



Review article

Acupuncture for the treatment of pediatric nocturnal enuresis: A systematic review and a meta-analysis of randomized and non-randomized studies[☆]



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ABSTRACT

Introduction: Nocturnal enuresis is a common clinical condition in the pediatric population. The aim of this study was to assess the effectiveness of acupuncture treatment on pediatric nocturnal enuresis.

Methods: The search of publications using “acupuncture” and “enuresis” or “bedwetting” as keywords was performed in 6 databases. To be included studies had to (1) compare acupuncture with conventional treatment or placebo; (2) investigate a pediatric sample; and (3) provide results at the end of treatment or follow-up. Languages included were English; Italian; and Chinese. Analysis was performed according to PRISMA guidelines. Primary outcome was reduction in wet nights. Side effects and dropouts were secondary outcomes.

Results: We included 10 studies (7 randomized controlled trials and 3 non-randomized controlled trials) covering a total of 888 patients. A favorable, but non significant, effect of acupuncture compared with conventional care and placebo emerged. The type of acupuncture was the main source of heterogeneity. No statistically significant differences emerged across non-randomized and randomized studies. No difference was found in dropouts. Side effects in the acupuncture group were minor but rarely reported.

Conclusions: Acupuncture seems to be an effective option for the treatment of nocturnal enuresis, though further large randomized trials are needed because no statistically significance emerged and low quality of the included studies might have overestimated results. Acupuncture treatment seems feasible and with minor side effects.

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1. Introduction

Nocturnal enuresis (NE) is defined as emptying of the bladder during sleep in a child aged at least 5 years [1]. NE is defined as

primary (PNE) if the child has not had a dry night for more than 6 months and as secondary if a period of dryness preceded the onset of bedwetting [2]. Monosymptomatic NE (MNE) is defined as involuntary urine voiding during sleep without other symptoms, at least twice per week for at least 3 consecutive months in a child over 5 years of age and not due to either a drug side-effect or a medical condition (i.e., without lower urinary tract symptoms or bladder dysfunction) [3]. Non-monosymptomatic NE denotes the coexistence of any symptoms among increased or decreased voiding frequency, incontinence, urgency, hesitancy, straining, weak or intermittent urine flow, incomplete emptying, post void dribble or dysuria [4].

NE is a common clinical condition in childhood and adolescence. The prevalence of NE is approximately 15%, 10% and 6% among 5-, 7-, and 12-year-old children, respectively; and moreover higher among males. NE shows a spontaneous improvement of 15% per year [5]. Further epidemiological studies of NE in adolescents and adults up to 40 years of age indicated that the prevalence remains stable (over 2% of adults) with no further significant drop after the age of 10 [6]. The overall prevalence of NE remains relatively constant irrespectively of geographical location [7].

Acupuncture is a traditional Chinese therapy with a 2000-year-old history [8] commonly used as a primary therapy for NE in Eastern medicine. A limited number of studies investigating the clinical usefulness of acupuncture as a treatment option for NE have been published in the last decades [9–20]. These studies reported a positive effect of acupuncture upon the number of enuresis episodes, the storage capacity of the bladder and the ease of arousing from sleep to void [9,10]. A systematic review published in 2005 provided limited evidence for the efficacy of acupuncture for the treatment of NE; however, due to the low methodological quality of the included studies, evidence to identify, which parameters of acupuncture work best, was lacking [21]. In 2011, a Cochrane meta-analysis concluded that there is little evidence on the effectiveness of acupuncture for the treatment of NE [5].

We carried out an updated systematic review and meta-analysis of both randomized and non-randomized published studies aimed to investigate and quantify the effectiveness (i.e., reduction of wet nights) of acupuncture (i.e., conventional, electroacupuncture, or laser acupuncture) compared to conventional drug therapy or placebo/sham acupuncture as a treatment option for pediatric NE.

