

Review Paper

Traditional, Complementary, and Alternative Medicine in Nocturnal Enuresis in Children

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Citation Motaharifard MS, Mohkam M. Traditional, Complementary, and Alternative Medicine in Nocturnal Enuresis in Children. *Journal of Pediatrics Review*. 2022; 10(1):47-56. <http://dx.doi.org/10.32598/jpr.10.1.1003.1>

 <http://dx.doi.org/10.32598/jpr.10.1.1003.1>

**Article info:**

Received: 08 Aug 2021

First Revision: 15 Nov 2021

Accepted: 26 Dec 2021

Published: 01 Jan 2022

Keywords:

Nocturnal enuresis,
Complementary Therapies,
CAM, Persian medicine,
Children

ABSTRACT

Background: The use of complementary and alternative medicine (CAM) treatments in children is increasing. Due to the ineffectiveness of some pharmacological interventions or intolerance to their side effects, different types of CAM are used in various problems, such as enuresis in children. This study aimed to introduce the most common complementary and alternative medicine methods used for enuresis in the pediatric population.

Objectives: This study aimed to introduce the most common complementary and alternative medicine methods used for enuresis in the pediatric population.

Methods: Medical literature search was performed in several databases for a variety of Traditional, Complementary, and Alternative Medicine in nocturnal enuresis in children. Databases used were Google Scholar, Web of Science, Scopus, Cochrane Library, PubMed, and a number of Persian databases, including Magiran and SID. Clinical trials, case series, or case reports that had evaluated the effectiveness of these therapies in nocturnal enuresis in children were included. Data were collected in English or Persian from inception to early 2021.

Results: Most studies had been performed on some CAM methods, such as acupuncture. In some methods, such as reflexology, the studies were limited to case reports and in others, such as aromatherapy, there was no study related to children's enuresis. Based on the results, most CAM methods have positive effects in the treatment of nocturnal enuresis and have their unique theories about the concepts of etiology, diagnosis, and treatment of disease.

Conclusions: Despite the relatively high use of CAM treatments in nocturnal enuresis among children, evidence of their effectiveness is not enough. More clinical trials are required to evaluate the safety and efficacy of these methods.

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1. Context

Dating back to 1550 BC, a wide range of complementary and alternative medicine (CAM) therapies have been used to treat nocturnal enuresis (NE) (1). Different types of CAM are used in different parts of the world that are influenced by culture, history, level of education, and personal interests. Several studies have suggested that CAM treatments are highly used in pediatric populations as in adults (2). The American Academy of Pediatrics (AAP) reports that 20-40% of healthy children and 50% of children with the chronic disease receive CAM treatment, which is different in various countries (3). Acupuncture, homeopathy, chiropractic, diet recommendations, hypnosis, medicinal herbs, and traditional medicines are used to treat various problems, including enuresis in children.

Nocturnal Enuresis (NE) is one of the major problems in young children. It can be defined as involuntary bed-wetting during sleep at least twice per week in the past three months, in the absence of organic disease, in a child aged five years or more (4). NE is a complex and heterogeneous disorder, which affects around 15% to 20% of five-year-old children and usually declines with age (5).

Although enuresis is a benign problem and has a high percentage of spontaneous improvement, it is a socially disruptive and stressful condition for the child and his/her family. We can help them with effective pharmacological or non-pharmacological treatments. Behavioral interventions are usually considered as the first line and medical treatments in the second step. These treatments are usually effective in reducing the number of bedwetting, but in lots of children, enuresis relapse after stopping treatments or they do not tolerate their side effects of them (6). Therefore, some parents use complementary and alternative methods to treat their children, but the review of trials did not provide strong evidence to support this.

This review aimed to critically review the literature to summarize the data on CAM treatments used in pediatric populations with NE.

2. Evidence Acquisition

We established literature search in scientific databases, including Google Scholar, PubMed, Web of Science, Scopus, Cochrane library, and Magiran and SID (the last two are Iranian databases). Search terms for extracting articles were “nocturnal enuresis” or “bed wetting” com-

bined with a series of keywords like “child”, “children” and “pediatrics”. We defined CAM using the definition from the WHO Traditional Medicine Strategy, where CAM refers to a broad set of health care practices that are not part of that country’s own tradition or conventional medicine and are not fully integrated into the dominant healthcare system (7). CAM are those therapies that may either be provided alongside conventional medicine (as complementary) or may act as an alternative for it.

