

# A Systematic Review and a Meta-Analysis of Using Acupuncture for the Treatment of Nocturnal Enuresis

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## Abstract

**Background:** Acupuncture has been an interesting portion of Traditional Chinese Medicine. Many studies have shown that pediatric acupuncture is also acceptable and feasible. Nocturnal enuresis (NE) is defined as evacuating the bladder during sleep in a child older than five years old. Acupuncture and laser acupuncture may be more effective than sham procedures at reducing enuresis and relapse rates; however, the evidence is weak. The purpose of this study is to evaluate the effect of acupuncture therapy in the treatment of nocturnal enuresis on randomized controlled trials (RCTs).

**Method:** An electronic literature search was conducted to identify appropriated trial studies. The outcomes were presented as relative risk, with 95% confidence intervals (CI).

**Results:** We found only seven trials that fulfilled our inclusion criteria. Only seven trials from five studies were included in meta-analysis. Final relative risk (RR) was not statistically significant (RR (range) = 1.312(0.939-1.832)) but evidences from independent review of each study suggested effective roll of acupuncture in treatment of NE.

**Conclusion:** In summary, the results of this study show that acupuncture seems to be an effective treatment for NE, but further large randomized trials are suggested.

**Keywords:** Meta-analysis; Acupuncture; Nocturnal enuresis

## Introduction

Acupuncture has been an interesting portion of traditional Chinese medicine (TCM) for over 2000 years [1]. Acupuncture and its connected therapies, such as laser acupuncture, acupressure and electro-acupuncture, are used throughout East Asia to treat and prevent a great array of diseases. Acupuncture has been adopted by the Western world as complementary treatments for many diseases. Many studies have shown that pediatric acupuncture is acceptable and feasible [1,2]. Nocturnal enuresis (NE) is defined as evacuation of bladder during sleep in a child older than five years old [3]. It has two types: monosymptomatic nocturnal enuresis (MNE) with no urinary symptoms in daytime, and nonmonosymptomatic nocturnal enuresis (NMNE) which includes daytime urinary symptoms [4]. Nocturnal enuresis (NE) occurs in 15% to 20% of 5-year-old children, 5% of 10-year-old children, and 1% to 2% of persons aged 15 years and older. Each year, 15% of children suffering from NE are cured without any treatment. Nocturnal enuresis can cause significant distress for parents and children [1]. Three mechanisms were imaged for NE including: bladder over-activity, failure to awaken in response to bladder sensations, and excessive nocturnal urine production [5]. The current acceptable treatments for NE are oral pharmacological therapies, including desmopressin, tricyclics, and oxybutynin, and behavioral

therapies [6]. Desmopressin has been proven to have reliable effects on one third of the unselected enuretic children. However, when the medication is not taken anymore, the clinical drug effects cannot be continued, and the side effects of drugs may cause the patients to oppose taking them for a long time [7]. Complementary and alternative medicine (CAM) widely helped to encounter the increasing demand for nonpharmacological approaches [6].

Acupuncture and laser acupuncture may be more effective than sham procedures at reducing enuresis and relapse rates; however, the evidence is weak [8]. Compared to formal treatment, safety and cost effectiveness of acupuncture cause the maintenance of patients' compliance [6]. The purpose of this study is to evaluate the effect of acupuncture therapy in the treatment of nocturnal enuresis on randomized controlled trials (RCTs).

## Literature Survey

Alsharnoubi designed a RCT studies including 45 children with NE, patients were randomized into three equal groups (Table 1). A statistically significant higher cure rate was reported in laser acupuncture group 73.3%, than other two groups. This study concluded that laser acupuncture is noninvasive, painless, with no side effects and its recurrence rate is very low which can be used as an alternative therapy for patients with NE [11].

Mogahed conducted a RCT study which included 50 children with NE who were randomly assigned to two groups of equal numbers. The results of this study suggested that low level laser acupuncture has an effect on bladder reservoir function and decreasing bedwetting in nocturnal enuresis [12].

The aim of MOURSY RCT study was to evaluate the efficacy of combined laser acupuncture and desmopressin in managing patients with NE to compare with their efficacy when used as monotherapy. The study included 186 patients. They were randomized into three equal groups. A statistically significant higher cure rate was reported in the group with a combination of laser acupuncture and desmopressin [13].

