# A Systematic Review and Meta-analysis of Using Acupuncture and Acupressure for Uremic Pruritus

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Review

**Introduction.** Uremic pruritus is characterized by an uncomfortable and unlimited sensation which leads to scratch, which strongly reduces the quality of life. Pruritus is a common symptom in patients with end-stage renal disease. Various clinical trial studies have examined the effects of acupuncture and acupressure on treatment of uremic pruritus. This systematic review meta-analysis aimed to evaluate the effectiveness based on published studies.

**Materials and Methods.** An electronic literature search was conducted to identify appropriate trial studies. The results for continuous outcomes were presented as weighted mean difference, with 95% confidence intervals.

**Results.** A total of 5 articles, including 6 trials, were enrolled in this systematic review. Only 3 of the six trial studies used a visual analogue scale score for assessing pruritus and acupressure for intervention regime, which were considered for meta-analysis. The combined results showed that acupuncture or acupressure was effective in treatment of uremic pruritus (pooled mean difference, -1.994; 95% confidence interval, -2.544 to -1.445).

**Conclusions.** This study confirms that using acupuncture and acupressure is effective in treatment of uremic pruritus. However, further vigorous studies are needed to verify these findings.

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## INTRODUCTION

Uremic pruritus (UP) is defined as an uncomfortable and unlimited sensation which leads to scratch and strongly reduces the patient's quality of life. Uremic pruritus is a common symptom in patients with end-stage renal disease (ESRD).[1] About 42% of patients reported moderate to severe pruritus. The existing data revealed that some patient's characteristics and dialysis parameters, such as older age, higher serum C-reactive protein levels, male sex, current or recent smoking habit, lower dialysis adequacy, use of low-flux (versus high-flux) dialysis membrane, higher serum calcium and phosphorus levels, low serum albumin levels, hepatitis C virus positivity, elevated ferritin levels, and underlying depression, have been associated with the pathogenesis of UP.[2] In addition, newer studies concentrated on opioid-receptor derangements and micro-inflammation as possible causes of UP.[3]

Most physicians recommend taking a stepwise approach for treating uremic pruritus that begins with optimization of dialysis adequacy, adjustment of calcium and phosphorus levels, skin hydration, nutrition control, and education on the importance of avoiding scratching. If symptoms persist, doctors may suggest pharmacological or nonpharmacological therapy (such as acupuncture

or acupressure).[2]

An effective approach to treat UP is acupuncture.[3] Acupuncture is a complex intervention originated from East-Asian countries. The word 'acupuncture' refers to involving acupuncture needles on body points or to a multicomponent treatment that involves taking patient's history, physical examination, diagnosis, and patient's education based on the East-Asian medicine.[4] Acupressure is commonly applied to acupuncture points on the energy-carrying meridians of the body using fingertips, palms, small beads, and especially-designed stimulation devices.[5]

A randomized control trial that was conducted in Turkey also suggested that acupressure provided to hemodialysis patients was effective in reducing UP.[6] This study showed that acupressure can decrease pruritus by reducing the frequency and severity of uremic pruritus associated with hemodialysis. The authors suggested the application of acupressure should be expanded by informing nurses and patients about the benefits of acupressure.[6] The present study intended to review trial studies that focused on acupuncture or acupressure for treating UP.

## MATERIALS AND METHODS

### Search Strategy and Selection Criteria

We searched the PubMed, Cochrane Library, Science Direct, Scopus, and Web of Science (updated up to January 2017). Search terms were ''(acupuncture or acupressure) AND (UP OR pruritus OR itch OR itching OR chronic renal disease OR chronic renal failure OR chronic kidney disease OR chronic kidney failure OR ESRD OR hemodialysis OR peritoneal dialysis)." We scanned bibliographies of relevant articles and conference proceedings. Studies by the same author were checked for possible overlapping participant groups. If the study was reported as duplicate, only the most recent or complete study was included. The following selection criteria were applied: (1) randomized clinical trials that used needle acupuncture as the only treatment or as an adjunct to other treatments were included if they had been conducted in humans; and (2) comparison of acupuncture treatment group with control group that take no acupuncture treatment for uremic pruritus treatment.

