RESEARCH ARTICLE

ORAL VERSUS NASAL VASOPRESSIN IN THE TREATMENT OF NOCTURNAL ENURESIS IN 5- TO 12-YEAR-OLD CHILDREN

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Abstract

Objective

Nocturnal enuresis is a common childhood problem and has various treatments. This study was carried out to compare oral and nasal vasopressin in the treatment of nocturnal enuresis in 5- to 12-year-old children who were referred to the Shahid Beheshti Clinic in 2008.

Materials & Methods

This study included 100 children (62 males and 38 females) with nocturnal enuresis. One group (50 patients) received 20 mcg nasal vasopressin which increased up to 40 mcg, depending on the patients' response. The other group (50 patients) received 0.2 mg oral vasopressin which increased up to 0.4 mg. The patients were followed up for one month after response to the last dose of drug. Data were recorded in prepared forms and analyzed using Chi-Square and Fisher Test.

Results

The success rate with oral and nasal method was 80% and 92%, respectively (P=0.08). Only 2% of the children had complications during the treatment; one child treated orally developed gastroenteritis and another child treated with the nasal method developed convulsions (P=1). Sixteen percent of the children treated with the oral method and 28% of the children treated with the nasal method had recurrence (P=0.148).

Conclusion

Oral and nasal forms of vasopressin have equal therapeutic effects. However, oral form of the treatment has fewer serious side effects and is easier to use. Therefore, the use of oral medicine is recommended.

Keywords: Nasal vasopressin, Nocturnal enuresis, Oral vasopressin

Introduction

Nocturnal enuresis is involuntary voiding during the night's sleep after the age of five when children usually have developed sphincter control. Its prevalence is 7% for five- year- old male children and 3% for females and is reduced to 3% and 2% at the age of 10, respectively. The most common form of the condition is the primary one in which the patient has no control over voiding at all while in secondary cases, enuresis re-appears after a period of normal control.

The possible causes of enuresis are delay in the development of nervous pathways which control voiding, reduction of antidiuretic hormone (ADH) level during the night, genetic background, and finally some sleep disorders (1). It may lead to serious consequences, including lack of child's self confidence through self image

disorder, chronic anxiety, parental anxiety, physical punishment, and even child abuse (2).

There are various pharmaceutical and non-pharmaceutical treatments. The basis of non-pharmaceutical treatments is on limiting the use of liquids at night or hours before sleeping, behavior therapy alarms with sensors that go off when they wet themselves, and finally motivation therapy including child encouragement and rewarding for dry nights (3). One of the oldest drugs used is imipramin, a tricyclic antidepressant which considerably controls symptoms during its use. However, recurrence is high after treatment is stopped (2). Vasopressin, the synthetic analogue of ADH, has been recently used effectively. There are many published trials of desmopressin for treating enuresis which conclude that desmopressin is superior to placebo in reducing the number of wet nights. To date, few adverse effects have been reported with desmopressin. Because minor side effects are common with the tricyclic antidepressants and because they are hazardous medications (due to the risk of accidental overdose), desmopressin may be a safer choice. This medicine was only available as nasal spray in the past but is now also available as oral tablets (4). Its nasal spray has a considerable effect on nocturnal enuresis. It showed to increase the average of dry nights from 0.6 to 4.3 per week in a study in Finland (5) while its oral form reduced the number of wet nights for at least 1 night per week in a study in England (6). In other studies, the efficiency of oral tablets and nasal sprays have been reported to be almost equal (7,8). The drug is effective in patients who do not have a vasopressin diurnal rhythm and their maximum anti-diuretic hormone concentration decreases at night. It reaches maximum concentration 0.5-1 hour after administration and has a half life of 4-6 hours. It increases the renal reabsorption of water and reduces urine output during the night to less than the functional capacity of the bladder. Major side effects of the medicine include hyponatremia, headache, convulsions, and coma (1).

Since the oral medicine has been recently introduced to the Iranian market and because the Desmopressine Argenine Vasopressin (DAVP) tablet has a good absorption, good biologic effects and few side effects similar to the intranasal spray, treatment with tablets is a good alternative to the intranasal route for primary nocturnal enuresis.

Materials & Methods

In a 12-month period in 2008, 100 children between 5 and 12 years of age who were visited at the pediatrics clinics of Shahid Beheshti University for nocturnal enuresis (involuntary voiding at night at least once a week) were included in this study. Those with diabetes insipidus, diabetes mellitus, urinary tract infection, renal anomalies, psychologic problems, and simultaneous use of other nocturnal enuresis medicines were excluded from the study after appropriate evaluation by CBC, FBS, U/A, U/C tests, and renal sonography. After the approval of the ethics committee, informed consent forms were signed by either the patients or their parents.