In Radvanska RCT study, a total of 31 patients with NE enrolled in the study. They compared laser acupuncture with placebo groups (control 1= red light and skin contact, and control 2= with red light without skin contact), but they found no significant effect of active laser acupuncture compared with placebo groups. They concluded that laser acupuncture is a safe but inefficient treatment for NE [14].

The Karaman RCT study was done with 91 children with NE. The children were randomized into two groups. They suggested that laser acupuncture therapy was significantly more effective compared to placebo in terms of complete dryness, partial improvement and a decrease in the mean number of weekly bedwetting episodes. This study suggested that laser acupuncture therapy can be considered as an alternative therapy for patients with NE [15].

In Yuksek study, 24 people enrolled. In this study, complete and partial responses in acupuncture group were seen in respectively 83.3% and 16.7% of patients treated with acupressure, after 6 months of treatment. In children who received oxybutynin, complete and partial responses were seen in respectively 58.3% and 33.3% of patients. They concluded that acupressure could be an alternative non-drug therapy for NE [16].

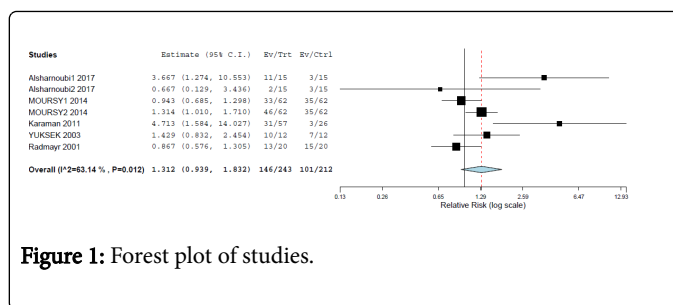
Honjo conducted a before-after clinical trial. They included 15 patients with NE who were treated by acupuncture. Nocturnal enuresis improvement rates were 40% just after the treatment and 47% two months after. They concluded that acupuncture may be useful in the treatment of nocturnal enuresis, and can be used an alternative therapy for NE [9].

Serel, T conducted a before-after clinical trial on 50 children suffering from NE. They showed that the efficacy of treatment was high. Within 6 months, 43 (86%) had improvements. They suggested that using acupuncture in patients with NE appeared to be the most efficacious [10].

In Radmayr study, forty children with NE were enrolled. Then, the children were randomized into two groups: group A children were treated with desmopressin, and group B children took laser acupuncture. Response rate in group B was 65% but in group A was 75%. Success rates indicated no statistically significant differences between two groups but they suggested that laser acupuncture should be considered as an alternative, noninvasive, painless, cost-effective, and short-term therapy for children with NE [17].

### Quantitative synthesis

Only seven trials from five studies were included in meta-analysis because of disparity in outcome measures. Results are summarized in forest plot (Figure 1).



**Figure 1:** Forest plot of studies.

### Methods

We searched PubMed, the Cochrane Library, Science Direct, Scopus, and Web of Science (updated on January 2017). Search terms were “(enuresis OR nocturnal enuresis OR nighttime urinary incontinence OR bedwetting) AND (acupuncture OR laser acupuncture OR electro acupuncture OR auricular acupuncture OR ear acupuncture OR scalp acupuncture OR acupoint OR moxibustion OR acupressure OR acustimulation)”. We scanned bibliographies in relevant articles and conference proceedings. Studies by the same authors were checked for possible overlapping participant groups. If the study was reported as duplicate, only the most recent or complete study was included. Our selection criteria were:

- (1) RCTs (randomized clinical trials) that used acupuncture as the only treatment or as an adjunct to other treatments, if they had been conducted in humans;
- (2) Comparison of acupuncture treatment group with control group that take no acupuncture treatment for nocturnal enuresis. We had restrictions 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 third reviewer. The quality of RCT studies was assessed using the Jaded score system.