We did not include supplements (minerals and vitamins) in our definition of CAM but included acupuncture, Ayurveda, massage (of any form), cupping therapy, dietary recommendation, reflexology, phytotherapy/herbal medicine, chiropractic, exercise therapy, homeopathy, hypnotherapy/hypnosis, yoga, aromatherapy, traditional Chinese medicine (TCM), and Persian medicine (PM). We also included the names of these CAM methods in the search terms. Clinical trials, case series, or case reports that had evaluated the effectiveness of these therapies in nocturnal enuresis in children were included. Data were collected in English or Persian from inception to early 2021.

3. Results

Based on our searches, more clinical studies have been performed on some CAM methods, such as acupuncture. In some methods, such as reflexology, the studies are limited to case reports and in some methods, such as aromatherapy, we did not find any studies on children’s enuresis.

Dietary recommendation

Many studies show that some foods and beverages can promote diuresis, which can exacerbate NE in some children. Dietary restrictions, such as avoiding fluids and diuretics before bedtime, are usually recommended in the treatment of pediatric enuresis. In some children, enuresis may be associated with food allergies and may be provoked by some foods; thus, avoiding food allergens and provoking foods have been suggested for the management of these patients (5, 8). High omega-6 polyunsaturated fatty acid (PUFA) in the diet has been shown to increase nocturnal diuresis by increasing PGE2 levels (9). The results of a study showed that vitamin D and omega-3 supplementation could reduce the number of wet nights among children with nocturnal enuresis (10). Therefore, adjusting the intake of some dietary fatty acids may be effective in this problem. The study conducted by Valenti et al. on 46 enuretic children, clearly demonstrated that a low-calcium diet (~500 mg/

day) in hypercalciuric enuretic children may ameliorate clinical symptoms by restoring aquaporin 2 excretion (11). In another study, restricted diet in those who responded increased bladder capacity and reduced the frequency of daily incontinence (12).

A study by Ferrara et al. showed that specific dietary advice was effective in the management of primary NE. The results showed a higher response rate and a lower number of relapses in those who received desmopressin and dietary advice compared to those who received desmopressin alone (13). Another study by Tsuji et al. in Japan showed that the high daily salt intake significantly reduced the efficacy of desmopressin in the treatment of nocturnal enuresis; thus, salt consumption should be controlled in children with nocturnal enuresis (14).

Chiropractic

Chiropractic is an alternative treatment that is interested in the diagnosis and treatment of mechanical disorders of the musculoskeletal system, especially the spine. It usually works by manipulating the spine and other body structures (5). Only two clinical trials have been published on this subject. A controlled clinical trial on forty-six enuretic children strongly suggests the effectiveness of chiropractic treatment for primary nocturnal enuresis (15). In another trial on 171 children, the number of wet nights had decreased with chiropractic care (16). Two case reports described the resolution of nocturnal enuresis in an 8-year-old girl and a 6-year-old boy after chiropractic manipulations (17, 18). In a case series of 33 consecutive children and teenagers with NE, the therapeutic response rate of chiropractic treatment was 66.6% with no relapse, which indicates the possible effectiveness of this treatment (19).

Homeopathy

Homeopathy is one of the alternative methods and homeopaths have used animal, herbal and mineral medicines for many years to treat a variety of diseases based on the principles of homeopathy (20). Homeopathic treatments seem to have a potential effect on NE. In a small trial, 20 children suffering from enuresis were treated with homeopathic remedies for two months. Enuresis completely disappeared and psychological symptoms improved in 50% of cases (21). A prospective observational trial by Saha et al. on 34 cases showed that homeopathic remedies can have a promising therapeutic effect on enuresis. However, further studies with more methodological accuracy are needed (22). Another study compares homotoxicological reme-

dies with desmopressin and placebo in the treatment of NE. Homotoxicology is a form of therapy that is strongly influenced by homeopathy and uses homeopathic remedies to eliminate toxins from the body. The results showed that homotoxicological remedies were effective in reducing the number of wet nights compared to the placebo, while they are significantly less effective than desmopressin in this trial (23).