2. Methods

2.1. Identification of studies and data collection

This meta-analysis was conducted according to the guidelines developed by PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [22]. Two authors (F.S. and C.M.) independently carried out a systematic literature search of all studies published as original articles, up to July 31st 2014, investigating the use of acupuncture for NE, in the following databases: Medline, Cinahl, Embase, Scopus, Web of Science (including Chinese Science Citation Database), Scopus, Ovid, Psycinfo, and Cochrane Library databases. We used the following search string: “acupuncture” and “bedwetting” OR “enuresis”. Languages included were English, Italian, and Chinese. Acceptable interventions included conventional acupuncture, electroacupuncture, and laser acupuncture using any combination of parameters.

To be included in this meta-analysis, studies had to: (1) compare acupuncture with conventional drug treatment, no treatment, or placebo, (2) investigate a pediatric sample (as defined by the trialists), and (3) provide results (i.e., reduction in wet nights) at the end of treatment or at the last follow-up visit. Randomized and non-randomized studies which used acupuncture in at least one arm of the study were included. Treatment duration was not considered an

exclusion criterion. Studies comparing acupuncture plus conventional drug treatment versus drug conventional treatment or acupuncture were excluded from this meta-analysis.

Outcomes considered were response rate and partial response rate, after treatment or at the last follow up visit. Response rate (R) was defined as having a minimum reduction of wet nights of 90%; partial response rate (PR) as having a minimum reduction nights of 50% in the number of wet night [23].

For each study F.S. and C.M. extracted using a standard form the following information: study design, country, number of subjects treated with acupuncture and with the conventional drug treatment or placebo, duration of treatment, duration of follow up, and effectiveness of acupuncture and of the conventional drug treatment or placebo as defined above by reduction of the numbers of wet nights. Differences were resolved by discussion.

Risk of bias in included studies was assessed according to Cochrane Handbook for Systematic Reviews of Interventions [24]. Evaluated sources of bias were: allocation concealment, randomization, blinding of assessors, subjects and data analysis personnel, intention-to-treat analysis and withdrawal or loss to follow-up.

F.S. analyzed the risk of bias assessment.

2.2. Statistical analysis

Comparison was performed between acupuncture treatment versus conventional drug treatment and between acupuncture treatment versus sham acupuncture/placebo. Specific subgroup analyses according to acupuncture type (body vs laser) and study type (randomized vs non-randomized) have been also carried out. Electro acupuncture was considered within the body acupuncture subgroup as it involves the insertion of needles into specific exterior body locations.

We used the Relative Risk (RR) as the association measure. $RR < 1$ indicates favorable effect of acupuncture as compared to the conventional drug treatment.

We tested for between-studies heterogeneity using the χ^2 test, and quantified inconsistency through the Higgins I^2 statistic, i.e., the proportion of total variation contributed by between-studies variance. Pooled meta-analytic estimates were derived using the fixed-effect model when no heterogeneity was found, and through the random effect model otherwise [25]. We applied the Yates 0.5 correction factor [26] in a study [11] containing zero events in treatment and placebo group in order to estimate the RR. Meta-analysis results were displayed in forest-plots; squares indicate study-specific RRs and horizontal lines their corresponding 95% confidence interval (CI) estimate. The size of each square is proportional to the precision (i.e., the inverse of the variance) of the RR. The pooled meta-analytic estimate is given by a diamond.

Visual inspection of funnel plot was used to assess publication bias.

Statistical analyses were performed by using the R meta package (Guido Schwarzer (2013). meta: Meta-Analysis with R. R package version 2.2-1. <http://CRAN.R-project.org/package=meta>

3. Results

Fig. 1 shows the strategy used to identify the relevant studies for inclusion in this meta-analysis. We retrieved a total of 327 studies and, on the basis of abstracts contents, 184 articles were evaluated as relevant for our meta-analysis. From the reference list of these articles, we identified 1 article of interest. From a total of 185 articles, 164 were excluded because they did not satisfy the inclusion criteria, i.e., for the following reasons: (i) multiple studies on the same study population; (ii) studies lacking quantifiable level of improvement after treatment; (iii) studies reporting only combined results for different kinds of treatment; (iv) studies lacking control group; (v)

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