The sample population was 100 individuals based on the previous studies (7,9,10). Each child was given a number and fifty numbers between 1 and 100 were randomly selected for oral treatment. The other 50 patients entered the nasal treatment group. Minimum oral or spray dose of 0.2 and 20 μg, respectively, started for the patients. The dose was increased by 50% after two weeks, and by 100% of the initial dose after another two weeks, if no acceptable response was observed. If no response was observed after these changes, they were identified as resistant, and the treatment stopped. Upon detecting improvement in any stage, the treatment continued for two weeks, tapered in the next two weeks and finally stopped. Recurrence was defined as re-appearance of the symptoms during or after tapering. Interview with mothers or children was done by a trained nurse. Data including demographic characteristics of the patients, and the degree of recovery as complete (absence of nocturnal enuresis two weeks after treatment), or partial recovery (reduction of nocturnal enuresis by more than 50%) were recorded in special forms and the results were compared in the two groups using chi-square and fisher exact tests.

Results

Out of 100 children with nocturnal enuresis, 62 were male (31 in each group) and 38 were female (19 in each group) (P = 1). Seventy four percent of the involved

children were in the age range of 5 to 8 and 26% were in the age range of 9 to 12 years (Table 1). In 36% of the children, one parent had a history of nocturnal enuresis. Eighty percent of the children recovered after oral and 92% recovered after nasal treatment. Chi-square showed no statistical difference between the two modes of treatment ($p<0.08$) (Table2).

Only 2% of children showed side effects, one in the oral and the other in the nasal group. The child in the nasal group developed convulsions (after hyponatremia) and the child in the oral group developed gastroenteritis. There was no significant difference in side effects between the two groups (Table2).

Nocturnal enuresis recurred in 22% of the children after treatment. Sixteen percent of the children with the oral and 28% with the nasal treatment experienced recurrence. Fisher test showed no significant difference between these groups ($p<0.148$, Table2).

Discussion

The distribution of age and sex in our patients was similar to other studies (8,13, 14,15,16,17,18,19). One parent had a history of childhood nocturnal enuresis in 36% of the cases while most of the others studies (1,9,14,17,18,19,20) have reported rates even up to 85% (5,2). This may be due to the effect of ethnic and racial differences in different studies.

In this study, 22% of the patients experienced recurrence. Recurrence rate was 16% in oral group and 28% in nasal group but the difference was not significant ($p<0.148$). The recurrence rate has been reported up to 80-100% in two studies (21,22). It is believed that gradual discontinuation of the drugs may reduce the possibility of recurrence (23).

Forty (80%) patients in the oral group and 46 (92%) in the nasal group showed improvement. The difference between the groups was not significant ($p<0.08$) as shown in other studies (1,12,9,13,15,16,17,18).

In a double blind study on 141 nocturnal enuresis patients between 5 and 17 years of age, 79% recovered after two weeks of treatment with vasopressin tablets (0.2mg) (9).

In a study, 15 children with nocturnal enuresis were treated with vasopressin tablets (0.2 mg) and 15 children were treated with 1 puff of vasopressin spray. Recovery (the number of dry nights per week) was significant (between 41% and 52%, $p<0.02$) in both groups and the difference between the groups was not significant (7).

In another study, 66 patients with nocturnal enuresis were treated with oral and nasal desmopressin and their recovery rate was then compared. No significant difference was found. Ninety six percent of the patients took and tolerated desmopressin tablets well. It was concluded that the desmopressin tablet was an effective alternative in nocturnal enuresis in this study (10).

Only 2% of our children had side effects; one in the oral group developed gastroenteritis and one in the nasal group developed convulsion after hyponatremia.

In a study on 34 children between 7 and 18 years of age in Singapore with 0.4 mg oral vasopressin for two weeks, no adverse effects were observed (11).

In a literature review including all the empirical studies from 1972 to 2005, out of 151 patients with hyponatremia, 145 were treated with nasal vasopressin and only 6 with oral vasopressin (8).

In Conclusion, Oral form of vasopressin is easier to use and is relatively safe. Therefore, it is recommended for the treatment of nocturnal enuresis in children.

Conflict of interest

This study was not supported by any pharmaceutical companies and no economic benefits were considered for the authors.

Table 1. Prevalence distribution of nocturnal enuresis recovery versus treatment method, age and sex

Treatment Method / Parameters	Oral	Nasal	PV
Male	25 (80.6)	28 (90.3)	0.473
Female	15 (78.9)	18 (94.7)	0.34
5-8 year	28 (82.4)	37 (92.5)	0.286
9-12 year	12 (75)	9 (90)	0.617

Table 2. Prevalence distribution of complete and partial recovery of children with natural enuresis versus treatment method, Age & Sex

Treatment Method / parameters	Nasal	Oral	PV
Recovery	46 (93)	40 (80)	0.08
Side effect	1 (2)	1 (20)	1
Recurrency	14 (28)	8 (16)	0.148

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