

In conclusion acupuncture is an effective inhibitor of histamine-induced and atopic dermatitis itch and wheal/flare size compared to placebo-acupuncture and no treatment, whereas it does not have the same effect on psoriatic lesions. Regarding the preventive influence of acupuncture on histamine-induced itch, the specific effect diminished itch sensation and increased the suppression of skin-prick reactions.⁷

While evidence provided by these studies supports the use of acupuncture to reduce itch and wheal/flare size, the sample size was limited and duration of treatment was short term, both warranting further research. It is difficult to explain the mechanisms of the observed effects as acupuncture studies are rare. Further studies need to particularly focus on the pathways of acupuncture action in the pathophysiology of itch or allergic skin reactions.⁷

Despite these limitations, the results conveyed by the studies in this review suggest that acupuncture might be a useful adjunctive therapy against itch sensation in atopic patients.

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