Exercise therapy

Pelvic floor muscle exercises and diaphragmatic breathing are simple and easy to learn for many children. These exercises in combination with standard urotherapy are useful for dysfunctional voiding, including NE in children. In a clinical study, NE was cured in 14 out of 21 patients (63%) and enuresis was improved in four boys (21%) during this type of treatment (24). The researchers investigated the effect of pelvic floor muscle exercises on enuresis in another prospective randomized study. In this study, the results showed no additional effect on treatment outcome or duration in children with bedwetting (25).

Since the upper airway obstruction and nocturnal snoring affect the nocturnal enuresis in some children, Khaleghipour et al. investigated the effects of breathing exercises on a reduction in NE in these children. The results showed that the frequency of breathing exercises reduce the nocturnal enuresis episodes in enuretic children with abnormal breathing pattern. Thus, this method can be used as a simple method with low cost and is more efficient than other approaches (26).

Hypnosis

Hypnotherapy as an alternative treatment has been used in children with nocturnal enuresis for many years (5). Many clinicians have reported that hypnosis is effective in treating enuresis. One trial suggested that the treatment of NE using hypnosis with continued regular practice of self-hypnosis is more effective than treatment with imipramine in children above seven years of age (27). The results of another study on 48 enuretic boys showed that hypnotherapy was associated with notable improvement in enuresis during the treatment and its effects were maintained during six months of follow-up (28). In a randomized clinical trial comparing hypnosis and alarm therapy, it was less effective than alarm therapy in achieving dryness in children during and after stopping treatment (29).

Ayurveda

Ayurvedic medicine (Indian traditional medicine) includes various therapies that are usually based on complex herbal compounds, minerals, and metal substances. This alternative method suggests special herbs that are highly effective for managing NE (30). In a recent study, a combination of Ayurvedic medicines compared to the placebo was effective in reducing the signs and symptoms of NE in children (31). Another clinical study showed that an Ayurvedic compound was effective in the treatment of enuresis and showed better results according to the percentage of improvement in comparison to the placebo group (89.6% compared with 48.7%) (32). Bimbimoola Vati (an Ayurvedic drug) showed highly significant results in improving NE symptoms with no adverse drug reactions (33).

Reflexology

Zone therapy or reflexology is a complementary treatment that is performed using deep hand massage in specific areas of the ears, hands, and feet that are related to the internal organs of the body (34). It is a non-invasive and easy method to apply to children. To the best of our knowledge, no clinical study has assessed the effects of reflexology on NE in English or Persian. We only found two case reports in this regard. The outcome of a single case report in a 6-year-old boy with NE showed that the bed-wetting stopped and showed no recur after five months (35). In another case report, an 8-year-old child with ADHD and nocturnal enuresis was treated with foot reflexotherapy for eight weeks and his enuresis disappeared completely after treatment. The results of this case study suggest that foot reflexology can be applied to treat NE in children (36).

Chinese medicine

Moxibustion is a type of traditional Chinese medicine (TCM) treatment that uses ignited materials (usually moxa) on particular points on the body to heat selected areas of the skin. It is promoted as a treatment for a wide variety of conditions, such as urinary incontinence (36). In a study in China, Ginger-partitioned Moxibustion plus cupping therapy was compared with Chinese herbal medicine in the treatment of enuresis in 158 cases. This method plus cupping therapy was better than Chinese herbal medicine with an 84.1% effective rate (37). Acupuncture, massage, and medicinal herbs are also used in TCM.

Acupuncture

Acupuncture is one of the main components of TCM, in which thin needles are inserted into different parts of the body. It is claimed that acupuncture is effective in treating virtually all diseases, including enuresis. Numerous studies have examined the effect of acupuncture on pediatric enuresis but most of them are in Chinese. Efficacy of this method for enuresis has been reported from 76% to 98% in different studies (38). Laser acupuncture has a significantly higher cure rate (73.3 %) compared to desmopressin (20%) in a randomized clinical study (39). In a short study done for the treatment of NE with acupuncture, including 20 subjects, the treatment succeeded, and sleep and quality of life improved (40). In another study on 50 children, the cure rate with acupuncture therapy at six months was 76% (41). A systematic review included 21 RCTs and concluded that acupuncture therapy is more effective than the placebo or pharmacotherapy in treating NE (42). Another systematic review was done in 2017 and seven studies were eligible for data extraction. This study suggested that acupuncture seems to be an effective treatment for NE, but further rigorous research is needed (43).