We had limitations for translation from Chinese language, so we did not search Chinese databases. Studies that failed to meet the inclusion criteria were excluded.

### Data Extraction and Quality Assessment

Two independent reviewers extracted data from the articles according to the selection criteria. Disagreements were resolved by discussion between the two reviewers considering the opinion of a 3rd reviewer. The quality of randomized controlled trial studies was assessed using the Jaded score system: (1) randomization (the study was described as randomized), (2) double blinding (participant masking and researcher masking), (3) reporting of the number of dropouts and reasons for withdrawal, (4) allocation concealment, and (5) generation of random numbers (by using computer, random numbers table, shuffled cards, or tossed coins).[7]

The following information were abstracted from each included study: first author and year of publication, design of study, sample size, mean age of patients, intervention regime, follow-up duration, concomitant treatment, tools for assessment pruritus, and outcome measures for each group. All the analyses were based on previously published studies, thus no ethical approval or patient consent was required.

### Quantitative Data Synthesis and Data Analysis

We extracted data and then used comprehensive meta-analysis to pool them for summary estimates. To facilitate studying the outcomes, we divided them into 2 types of intergroup and within group outcomes. For intergroup outcomes, we compared pruritus grade between the cases and the controls, and for the within group outcomes, we compared outcomes in the cases or the controls with their baselines.

We expressed the results for continuous outcomes as weighted mean difference, with 95% confidence intervals. We checked heterogeneity among our studies by the chi-square-based Cochran Q and the $I^2$ statistics to measure the proportion of total variation due to heterogeneity beyond chance. If $I^2$ was greater than 50%, heterogeneity was considered significant and data was analyzed using a random effect model. Otherwise, the fixed-effects model was applied as the preferred method. We used fixed effects model in this study, and a $P$ value less than .05 was considered significant.

## RESULTS

### Search Results and Characteristics

The literature search and reference mining yielded 494 potential relevant articles. We removed 28 articles because of duplication. We also excluded 404 articles after reviewing the titles and abstracts because they were books, book sections, or review papers, and therefore not relevant. Then, we reviewed full texts of selected articles and removed 57 studies because topics were not relevant to the subject. Finally, 5 studies reporting 6 trials were included in the systematic review (all of them were randomized clinical trial,[1,5,7-9] except one by Duo that was a cross-over clinical trial.[7] The flow diagram of study selection is depicted in Figure 1. The main characteristics and the details of the studies are summarized in Tables 1 and 2.

### Review Articles

Duo[7] designed a cross-over study. Electro-acupuncture was conducted 3 times a week during a mean of 24.7 days per 1 course of treatment. Three patients received 3 courses of treatment and 2 had 1 course. In all the patients, electro-acupuncture alleviated UP symptoms and improved the number of sleep hours during and after the treatment, whereas superficial electrical stimulation failed to do so.[7] In Che-Yi and colleagues' study,[8] the study compared acupuncture with sham acupuncture in 40 hemodialysis patients suffering from UP. Compared with baseline, the acupuncture group had a significantly decreased pruritus score in the posttreatment time and 3 months afterwards. However, the sham acupuncture group did not have any difference from their baseline.[8] A nonrandomized controlled trial by Akca and colleagues took place at 4 hemodialysis centers in Turkey.[5] Seventy-eight patients participated in this study. The intervention group received acupressure that was applied with transcutaneous electrical nerve stimulation, and the other group did not receive any treatment. The outcome data