The following information was abstracted from each included study: the first author and year of publication, design of study, sample size, mean age of patients, intervention regime, follow-up duration, 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. We expressed the results with relative risk with 95% confidence intervals. We checked heterogeneity among our studies by the Chi-square-based Cochran's Q and I<sup>2</sup> statistics to measure the proportion of total variation due to heterogeneity beyond chance. If I<sup>2</sup> > 50%, heterogeneity was considered statistically significant and data was analyzed using a random effect model. Otherwise, the fixed-effects model was applied as the preferred method. We used random effects model in this study, and in the whole study, P<0.05 was considered as statistically significant.

## Results

### Search results and characteristics

The literature search and reference mining yielded 508 potential relevant articles. We removed some articles because of duplication. We also excluded some articles after reviewing the titles and abstracts because they were books, book sections, review papers and therefore not relevant. Then, we reviewed full-text of selected articles and removed some other studies because their topics were not relevant to the subject. At last, remaining studies and trials were included in the systematic review (all of them were randomized clinical trial (RCT) except trial number 9 [9] and 10 [10] that were clinical trial before-after. The flow diagram of study selection is given in Figure 2. The main characteristics and the details of the studies are summarized in Table 1.

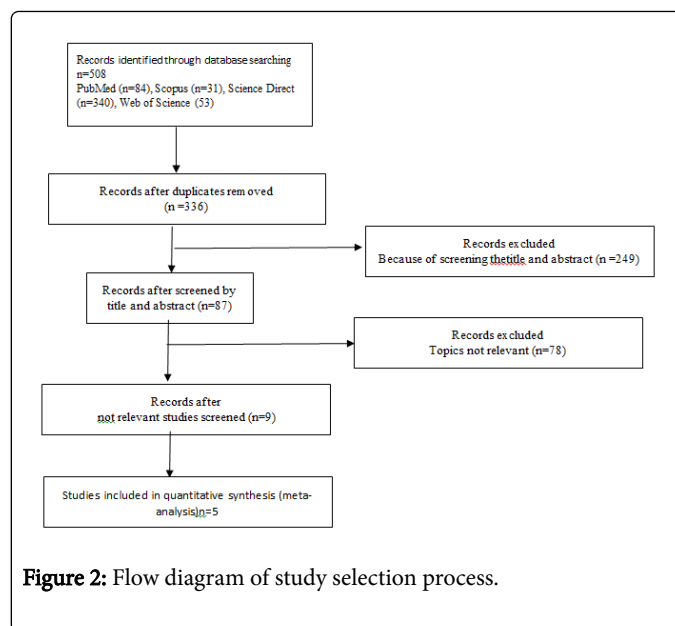


Figure 2: Flow diagram of study selection process.

Number	Name	Design	Sample size case	Sample size control	Age (mean) case	Age (mean) control	Intervention regime case	Intervention regime control	Follow-up (month)
1	Alsharnoubi [11]	RCT	15	15	8.8 ± 3.18	9.43 ± 2.77	laser acupuncture	desmopressin acetate	6
2	Alsharnoubi [11]	RCT	15	15	9.93 ± 3.16	9.43 ± 2.77	laser acupuncture	desmopressin acetate	6
							desmopressin acetate		
3	Mogahed [12]	RCT	25	25	10.84 ± 3.31	10.28 ± 3.27	laser acupuncture	sham laser	1
4	Moursy [13]	RCT	62	62	15.6	15.9	laser acupuncture	desmopressin acetate	9
					(10–21)	(11–21)			
5	Moursy [13]	RCT	62	62	15.8	15.9	laser acupuncture	desmopressin acetate	9
					(11–21)	(11–21)	desmopressin acetate		
6	Radvanska [14]	RCT	16	13	8	8.6	laser acupuncture	CONTROL1: placebo treatment with red light and skin contact	6
					5–14	5–16		CONTROL2: placebo treatment with red light without skin contact	
7	Karaman [15]	RCT	57	26	8.5 ± 3.2	8.9 ± 3.3	laser acupuncture	Non-laser light (placebo)	6
8	Yukse [16]	RCT	12	12	7.67 ± 2.34	7.41 ± 2.67	Acupressure	oxybutynin	6
9	Honjo [9]	CT before-after	15				acupuncture		
10	Serel [10]	CT before-after	50		10.3 (9–18)		acupuncture		6

11	Radmayr [17]	RCT	20	20	8 (5–14)	8.6 (5-16)	laser acupuncture	desmopressin	6
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**Table 1:** Characteristics of trials included in review.