Massage

Different types of massage are used as an alternative therapy for various diseases. Pediatric Tuina (a kind of TCM massage) has been widely used in the treatment of NE in China (44). The auricular point pressure is also an important component in TCM plus Tuina massage. This method is safe and painless and usually has no side effects. In a study, 92 cases of enuresis were treated with auricular point pressure plus Tuina. After treatment, in 61 cases, enuresis and other symptoms disappeared with no recurrence and in 28 cases, the wet bedding was greatly reduced. The effective rate was 96.7% (45). Other methods, such as abdominal massage, kneading, and spine-pinching in 89 cases aged 3.5 to 10 years showed cure in 54 cases and enuresis decreased obviously in 32 cases (46). In one study the use of massage with olive oil reduced enuresis in preschool children. The response rate was 63.3% in this study (47).

Herbal Medicine

Herbal medicine as a kind of CAM is mainly made from natural plants and usually uses one or several medicinal herbs to treat the diseases. There are few studies on the effect of herbal medicines for NE, especially in children. In three separate trials, different combinations of Chinese herbal medicine were compared with imipramine

and the herbs appeared to be better than imipramine both during and after the treatment (5).

One of the herbal medicines is Suoquan, which has been widely used to treat the symptoms of NE in Traditional Korean Medicine (TKM) and TCM. Numerous studies have examined and confirmed the use of Suoquan in children's enuresis (48). In a clinical trial, Suoquan was compared with desmopressin in 369 cases. The results showed that the combined treatment with Suoquan and desmopressin in children with NE was effective and had a low relapse rate (49).

Yokukansan is a Japanese traditional herbal prescription that is comprised of seven herbs and has been used in Japan for more than 400 years for different problems. In a small trial, Yokukansan with desmopressin was prescribed to 18 children who did not respond to desmopressin alone. This combination therapy was effective in 12 out of the 18 cases with no serious adverse effects (50).

A randomized double-blind placebo-controlled clinical trial assessed the efficacy of a herbal combination for the treatment of nocturnal enuresis in 80 children, but the results of this study have not yet been published (51).

Persian Medicine

Persian medicine, as traditional medicine, suggests many useful herbal remedies to manage NE in children. These medicinal herbs are used in various forms, including oral preparations, topical poultice, medicated oils, sitz baths, and fumigation (52). Only one clinical trial has been performed considering these suggestions. This study was conducted by Sharifi et al. on 80 enuretic children and demonstrated that topical use of *Matricaria recutita* (Chamomile) oil can decrease the frequency of nocturnal or daytime enuresis (53). In a recent study, the effect of topical use of *Saussurea costus* (Qost) oil as a Persian medicine product was assessed in pediatric nocturnal enuresis. The results showed that costus oil was effective in children with monosymptomatic nocturnal enuresis with a 74.5% response rate (54).

Yoga

Yoga therapy is a promising method for children's problems and was recommended to help the child to overcome bed wetting. Based on our searches, there is no clinical trial on the effect of yoga on enuresis. In a pilot study, yoga programs were recommended for ten children aged 6-10 years old. The results showed signifi-

cant improvement and a reduction in NE in the children. The total effective rate in this study was 96.6% (55).

4. Discussion

Nocturnal enuresis is a common problem in the pediatric population. It is usually a distressing problem for children and families (5). In addition to common pharmacological treatments, there are several safe, reasonable, and cost-effective options for treating NE. People often use complementary methods to treat their children's problems, such as enuresis, but the review of trials does not provide enough evidence to support this. This review focuses on the evidence of CAM treatments on nocturnal enuresis.