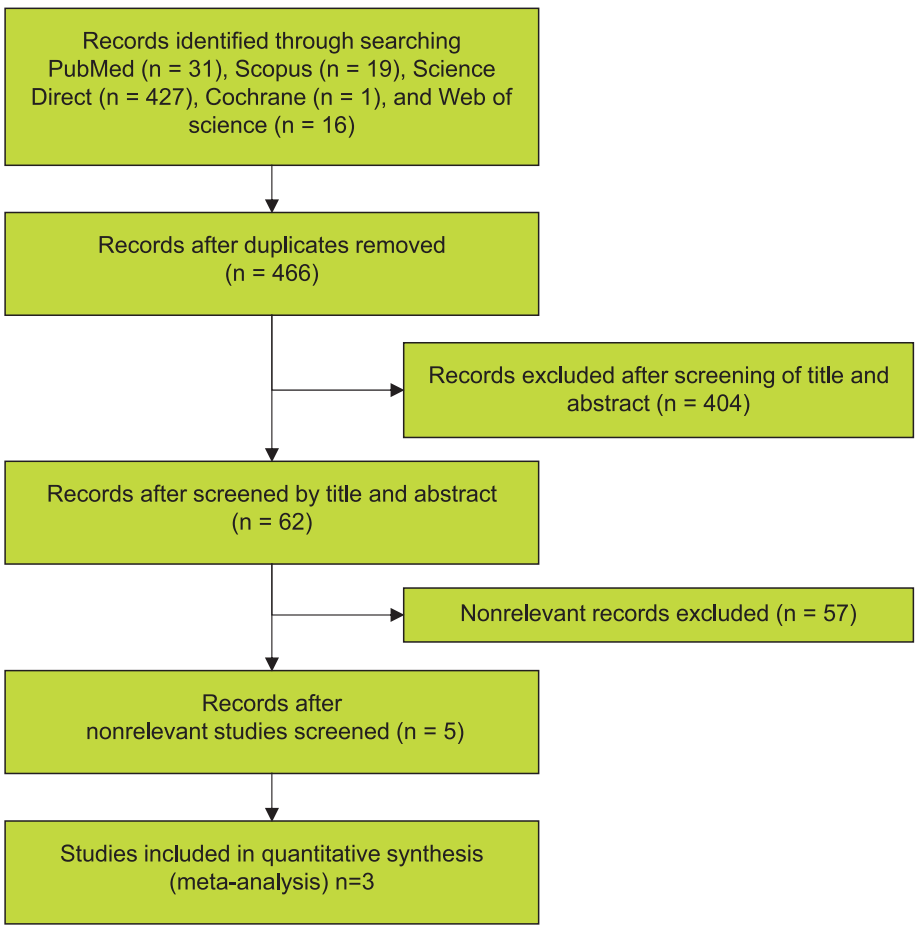


**Figure 1.** Flow diagram of study selection process.

**Table 1.** Characteristics of Published Clinical Trials Included in Systematic Review

| Study | Publication Year | Design | Sample size | | Mean Age, y | | Intervention Regime Case | Intervention Regime Control | Follow-up, mo | Concomitant Treatment Used for Both Groups | Jaded Score |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Case | Control | Case | Control | | | | | |
| Duo[7] | 1987 | Cross-over clinical trial | 6 | 3 | 50.5 | … | Electro acupuncture, 3 times weekly | Superficial electrical stimulation, n = 3 | 1 | Sleeping pills (n = 2) | 1 |
| Che-Yi et al[8] | 2005 | Randomized clinical trial | 20 | 20 | 62.4 | 63.2 | Acupuncture, 1 hour 3 times weekly for 4 weeks | Sham acupuncture (penetrating, no acupuncture point) | 3 | Antihistamines and phosphate binders | 2 |
| Akca et al[5] | 2013 | Nonrandomized clinical trial | 38 | 40 | 47.5 | 44.5 | Transcutaneous electrical nerve stimulation, acupressure apparatus, 3 times weekly for 6 week | None | 1.5 | Antihistaminic tablets | 1 |
| Yan et al[9] | 2015 | Randomized clinical trial | 32 | 30 | 54.00 | 56.63 | Auricular acupressure treatment, 3 times a week for 6 weeks | None | 1.5 | Routine medications | 2 |
| Akca et al[1] | 2016 | Randomized clinical trial | 24 | 25 | 48.08 | 45.84 | Transcutaneous electrical acupoint stimulation, 3 times per week | Normal clinical treatment | 1 | Antihistaminic tablets | 2 |
| Akca et al[1] | 2016 | Randomized clinical trial | 25 | 25 | 55.24 | 45.84 | Acupressure, 3 times per week | Normal clinical treatment | 1 | Antihistaminic tablets | 2 |

