Desmopressin in nocturnal enuresis

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Summary The response of desamino-D-arginine vasopressin (DDAVP) was investigated in 32 enuretic children in a double-blind clinical study. The 15 children treated with DDAVP showed a significant reduction in the incidence of bed wetting—from 18.7 ± 6.5 to 6.5 ± 9.2 wet nights per 30 days. In 6 children bed wetting stopped entirely, in 6 there was a satisfactory response, and in 3 the response was marginal or there was none. When DDAVP was stopped most children reverted to their earlier bedwetting habits (15.7 ± 8.9 nights a month). Response to DDAVP was significantly better in children aged more than 10 years (mean age for the entire group). The administration of DDAVP was not associated with any appreciable change in morning urine osmolalities. No adverse effects were noted. It is concluded that DDAVP is effective in nocturnal enuresis, particularly in older children. It is suggested that the cessation of bed wetting may, in part, reflect functional properties of DDAVP rather than antidiuresis.

Enuresis nocturna (EN) is a common, age-related complaint in childhood for which there is as yet no clear treatment. Antidepressant drugs and electrical conditioning devices have been used with a modicum of success, despite side effects.

Recently DDAVP was administered with considerable success to children with EN, and its beneficial effects were attributed to antidiuretic properties. The aim of this study was to evaluate the response of children with EN during and after the administration of DDAVP, and to assess the effect of this drug on morning urine concentration.

Material and methods

Thirty-two (15 boys and 17 girls) children with EN, whose ages ranged from 7 to 15 years, took part in a double-blind study. Any child known to have an organic disease of the urinary tract was excluded; however, 3 patients had a history of urinary tract infections and of healed vesicoureteric reflux.

A complete case history was taken and physical examination, urine analysis, and urine culture were performed at the start of the study, and repeated thereafter.

The children were studied during three 30-day periods, before, during, and after the treatment. The treatment consisted of DDAVP (desamino-D-arginine vasopressin, Ferring AB, Sweden), 10 μg, or placebo, administered intranasally, before bedtime, every day, for 30 days. The study was randomised and the code was known to neither participants nor investigators. Bed-wetting episodes were recorded every morning for 90 days. A night in which bedwetting had occurred at least once was called a ‘wet’ night.

Since the first morning urine in children with persistent EN is probably the product of the last hours of the night, its osmolality may be higher than the first morning urine produced throughout the entire night by the children who do not wet their beds. For the purpose of assessing concentration capacity we therefore measured the osmolality of the second morning urine sample before any fluid intake.

Informed consent was obtained in each case from one of the parents.

Data were analysed by the Student’s t test and are presented as mean ± SD.

Results

Fifteen (7 boys and 8 girls) children received DDAVP, and 17 (8 boys and 9 girls) children received placebo (Table 1). In the DDAVP group 12 children had been treated previously with chlorimipramine hydrochloride, 2 of whom had responded; in the placebo group 3 of the 11 patients who had been treated in the past with chlorimipramine hydrochloride had responded well to the drug.

A familial history of EN was elicited in 4 children
Table 1  Clinical data and second morning urine osmolalities in the DDAVP and placebo-treated children

<table>
<thead>
<tr>
<th></th>
<th>DDAVP (n=15)</th>
<th>Placebo (n=17)</th>
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</thead>
<tbody>
<tr>
<td>Boys</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Girls</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Age (years)</td>
<td>10.5 ± 2.2</td>
<td>10.0 ± 2.5</td>
</tr>
<tr>
<td>Patients with a family history of enuresis</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Urine osmolality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before treatment</td>
<td>1032 ± 147</td>
<td>920 ± 135</td>
</tr>
<tr>
<td>During treatment</td>
<td>1006 ± 210</td>
<td>918 ± 164</td>
</tr>
<tr>
<td>After treatment</td>
<td>919 ± 181</td>
<td>911 ± 165</td>
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</table>

of the DDAVP group, and in 6 of the control group. Mean age was 10.5 ± 2.2 (median 10.0) and 10.0 ± 2.5 (median 9.5) years in the DDAVP and control groups respectively.

Second morning urine osmolalities before, during, and after treatment were 1032 ± 147, 1006 ± 210, and 919 ± 181 mmol/l in the DDAVP group and 920 ± 135, 918 ± 164, and 911 ± 165 mmol/l in the placebo group. There were no significant differences in urine osmolality between the two groups in any of the study periods. Morning urine osmolality did not change after administration of DDAVP.

Placebo administration was not associated with any significant change in the number of wet nights: 21.3 ± 8.5, 18.8 ± 8.3, and 16.9 ± 9.4 during the three periods—before, during, and after the administration of the placebo.

In the group of children on DDAVP the number of wet nights decreased significantly from 18.7 ± 6.5 to 6.5 ± 9.2 (P<0.01). Response was prompt and could be seen as early as 1–3 days after drug administration. When the treatment was stopped the number of wet nights rose to 15.7 ± 8.9, a value not significantly different from that observed before DDAVP (Figure).

Results were assessed as excellent (no wetting), satisfactory (fewer than 7 wet nights per 30-day period), or unsatisfactory. The administration of DDAVP resulted in excellent results in 6 children, and in satisfactory results in 6 others. In 3 patients the results were unsatisfactory: the number of wet nights was changed from 27 to 12 in one child, from 28 to 25 in another, and from 24 to 30 in the third. In the children of the placebo group only one child had an excellent response and one had a satisfactory response (Table 2).

If the children taking DDAVP are placed in two groups according to their ages, the older children (mean age >10 years) had better results (6 children with excellent results and one in whom the response was satisfactory); in the younger group (mean age <10 years) results were less satisfactory (5 had satisfactory responses and 3 failed to respond to DDAVP) (Table 3). The difference between the responses in the two age groups was significant (P<0.01).

None of the children treated with DDAVP had any side effects.

Discussion

This double-blind study, similar to several others5–7 shows again that DDAVP is a potent drug in the prevention of EN. There were minimal side effects or none at all after the administration of DDAVP in this series, as in others.5–7

The response to DDAVP was particularly gratifying in children older than age 10 years. The results do not seem to favour the hypothesis of dose-related response curve. Response to treatment...
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Commentary

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The medical literature is littered with papers reporting the use of different drugs in the treatment of enuresis. There are few drugs that have not been tried! Unfortunately most of the drug trials have been conducted poorly. The authors of this paper have completed a carefully controlled trial. They found that DDAVP enabled a proportion of children to become dry while they were taking the drug. Previously the only clear evidence of successful drug therapy had come from the tricyclic antidepressant drugs—such as imipramine and amitriptyline. DDAVP can now be added to that list. However, as with the tricyclic drugs so with DDAVP, the beneficial effect appears to be temporary and once the drug is stopped the children start wetting again. No drug has yet been found to be effective in producing long-term cure for nocturnal enuresis. This limits the use of such drugs and many will feel that the drug should be used only for short periods—such as during an important visit or holiday.

It is interesting that the authors are unsure how the DDAVP is acting and in particular do not think it is related to its antidiuretic effect. Similarly with the tricyclic drugs it is not known why such drugs should be effective. It does not seem specifically to be related to any of their known properties—that is, why antidepressants don’t work, other anticholinergics

References


