Introduction

Nocturnal enuresis (NE) is characterized by the involuntary discharge of urine at night in those 5 years of age or older. Primary NE (PNE) is diagnosed in an individual who has never achieved nighttime dryness; in secondary NE (SNE), incontinence follows a dry period of at least 6 months. In either, the enuresis must not be due exclusively to a medical condition or diuretic therapy. Prevalence is estimated at 5% to 10% among 5-year-olds, 3% to 5% among 10-year-olds, and 1% among those 15 years of age and older. Between 5% and 10% of cases resolve annually without treatment. (1) The causes of PNE and SNE remain unclear, although physical, neurologic, and psychological factors; genetics; sleep structure; and other medical conditions have been implicated. (2)

Treatment for NE includes pharmacologic and nonpharmacologic options, and many families are interested in complementary and integrative approaches. This review assesses the efficacy and safety of acupuncture/acupressure, hypnosis, and biofeedback in treating NE.

Acupuncture/Acupressure

Originally developed as a health-care tool in China thousands of years ago, the stimulation of specific points on the body (called acupoints) may be carried out by a variety of techniques, including insertion of thin needles (acupuncture), surface pressure (acupressure), electricity (electro-acupuncture), and laser (laser acupuncture). The effect of acupuncture on PNE was assessed through two recent systematic reviews. (3)(4) The Cochrane review summarized the results of three randomized controlled trials (RCTs). (5)(6)(7)

In the first study, 111 patients ages 5 to 15 years were assigned randomly to two different forms of acupuncture. (5) In the treatment group, a needle was embedded under the skin and left in place; in the control group, a needle was placed on the skin surface for 30 minutes each day. The number of treatment courses (of 6 days each) depended on response; follow-up times were not reported. At the end of the study, 54% (30/56) of patients in the treatment group attained 14 consecutive dry nights compared with 31% (17/55) in the control group. Adverse events were not mentioned.

In the second study, 100 patients were assigned to two groups: 80 to the acupuncture group and 20 to the drug group. (6) Patient ages were reported only for the acupuncture group, with most patients between 5 and 21 years of age. In this group, patients received needle acupuncture daily for 10 days. In the drug group, patients received a combination of drugs: meclofenoxate (200 mg four times a day), oryzanol (20 mg three times a day), and thiamine (25 mg three times a day) for 10 days. The number of treatment courses (of 10 days each) varied. At the end of the study, 73% (58/80) of patients in the acupuncture group reached 14 consecutive dry nights compared with 10% (2/20) in the drug group. Adverse events were not mentioned. The conclusions from this study are limited because reporting of methods and patient demographics were incomplete.

In the third study, 40 patients ages 5 to 16 years were assigned randomly to laser acupuncture or pharmacotherapy for 3 months. (7) In the acupuncture group, patients received laser acupuncture (for 30 seconds three times per week to a maximum of 15 treatments). In the drug group, patients received intranasal desmopressin (between 20 and 40 mcg, as needed). Response was defined as a decrease in wet nights of 90%, partial
response as a decrease of 50%, and nonresponse as a decrease of less than 50%. At the end of the study, response was reported to be 80% (16/20) for the acupuncture group and 70% (14/20) for the drug group. A similar level of response was reported 6 months after the study. No adverse events occurred in either group. The conclusions from this study are limited because of the small sample size and subsequent lack of statistical power.

A second systematic review identified 10 additional studies that compared acupuncture with either a different form of acupuncture or another traditional Chinese medicine therapy such as herbs. (4) Few study details were provided in the review. The authors concluded that although there was tentative evidence for the efficacy of acupuncture in NE, the quality of the included studies was very low. Because of the types of comparison groups used, the usefulness of the studies in the context of Western medicine is limited.