Although in this study we tried to include more CAM methods in our searches, we did not find sufficient evidence about the use of some methods of complementary and alternative medicine. Most complementary medicine methods have their unique theories about the concepts of etiology, diagnosis, and treatment of diseases different from Western medicine. However, more studies are needed to understand the exact mechanism of action of CAM interventions, most of them seem to have positive effects in the treatment of enuresis with their own rationales.

Several potential mechanisms may be involved in the effect of the enuresis diet. Enuresis in some children may be related to dietary responses that provoke bladder instability. It is believed that enuretic children have small bladders, which expand with a successful diet (8). Many studies have shown that some foods and beverages have a diuretic effect leading to overactive detrusor muscle and can exacerbate NE (9). It has been reported that dietary components play important roles in the regulation of nocturnal urine production through prostaglandin (PG) changes (56) so that the elevated PGE2 levels may increase nocturnal diuresis with increasing instability and overcontractility of the bladder muscles (9).

Based on chiropractic theories, some of the neurological problems associated with bed-wetting may be due to spinal cord subluxation or lumbosacral spinal misalignment that affects the bladder and kidneys. Chiropractic can be effective at restoring bladder control by correcting structural deviations and misalignment (5). Breathing exercises in enuretic children with sleep-disordered breathing, cause a better response to antidiuretic hormone and better control of bladder muscles by increasing the oxygen level (26). The exact mechanism for hyp-

nosis effectiveness in improving NE is unknown and it seems to work by its own specific rationales in enuresis.

The improvement of enuresis by some Ayurvedic medicines may be due to increased strength of the bladder sphincters and increased bladder retention capacity (31). Foot reflexology, based on the principle of activating specific reflex zones of the feet, which are related to the brain and urinary system may aid in reducing the symptoms of NE (34).

Based on Chinese medicine principles, cupping therapy in special points is able to warm up and dredge the kidney yang and calm the heart and mind; thus, enuresis can be controlled (37). Acupuncture is thought to restore health by removing energy imbalances and blockages. Studies suggest that acupuncture decreases uninhibited contractions of the detrusor muscle (38) or increases the maximum bladder capacity (40). Tuina massage can warm the kidneys, astringe the bladder and coordinate yin-yang in the treatment of enuresis according to Chinese medicine (45). In herbal medicine, each plant has a different mechanism of action and the different ingredients in each plant work synergistically to balance the body of patients with enuresis (5). For example, Suoquan has a good effect on strengthening the kidney and plays an effect on enuresis by reducing the amount of urine and the irritability of bladder detrusor (49). Though the specific mechanisms of action of Persian medicine products are not exactly known, most of them are bladder tonic and have antidiuretic, antispasmodic, or anticholinergic activity (52). The probable mechanism of yoga on enuresis is to help strengthen the muscles that control urination and increase bladder capacity (55).

There are differences in treatment methods between different complementary medicines that may influence relevant research. For example, there are limitations to blind the studies in some CAM interventions. Designing a placebo for methods, such as acupuncture, manual therapies, such as massage and reflexology, and herbal remedies with a specific smell and taste is associated with certain problems and in many cases is not possible.

Our study had many limitations, such as language, because we only reviewed English or Persian articles while many related articles are in Chinese. We tried to search most CAM methods in enuresis, but because CAM treatments are so diverse, we may miss some types of CAM therapies. We only included published articles in this study; however, there are unpublished studies on this subject that are not included in our study. According to the Iranian Registry of Clinical Trials (IRCT), several studies have been

conducted on the effect of herbal medicines and PM in NE in Children, but the results have not been published yet. Based on our review, most CAM interventions had positive effects on children's enuresis, but for better results, more studies with better qualities are required.

5. Conclusion

Some evidence suggests that CAM methods can be effective for pediatric enuresis, but there was little reliable information comparing complementary methods with established effective methods. Despite the wide use of many of these alternative therapies for different problems of children, the evidence does not support those until properly randomized trials have been done to demonstrate their effectiveness. More clinical trials are required to evaluate the safety and efficacy of these methods.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles were considered in this article.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

Conceptualization, investigation, writing - original draft: Monireh Sadat Motaharifard; Writing - review, and editing: Masoumeh Mohkam; Reading and approving the final manuscript: Both authors.

Conflicts of interest

The authors declared no conflicts of interests.

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