**Table 2.** Outcomes of Clinical Trials

| Study | Publication Year | Assessment Tool | Mean Visual Analogue Scale Score | | Intergroup Results | Within Group Results |
|---|---|---|---|---|---|---|
| | | | Case | Control | | |
| Duo[7] | 1987 | Pruritic score scale | … | … | … | Decreased pruritic scores and increased sleeping hours (6 of 6) |
| Che-Yi et al[8] | 2005 | Pruritus score questionnaire | … | … | After treatment ($P < .001$), Three months later ($P < .001$) | Decreased pruritus in case group ($P < .001$) at posttreatment and 3 months later |
| Akca et al[5] | 2013 | Visual Analogue Scale and a pruritus score | 2.66 ± 1.96 | 4.98 ± 1.69 | Significant different between case group and control group in visual analogue scale scores at 18 weeks ($P < .001$) | Significant decrease in visual analogue scale and pruritus scores of both case and control groups at 18 weeks ($P < .001$) |
| Yan et al[9] | 2015 | Visual Analogue Scale | 3.844 ± 1.687 | 5.567 ± 2.285 | Significant difference in mean visual analogue scale scores between the acupressure and control ($P < .001$) | Significant decrease in visual analogue scale and pruritus scores of both case and control groups at 18 weeks in their follow-up assessment |
| Akca et al[1] | 2016 | Visual Analogue Scale | 3.12 ± 2.15 | 5.08 ± 1.55 | Transcutaneous electrical acupoint stimulation group versus control group ($P = .01$) | Transcutaneous electrical acupoint stimulation group had significant reductions from baseline to posttreatment in their levels of discomfort from uremic pruritus ($P < .001$) compared with control group ($P < .05$) |
| Akca et al[1] | 2016 | VAS scores | 3.36 ±2.37 | 5.08 ± 1.55 | Acupressure group versus control group ($P = .004$) | Significant reductions from baseline to posttreatment in levels of discomfort from uremic pruritus of acupressure group ($P < .001$) compared with control group ($P < .05$) |

was collected using visual analogue scale (VAS). It was found that the intervention group mean VAS score significantly decreased at 6 weeks ($P < .001$), compared with the control group, and also they took less medication.[5] Yan and colleagues' study aimed to determine the effect of auricular acupressure therapy on UP.[9] The intervention group received auricular acupressure treatment 3 times per week for 6 weeks, but the control group did not have it. They used VAS scores for assessing pruritus. There was a significant difference in the mean VAS scores between the intervention and control groups during the follow-up. They suggested that auricular acupressure may be a useful treatment for UP.[9] Akca and colleagues also carried out a randomized controlled trial that aimed to test the effect of acupressure and transcutaneous electrical acupoint stimulation (TEAS) on UP in patients on routine hemodialysis treatment.[1] Patients were randomly assigned to three groups: the acupressure group (intervention group), the TEAS group (intervention group), and the control group.[1] The authors used the VAS score for assessing patients' pruritus. The two intervention groups received their treatment on the large intestine acupuncture points in the arm. In terms of outcome measures, there were no differences between the acupressure and the TEAS groups, but patients in the acupressure and TEAS groups had significant reductions in the level of pruritus score from baseline, compared with patients in the control group. In that study, it was concluded that acupressure and TEAS used for treatment of hemodialysis patients were effective in reducing uremic pruritus.

### Quantitative Synthesis

Only three trial studies used the VAS score to assess pruritus and acupressure for intervention regime, so they were included in the meta-analysis.[1,5,9] Results are summarized in a forest plot (Figure 2).