One additional RCT compared acupressure with oxybutynin therapy in 24 patients ages 4 to 13 years. (8) Three patients had experienced unsuccessful pharmacologic treatments previously and were assigned to receive acupressure. The acupressure group received daily acupressure from their parents; the other group received 0.4 mg/kg of oxybutynin daily. Response was classified as complete, partial promising, but the scientific and clinical relevance of these studies is limited due to the methodologic points identified for each. To strengthen the evidence of the utility of acupuncture in treating PNE, studies must be conducted with increased methodologic rigor and verified by replication. Additional comparative effectiveness research would help clarify the optimal role of acupuncture in the context of Western conventional care. No adverse events were reported.

Mind/Body

Hypnosis

The use of hypnosis for PNE was summarized in a recent Cochrane systematic review that presented the results of two studies, an RCT and a controlled clinical trial. (3) In the RCT, 48 boys ages 8 to 13 years were assigned randomly to one of four groups: trance plus suggestions (group A), suggestions without trance (group B), trance alone (group C), and wait list (group D). (9) Groups A, B, and C received 1-hour sessions each week for 6 weeks. The mean number of dry nights after the trial were higher for these groups than for group D. Improvements were observed after 6 months for groups A, B, and C but not for group D; however, the study authors reported that only groups A and B showed significant improvement and that the effect may have been due to the suggestions rather than to the hypnosis. The conclusions for this study are limited because of small sample size and incomplete reporting of methods and results. In addition, the four groups differed with respect to number of dry nights at baseline.

In the controlled clinical trial, 50 patients ages 5 to 16 years were assigned alternately to hypnosis or imipramine therapy for 3 months. (10) Patients in the hypnosis group received two 30-minute sessions in week 1, one session in week 2, then sessions every 1 to 2 weeks. The imipramine patients received 25 mg each night, which was increased weekly if there was no response. The number of patients who were dry or improved at 3 months was similar between groups (18/25 for hypnosis compared with 19/25 for imipramine). However, after treatment ended, many more patients relapsed who received imipramine than hypnosis (13/19 versus 1/18).

In one additional RCT, 89 patients ages 7 to 12 years who had PNE were randomized to either hypnosis or alarms. (11) Patients in the hypnosis group received an audiotape for use at bedtime until they were dry. Patients in the alarm group received instruction on using an alarm. A successful outcome was achieved by 19% of the hypnosis group compared with 55% of the alarm group.
### Biofeedback Studies

<table>
<thead>
<tr>
<th>Author/Date</th>
<th>Sample Size/# Who Had NE</th>
<th>Age/Sex</th>
<th>Diagnosis</th>
<th>*Biofeedback Type &amp; Details</th>
<th>Concurrent Treatments</th>
<th>NE Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kibar 2007  (14)</td>
<td>78/22</td>
<td>5 to 14 yr; mean 7.2 yr; 8 male, 70 female</td>
<td>Voiding dysfunction and VUR</td>
<td>Type I; one session every week to start, then once every 3 to 4 weeks up to 6 months; 30 sets per session, sessions ranged from 2 to 14, median 6, mean 4.4±2.2</td>
<td>Laxatives as needed</td>
<td>Positive; 18 (82%) had pronounced improvement (&gt;90% decrease)</td>
</tr>
<tr>
<td>Yagci 2005 (12)</td>
<td>168/79</td>
<td>5 to 14 yr; median 8 yr; 16 male, 152 female</td>
<td>Voiding dysfunction</td>
<td>Type I; one session every week to start, then once every 3 to 4 weeks up to 6 months; sessions ranged from 3 to 14, median 6, mean 4.3±2.1</td>
<td>Laxatives as needed</td>
<td>Positive; improvement at 6 months=64 (81%), at 2 years=66 (84%)</td>
</tr>
<tr>
<td>McKenna 1999 (13)</td>
<td>41/21</td>
<td>5 to 11 yr; mean 7.2 yr; 8 male, 33 female</td>
<td>Abnormal voiding patterns</td>
<td>Type I; sessions ranged from 2 to 11, mean 6; hourly sessions.</td>
<td>NR</td>
<td>Positive; at treatment midpoint, improvements in 57%, of whom 33% were cured; at endpoint, improvements in 90%, of whom 52% were cured</td>
</tr>
<tr>
<td>Hoekx 1998 (16)</td>
<td>27/27</td>
<td>6 to 19 yr, mean 10.4 yr; 23 male, 4 female</td>
<td>Primary NE</td>
<td>Type II; weekly 1-hour sessions for 1 month, then every 2 weeks; mean treatment period, 8.3 weeks</td>
<td>Prophylactic antibiotics at each session</td>
<td>Positive; 24 evaluated; 17 (71%) cured, 6 (25%) improved</td>
</tr>
<tr>
<td>Sugar 1982 (15)</td>
<td>10/4</td>
<td>6 to 16 yr, sex NR</td>
<td>Vesical voluntary sphincter/pelvic floor dyssynergia</td>
<td>Type I with visual display; treatment details NR; for 1- to 3-year duration</td>
<td>2 patients received imipramine</td>
<td>Positive; after biofeedback for 1 to 3 years, NE resolved in 3 of 4 children (1 child continued to have NE once every 3 weeks)</td>
</tr>
</tbody>
</table>

