Editorial

Dr. — Thought you would find this article interesting!

Risk/Benefit Ratio in Enuresis Therapy

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Enuresis is a common problem affecting 15% to 20% of five-year-olds. By adolescence, the frequency declines to only 1% to 2%.[1-3] The natural history of the disease is that most patients have a spontaneous resolution of their symptoms with or without therapy. Unfortunately, enuresis can carry a significant emotional stigma that concerns large numbers of affected patients and their parents.[4] It is because of the emotional factors and inconvenience that enuresis needs to be treated. The natural resolution of enuresis leads to difficulties in evaluating new therapies. When evaluating a treatment, the 15% spontaneous resolution per year must be considered. Therefore, any treatment must demonstrate an improvement rate greater than 15% per year before it can be considered effective.[1] Second, it is important to remember that enuresis is pathologically benign, so any treatment must be extremely safe, with minimal side effects, to achieve an acceptable risk/benefit ratio.

There are currently several modes of therapy used in the treatment of enuresis, each based on a particular bias about its cause. The treatments can be broken down into five groups: psycho- and hypnotherapy, motivational therapy, bladder training, pharmacologic manipulation, and alarm systems. These treatments are frequently used in combination.

The first approach is psychological counseling and hypnotherapy. While counseling is frequently helpful for patients with behavioral or emotional problems, this group is decidedly a minority of the patients treated.[5] Hypnosis has been used, but so rarely that reliable figures on its general usefulness are difficult to obtain.[6]

Motivational therapy is a treatment approach that involves two general principles. First, an attempt is made to limit the guilt feelings the patient may feel about the condition by reinforcing the idea that this is a disease and not something the patient brought on him- or herself. Second, while the condition is not the patient's fault, its treatment is the patient's responsibility.[7,8] The patient is given positive reinforcement, such as pasting stars on a calendar, for dry nights but no negative reinforcement for wet ones. In this way the patient's behavior is gradually shaped until enuresis is gradually controlled. When motivational therapy is used alone, the cure rate is approximately 25%, but the relapse rate is low, at only 5%.[7] Because of the low cure rate, it is not recommended for use alone. However, its precepts are useful in combination with all the other therapies available. In fact, in our clinic we do not use any method of treatment unless it is supported by a motivational approach and assures that the patient will be involved in his or her own treatment plan.

There has been much written about the notion that children with enuresis have a small bladder capacity.[9] To correct this problem some authors have suggested using bladder augmentation exercises. In this process the patient systematically drinks fluids and attempts to increase the length of time between voiding. The progress is documented by having the patient urinate into a measuring cup at predetermined intervals, or hold the urine in the bladder as long as possible prior to voiding. Although most studies demonstrate an increase in bladder capacity, the cure rate is only around 30%.[10,11]

The pharmacologic options in the treatment of enuresis consist of anticholinergics such as oxybutynin; an antidepressant, imipramine (Tofranil); and an antidiuretic, DDAVP (desmopressin). Anticholinergics work by blocking the effects of acetylcholine on the detrusor muscle and limiting uninhibited bladder contractions. While this approach is useful in the treatment of neurogenic bladder and diurnal enuresis, it has not been shown to be effective in primary

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nocturnal enuresis.[2,7]

The most commonly prescribed drug for enuresis is the tricyclic antidepressant imipramine. The exact mode of action has yet to be clearly defined. Imipramine is used in doses from 25 to 75 mg given at night about one to two hours before retiring. If the medication is effective, it is maintained for three to six months and then gradually tapered. The success rate is quoted as 50% in the short term. However, due to frequent relapses when the patient is off medication, there is a 25% overall cure rate.[2,7,12] Although well-tolerated in prescribed doses, if an overdosage is taken the side effects are serious. The triad of symptoms include coma, convulsions, and cardiac disturbances, for which the treatment consists of physostigmine and supportive care.[2] The risks of having a medication with potentially fatal side effects in the home for a self-limited benign condition make the risk/benefit ratio poor. Imipramine should be used only in stable home situations, preferably without toddlers, where close monitoring and proper use of the medication is likely.