## DISCUSSION

The main conclusion of our analysis was that there was insufficient evidence for using acupuncture or acupressure for treatment of pruritus in patients with ESRD. We found only 6 trial studies that fulfilled our inclusion criteria. All of them had control groups except the study by Duo which was a cross-over study.[7] The mean age of participants in all studies were between 47.5 and 55.24 years, expect in one with slightly older patients (62.4 years).[8] All of the studies concluded that acupuncture or acupressure were effective in treatment of UP. In most of those studies, the control groups did not receive any intervention except in 2 with superficial electrical stimulation and sham acupuncture.[7,8] Defining the intervention for a control group similar to acupuncture (like sham acupuncture) was difficult.

Due to disparity in assessing tools and type of interventions, only 3 of the selected articles included in the meta-analysis. We combined the VAS score results of 3 studies,[1,5,9] and as illustrated in Figure 2, we calculated low heterogeneity. We therefore used a fixed effect model for our study. The final mean difference was significant (mean different, -1.994; 95% confidence interval, -2.544 to -1.445). Evidence from meta-analysis suggested favorable effects of acupressure when combined with other common drugs in treating uremic pruritus. We could not find any meta-analysis that had studied the outcome of acupressure for curing UP. When we searched systematic reviews on UP, we found that a systematic review was done which evaluated the effectiveness of acupuncture for UP in patients with ESRD.[10] They searched 16 electronic databases from their inception to November 2009. All prospective

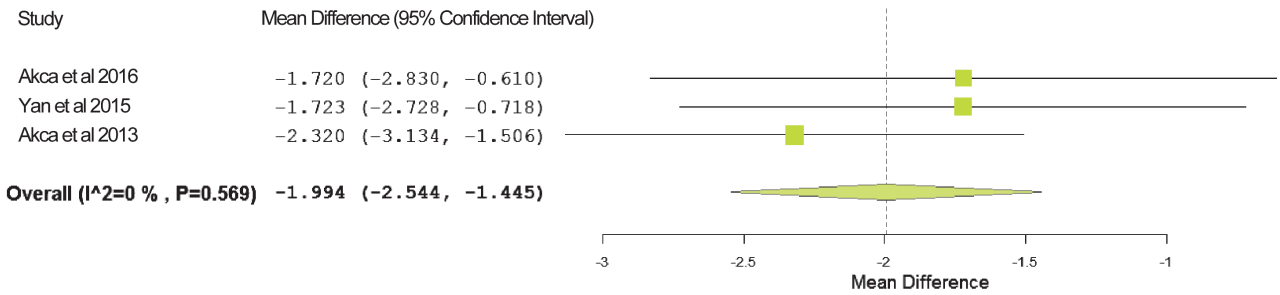


**Figure 2.** Forest plot of studies reporting changes in visual analogue scale scores for pruritus following treatment with acupuncture.

clinical studies of needle acupuncture for UP in patients with ESRD were included regardless of their design. Three randomized controlled trials and 3 observational studies were included in that study. All of the jointed trials reported effectiveness of acupuncture in UP, but the authors believed that most of the included trials had a high risk of being biased and reported that evidence was insufficient to have a strong conclusion.[10] One recent review study on acupuncture and related interventions for symptoms of chronic kidney disease included 24 studies.[4] The authors concluded that evidence was not enough to support the short-term effects of manual acupressure, as complement of other interventions for UP in patients undergoing regular hemodialysis.[4] Another review article that studied itch management generally also concluded that insufficient evidence existed to consider acupuncture as a physical therapy for pruritus, and suggested that further well-designed studies were needed.[12] Acupuncture does not have any significant adverse effects; therefore, it seems reasonable to offer it as an alternative therapy to patients with UP who do not respond to other treatments, who have problems with other systemic medications, or who have an interest to use acupuncture more than other therapies.[2]

A limitation of our study was that we could not search any Chinese databases, and we excluded 2 articles written in Chinese which did not have an English translation, because we had logistic and financial limitations for having access to a Chinese translator. To find a definitive answer for our study question, further rigorous research is needed. Future studies should investigate the effects and safety issues of acupuncture types for treatment of UP, for different stages of chronic kidney diseases.

## CONCLUSIONS

This study suggested that using acupuncture and acupressure may be effective in the treatment of UP, but the evidence is insufficient and other further vigorous studies are needed.

## CONFLICT OF INTEREST

None declared.

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