NR=not reported, NE=nocturnal enuresis, VUR=vesicoureteral reflux, UTI=urinary tract infection, *Type I=perianal electrodes, Type II=bladder filling.
hynosis group compared with 55% of the alarm group. Relapse was experienced by two hypnosis and six alarm patients.

As for the acupuncture studies, methodologic variation prevented the combining of data for analysis. Studies that have increased methodologic rigor would strengthen the evidence of hypnosis for PNE, as would replication of results. No adverse events were reported.

**Biofeedback**

To our knowledge, the use of biofeedback in NE has not been investigated through controlled clinical trials. We present the results from six prospective observational studies that specifically reported on the effect of biofeedback on NE of various causes (Table). The types of biofeedback used in these studies fall into two categories. In the first category (type I), voiding muscles are monitored with perianal electrodes. Children who have full bladders practice voiding control exercises and receive feedback of muscle activity on a visual display. The specific exercises generally consist of a series of muscle contractions to allow patients to understand how to relax their pelvic floor musculature and external urethral sphincter to help with coordinated voiding. Four studies used type I biofeedback in children who had voiding dysfunction alone (12)/(13) or who had vesicoureteral reflux (14) or vesical voluntary sphincter/pelvic floor dyssynergia. (15) Results for all studies were positive, resulting in most patients being cured or improving.

The second category of biofeedback (type II) is characterized by repeated cycles of bladder filling and voiding. A catheter is inserted into the bladder and used to fill the bladder with liquid, after which the patient practices controlled voiding, sometimes with a visual display showing muscle activity. One study using type II biofeedback in children who had PNE reported that 71% were cured and 25% improved. (16)

The conclusions for all of the included studies were limited by the observational designs used and some by small sample sizes. All of the identified studies showed benefit and little risk of harm, suggesting the need for methodologically rigorous studies, including RCTs, to determine the relative effect of biofeedback compared with that of various controls. No adverse events were reported.

**Conclusions**

Of the four studies investigating acupuncture/acupressure for PNE, results were either better than or similar to control techniques, including medications. Due to low quality and methodologic limitations, more rigorous studies are recommended. The results of the three hypnosis studies on PNE were mixed; replication of the studies would strengthen the evidence. Of the six observational studies of biofeedback, all reported cure or improvements over baseline. Controlled studies may provide more convincing evidence of the effect of biofeedback on NE. Studies suggest that acupuncture/acupressure, hypnosis, and biofeedback may offer nonpharmacologic treatments that can be used in conjunction with conventional interventions or when conventional interventions have failed or are contraindicated.

No adverse events were reported for any of the interventions, suggesting that they are safe. However, the sample size in many of the studies was small, limiting their ability to detect harmful effects. Although the safety of acupuncture has been well documented, (17) the safety of hypnosis and biofeedback has been less well defined. A recent review of mind-body techniques concluded that negative effects generally are mild and transitory. (18) In situations in which safety information is lacking, use of a safety/efficacy grid such as that proposed by Cohen and Eisenberg (19) may be warranted.

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## Complementary, Holistic, and Integrative Medicine: Nocturnal Enuresis

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