RESEARCH STUDY

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Efficacy & safety of Desmopressin in the treatment of pediatric nocturnal enuresis

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Back ground: primary nocturnal enuresis (PNE) is a socially distressing condition that can be troubling for children & their families. It affects 15-26% of five years olds. Several approaches are used to treat PNE including behavioral modification, alarms & drug therapy.

Aim of the study: to determine the efficacy and safety of nasal desmopressin treatment in children with PNE

Patients : fifty-four children with primary nocturnal enuresis with a mean age of (8.2) years (range 6-15), underwent a 2 week observation period followed by entrance into a randomized controlled study, comparing desmopressin & placebo, lasting 4 weeks. The efficacy of the drug was measured in reduction of the number of wet nights per week. The enuretic status of the children was documented for 4 weeks after the treatment was stopped.

Results: a significant reduction was found in the mean wet nights per week in the desmopressin group (p=0.001) as compared to placebo group (p = 0.83), from 4.3 wet nights during pretreatment to 0.6 & from 4.6 to 4.4 respectively, however this effect was not sustained after treatment was finished as only five children (18.5%) in the drug-treated group remained dry compared with one child (3.7%) in the placebo group. Side effects associated with the nasal adminstration of desmopressin were mild & infrequent.

Conclusion: desmopressin has a clinically significant & safe effect on children with primary nocturnal enuresis

Introduction

Nocturnal enuresis (NE), or bedwetting, is a common problem of childhood. It is not a serious medical disorder, but it can be very difficult to live with. Wetting in bed may interfere with a child's socialization & it can lead to significant stress within the family [(1)].

NE is defined as involuntary loss of urine at night during sleep in a child five years or older [(2)]. There are two types of bedwetting; primary and secondary. Primary nocturnal enuresis (PNE) is defined as bedwetting in a child who has never been dry for six consecutive months. Secondary nocturnal enuresis (SNE) is defined as bedwetting in a child who was dry for six consecutive months and then started wetting again [(3)]. A small percentage of bed wetters have wetting episodes when they are a wake. Diurnal enuresis or incontinence are the terms used to describe this situation.

The overall prevalence of enuresis at 5 years of age is 15-26 percent [(4)]. With each year of maturity, the percentage of bed-wetters declines by 15 percent. Boys are three times more likely to wet the bed than girls [(5)].

The causes of PNE are unclear. Genetic, familial & psychological factors, as well as bladder problems have been suggested [(6)]. Other factors which may contribute to bed-wetting include: constipation, sleep apnoea & upper airway obstructive symptoms [(7)]. Less than 3% of children with NE have a medical disorder that underlies their wetting. Bed-wetting has been reported with sickle cell disease [(8)], urinary tract infections [(9)], diabetes [(10)] & neurological problem [(11)]. Medical disorders are more likely to present with SNE.

There are several approaches to the treatment of NE including behavioral modification, alarms & drug therapy [(12)]. To better combat the problem, a combination of treatment modalities may be used if necessary. Unless an underlying medical cause is identified, primary & secondary bed-wetting are treated the same way [(3)]. Treatment with desmopressin has been proven in various studies. Desmopressin is an analogue of the human pituitary hormone arginine vasopressin. It exerts its action by reabsorbing water, reducing the amount of urine excreted into the bladder resulting in a decrease of bed-wetting episodes [(13)].

The present study was conducted to determine the efficacy & safety of nasal desmopresssin treatment in children with PNE.

Methods:

Fifty-four children with PNE who were referred to urology clinic of Al-Yarmouk Teaching Hospital, were enrolled in a randomized controlled study, comparing desmopressin & placebo, from January 2011 to January 2013.

After careful history taking & thorough physical examination children were studied by urinalysis, urine culture & abdominal ultrasound.

Patients with any history of day-time wetting, chronic UTI, chronic constipation, spine abnormalities, or neurological disease were excluded from the study.

The fifty-four patients who met the entry criteria were randomly distributed into two equal groups; A & B. participants in group A were treated with 20 micrograms intranasal desmopressin & group B with placebo each night for four weeks. All children were asked to keep a voiding diary for two weeks, noting the number of enuretic episodes prior to initiating any treatment. The efficacy of the drug was measured in reduction of the number of wet nights per week. Those using desmopressin (or their parents) were warned to avoid overdrinking before bedtime in order to avoid the possible risk of water intoxication. Patients were then followed up for at least four weeks post treatment to determine the relapse rate.

Results:

The study sample consisted of 54 children (40 males [74%] & 14 females [26%]) ranging in age from 6 to 15 years (mean 8.2 ± 2.73 years) The demographic findings of the patients are shown in table 1.

There was a significant reduction in the mean wet nights per week in the desmopressin group (p=0.001) as compared to placebo group (p = 0.83). This reduction was not influenced by gender or age. Table 2 summarizes the mean wet nights in the two groups before & after treatment.

Adverse effects were infrequent in the drug-treated group as opposed to placebo group, these included headache (the most frequent), nausea, nasal irritation & nose bleeds. The majority of these side effects were mild. (Table 3)

At the end of the study only 5 children (18.5%) in group A remained dry compared with 1 child (3.7%) in group B.

Table 1: the demographic findings of patients

Age (mean)	8.2 ± 2.73 years
Gender	74% males, 26% females
Duration of treatment (weeks)	4

Table 2: the mean wet nights before & after treatment in the two groups

Group	before treatment	after treatment	P value
Desmopressin	4.3 ± 1.13	0.6 ± 0.69	< 0.05
Placebo	4.6 ± 1.21	4.4 ± 1.18	> 0.05

Table 3: summary of adverse effects

Adverse group effects	Desmopressin group No. (%)	placebo No. (%)
Headache	6 (22.2)	2 (7.4)
Nausea	3 (11.1)	1 (3.7)
Nasal irritation	2 (7.4)	0
Nose bleed	2 (7.4)	0
Total	13 (48.1)	3 (11.1)

Discussion:

NE is one of the most prevalent disorders in children & the most distressing & stressful condition for children & their families.

In this study, desmopressin had significantly & rapidly reduced the number of nocturnal voids per week, compared to placebo. This finding is comparable with the results of previous studies (Schulman 2001 [14], Lister-Sharp 1997 [15], Uygur 1997 [16], Moffatt 1993 [17]).

Although desmopressin was beneficial while the drug was taken, many children in our study started wetting again after treatment stopped indicating that desmopressin works only on the nights when it is used, so it does not cure the problem in the long term. This is due to the persistent effect of several contributory factors to bedwetting including; genetic, familial, psychological factors in addition to bladder problems. This is consistent with the results reported in other studies (Fai-Ngo NG & Wong 2005 [18], Glazener & Evans 2002 [19]).

No serious side effects were observed in the desmopressin treated group & all were mild & infrequent. This is supported by the data reported in previous studies made by (Hjalmas 1993 [20], Miller 1989 [21], Klauber 1989 [22])

Conclusion:

Nasal desmopressin has a clinically significant & well tolerated effect on patients with PNE, but this effect is not sustained after treatment withdrawn.

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