### Outcome

The disparity of outcome measures seen in trials is shown in Table 2.

Number	Name	Outcome1 case	Outcome1 control	Outcome1 statistical significance	Outcome2 case	Outcome2 control	Outcome2 statistical significance
1	Alsharnoubi [11]	mean value bedwetting frequency= 1.13	mean value bedwetting frequency=5.8		cure rate=73.3%(11 of 15)	cure rate=20% (3 of 15)	significant
2	Alsharnoubi [11]	mean value bedwetting frequency=8.13	mean value bedwetting frequency=5.8		cure rate= 13.3%	cure rate=20%	significant
3	Mogahed [12]	complete dryness =52%	NR	significant	maximum voiding volume= 254.2 ± 63.86	maximum voiding volume= 222.2 ± 37.31	significant
4	Moursy [13]	Cure with no bed wetting=33 (53%)	Cure with no bed wetting=35(56.5%)	not significant	maximum voiding volume=340 ± 47.04	maximum voiding volume=286 ± 27.7	not significant
5	Moursy [13]	Cure with no bed wetting=46 (74%)	Cure with no bed wetting=35(56.5%)	significant	maximum voiding volume=346 ± 42.49	maximum voiding volume=286 ± 27.7	not significant
6	Radvanska [14]			Not significant	50% reduction of wet nights 3 of 16	50% reduction of wet nights' control 1+2= 1 of 13	not significant
7	Karaman [15]	the mean number of bed-wetting episodes 1.7 per week	the mean number of bed-wetting episodes 3.1 per week	significant	complete improvement 54.4% (31)	complete improvement 11.5% (3),	significant
8	Yuksekk [16]	complete responses 83.30%	complete responses 58.30%				
9	Honjo				complete cure rate 47% (7/15)		
10	Serel T [10]	completely dry 43 (86%)					
11	Radmayr [17]				response rate 13 (65%)	response rate 15 (75%)	

**Table 2:** Outcome of trials.

### Discussion

This study showed that there is no sufficient evidence to use acupuncture for treatment of NE. We found only seven trials that fulfilled our inclusion criteria. All of the studies had a control group except two [9,10]. The Mean ages of participants in all studies were between 7 to 11 years old except in MOURSY [13] study which was 15 years old. All the studies recommended the acupuncture as an alternative therapy for NE. We saw some disparity in sample sizes in found studies. Due to disparity in outcome measures, only seven trials from five studies were included in meta-analysis. We combined complete improvement percentage results of selected studies, and as can be seen in Figure 2, we calculated the heterogeneity (0.12=63.14%,

$p=0.012$ ), so we used random effect model for this study. The final relative risk (RR) was not statistically significant (RR (range) = 1.312(0.939-1.832)), but evidence from independent review of each study suggested effective roll of acupuncture in treatment of NE.

A systematic review was done and evaluated the effectiveness of acupuncture for NE. In this study, randomized controlled trials which compared acupuncture therapy and pharmacological therapy or placebo treatment were identified, and a meta-analysis was performed. The results of meta-analysis of this study showed that acupuncture therapy is more effective for clinical efficacy when compared with placebo or pharmacological treatment, but this study suggested additional RCTs with rigorous experimental design, large-scale high

quality methodological control, long follow-ups, and strict reporting specification [6]. Another systematic review was done about acupuncture for nocturnal enuresis in children. In that study, 11 studies were eligible for data extraction. That study suggested that acupuncture is useful for nocturnal enuresis when used in conjunction with other treatment (OR 3.98, CI: 2.2-7.2). They expressed that further rigorous studies were needed [18].

### Limitation

A limitation of our study was that we could not search any Chinese database, and we therefore excluded some Chinese articles that didn't have English Translation because Chinese translator was not available and there was no budget for that. Another limitation is that the number of studies included is small, as well as the number of studies in the subgroup meta-analysis.

### Suggestion

To find a definitive answer for this research question, further rigorous research is needed. Future studies should investigate the effects and safety of acupuncture types for treatment of NE.

### Conclusion

In summary, the results of this study show that acupuncture seems to be an effective treatment for NE, but further large randomized trials are suggested.

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