How effective is desmopressin for primary nocturnal enuresis?

EVIDENCE-BASED ANSWER

Desmopressin reduces the number of nights of primary noctural enuresis by at least 1 per week, and increases the likelihood of "cure" (defined as 14 consecutive dry nights) while treatment is continued (number needed to treat [NNT]=5–6) (strength of recommendation [SOR]: **A,** based on meta-analysis). Evidence suggests that the benefits of desmopressin are temporary, with a high relapse rate once treatment is discontinued (SOR: **B**). However, long-term therapy with occasional weaning attempts is a safe option (SOR: **B**). Evidence is inadequate to judge the relative efficacy of the nasal vs oral forms of desmopressin (SOR: **C**).

EVIDENCE SUMMARY

Desmopressin is an analogue of the natural pituitary hormone vasopressin acetate. It produces an antidiuretic effect, resulting in increased reabsorption of water from the kidney, a reduced volume of more concentrated urine entering the bladder, and a reduced 24-hour urine production.[1,2] Desmopressin is available in a nasal spray (10 µg/spray) and an oral tablet (0.2 mg), and is most often prescribed as 1 to 2 sprays per nostril or 1 to 3 tablets at bedtime, regardless of age or weight.[1]

A Cochrane review[1] of 16 randomized controlled trials found nasal desmopressin to be better than placebo in reducing the number of wet nights per week (mean 1.34 fewer wet nights/week; 95% confidence interval, 1.11–1.57). Desmopressin at doses of 20 µg, 40 µg, and 60 µg similarly increased the likelihood of a cure (14 consecutive dry nights during treatment) in 3 trials reporting this outcome (relative risk for failure to achieve 14 dry nights with 20 µg=0.84; NNT for cure=5.6).[3] No difference was found in cure rates after treatment was stopped. Data were insufficient to judge the effectiveness of the oral versus nasal route of desmopressin.[1]

One randomized controlled trial found a linear dose response for oral desmopressin in reducing wet nights. After 2 weeks of treatment, the number of wet nights was decreased by 27%, 30%, and 40% at doses of 0.2 mg, 0.4 mg, and 0.6 mg, respectively, compared with 10% with placebo.[1]

Snajderova and colleagues studied desmopressin as a long-term treatment for 55 children with primary nocturnal enuresis. Intranasal desmopressin was titrated upward until bedwetting stopped (7–21 µg; 89.1% responders); children in whom no response occurred to a maximum of 28 µg were excluded. Every 3 months, a weaning attempt was made; if relapse occurred, the previous successful dose was reinstated. At the end of each of the 3 years, the number of responders remained higher (72.7%, 70.9%, 61.6%) than the spontaneous cure rate of 15%.[4]

The Swedish Enuresis Trial (SWEET) demonstrated a similar outcome in an open-label study of 399 children.[5]

The main side effects of desmopressin are nasal discomfort, nose bleeds, headache, abdominal pain, rash, and (rare but serious) water intoxication. Restrict fluid to 240 mL (8 oz) on nights desmopressin is given.[1]

RECOMMENDATIONS FROM OTHERS

A University of California at San Diego Medical Group Guideline recommends using desmopressin for primary nocturnal enuresis in children aged >5 years when it occurs frequently and causes distress, as well as under specific circumstances, such as when a child shares a room or goes to camp, or a sleepover.

Therapy begins at 10 µg (1 nasal puff) each night, increasing weekly to a maximum of 40 µg. Younger children should be reassured, encouraged to limit fluids and void before

bedtime, partake in the responsibility to change bedding, and be praised for dry nights.[6]

The American Academy of Pediatrics also emphasizes support and encouragement of the child, and reassurance that the problem will get better in time. For children aged ≥7 years, alarm systems or bladder-stretching exercises might help.[7]

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CLINICAL COMMENTARY

Primary nocturnal enuresis can be challenging for the primary care physician, frustrating for the patient's parents, and embarrassing for the child. The physician's role is to help the child and parents realize that almost all children eventually maintain nocturnal continence whether or not pharmacotherapy is used.

Nonpharmacologic interventions, such as behavioral modification (eg, use of a nocturnal conditioning alarm with a moisture sensor) may be more acceptable to families, at least as a first attempt at therapy. In my experience, however, many children sleep through these alarms.

The decision to use medication should be made by a well-informed and motivated child and their parents. They should understand the limitations and expectations of pharmacotherapy. The authors of this clinical inquiry have provided the physician with an excellent summary of the evidence for the efficacy of desmopressin.

Children with enuresis associated with sleep arousal disorder should theoretically respond to older forms of pharmacotherapy, such as imipramine. However, due to potential toxicity, many clinicians are reluctant to use tricyclic antidepressants in their patients. The efficacy and low toxicity of desmopressin makes it an attractive choice for pharmacotherapy in enuretic children.

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