The newest drug to be used in this country for enuresis is DDAVP. A few small studies have shown that enuretic children lack a diurnal variation in arginine vasopressin (AVP) secretion, compared with normal controls. This lack of increased AVP secretion in the evening may contribute to enuretic children producing more urine at night. Although these studies are small, and it has yet to be proven that this is the sole cause for enuresis, it is clear that when enuretic children are given DDAVP, urine production is decreased.

The usual dose of DDAVP is 20 to 40 μg, delivered by a nasal spray at 10 μg per spray. The dosage produces a rapid response (our patients, on the average, responded within one to two nights), and it does achieve a good long-term response rate of approximately 60% while the patient is on medication.[13,14] However, relapse rates off medication are often reported to be 59% to 100%. Despite legitimate concerns over the possibility that DDAVP may cause electrolytic imbalances due to water retention, its extensive use in Europe has not shown this to occur. We tell our patients not to drink liquids until the next morning after an evening dose of DDAVP. The medication is, in general, well-tolerated, although some patients don't care for the local nasal irritation from the nasal spray, or rare headaches and nausea.

One of the major limitations of using DDAVP is the cost, as mentioned in the accompanying article by Key et al.[15] The cost to our patients is approximately $120 to $240 per month if the patient is using doses of 20 μg to 40 μg per day. Key et al were able to demonstrate a "satisfactory result" in 81% of the patients studied, although the cure rate of 54% is lower than that reported in some of the literature describing higher dosages. However, the study must be viewed with caution, since the number of patients was small, there were no controls, and the outcome criteria of a "conspicuous decrease" are vague. Despite these criticisms, if additional studies were to support a lower dose, the cost savings would justify the added inconvenience of not being able to tolerate the metered dose spray well. Until additional studies are done, we will continue to use 20 μg as our starting dose.

The most effective and one of the least used treatments of enuresis is the bed-wetting alarm. The long-term success (70%) of this method is generally better than that of any other treatment. The system works by placing a small sensor in the patient's underwear that sounds an alarm, even when a small amount of urine is released, awakening the patient. The patient gradually learns to associate the sensation of a full bladder with awakening and eventually with inhibition of micturition. We have found that having the patient, while awake, voluntarily interrupt the flow of urine at the sound of the alarm augments the process. It is generally three to six months from the time treatment is initiated before the patient can remain dry without the alarm.

The difficulty with this system is that its success is highly dependent on cooperation and motivation on the part of the patient as well as the parent. The advantages include a relatively low cost of about $50, high long-term success rates, no need for a systemic medication, and no side effects. For these reasons, it is our treatment of choice.

The use of dietary changes is, in general, not widely discussed by most authors of studies on enuresis. The accompanying study by Egger et al.[16] describes 21 children with enuresis concomitant with migraine and hyperkinesis who responded to a dietary restriction imposed for migraine with an improvement of their enuresis. While the response of migraine and hyperkinesis to diet has been documented in a previous article by the same author, the direct link between a specific food allergy, or allergy in general, and enuresis was poorly demonstrated. In this study, the possibility of a complex interaction between the original disorders and the enuresis make it difficult to establish a direct link between the dietary restrictions and the improvement of the enuresis. Although the therapy is reasonably

benign, given the difficulty of interpreting the data and, as pointed out by the authors, initiating the diet, additional studies need to be done before this can be recommended as a standard therapy.

In conclusion, the condition of primary enuresis is not completely understood. However, whatever the cause, it is self-limited and pathologically benign. Despite the benign nature of the condition, the emotional stress and inconvenience that it produces warrants treatment in those over six years of age. In evaluating treatments of enuresis, not only should the efficacy of the treatment be taken into account but, owing to the lack of severe consequences of the condition itself, the risks of the treatment must be kept extremely low. Not only the risk of the toxicity of the regimen should be considered but also its cost. There are multiple options available to the clinician: counseling, hypnosis, motivational therapy, bladder exercises, imipramine, oxybutynin, DDAVP, and diet therapy. We feel that the regimen with the best risk/benefit ratio is the use of the alarm system, supported by motivational principles. We reserve the use of DDAVP for those times (e.g., overnight camp, sleep-overs) when rapid reliable control is necessary or when the alarm method has failed after a six-month trial. We begin DDAVP at 20 μg to 40 μg a night two to three days before the time when dryness needs to be assured.

Other therapies seem to have a higher attendant risk than is warranted, meet with limited success, or require further evaluation before they can be routinely recommended.

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