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EFFICACY OF OXYBUTYNIN, PSEUDOEPHEDRINE AND INDOMETHACIN IN THE TREATMENT OF PRIMARY NOCTURNAL ENURESIS*

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SUMMARY: Varan B, Saatçi Ü, Özen S, Bakkaloğlu A, Beşbaş N. (Nephrology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Efficacy of oxybutynin, pseudoephedrine and indomethacin in the treatment of primary nocturnal enuresis. Turk J Pediatr 1996; 38: 155-159.

The efficacy of oxybutynin, pseudoephedrine and indomethacin treatment was investigated in 29 patients with primary nocturnal enuresis. Patients were randomly assigned to either oxybutynin (1st group, n = 9), pseudoephedrine (2nd group, n = 11) or indomethacin (3rd group, n = 9) treatments.

Oxybutynin and indomethacin did not cause a statistically significant difference in the number of dry nights ($p > 0.05$), but patients treated with pseudoephedrine had a significant increase in the number of dry nights ($p < 0.05$). Five patients in the oxybutynin and one patient in the indomethacin group experienced side effects. None of the patients in the pseudoephedrine group had any complaints with the drug. We therefore conclude that pseudoephedrine can be an alternative in the treatment of primary nocturnal enuresis.
Key words: enuresis, oxybutynin, pseudoephedrine, indomethacin.

Enuresis is a troublesome condition in childhood, affecting as many as 15-20 percent, five percent and one percent of five-year-olds, 10-year-olds and 15-year-olds, respectively[1]. The benign nature and high spontaneous cure rate of 15 percent annually necessitates a careful assessment of the risk-benefit ratio of therapy[2]. Tricyclic antidepressants and desmopressin are the most widely used and investigated drugs. The dangerous side effects of imipramine and the high cost and relapse rate of desmopressin led us to investigate alternative drugs. There are limited reports and controversial results regarding the drugs acting on the function of the urinary bladder. Thus, in this study the efficacies of oxybutynin, pseudoephedrine and indomethacin in children with primary nocturnal enuresis were evaluated.

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Material and Methods

Children admitted to Hacettepe University İhsan Doğramacı Children's Hospital, Department of Pediatric Nephrology with the complaint of bedwetting were the subject of this study. The inclusion criteria were: 1. age equal to or greater than six years; 2. absence of a six-month or longer period of dry nights; 3. absence of neurologic or renal disease, or recurrent urinary tract infections; 4. presence of at least three wet nights in a week in the last two-week period.

The age and sex of the patients, the socioeconomic condition of the family and the family history for enuresis were recorded. Urinalysis, urine culture and simultaneous urine and blood osmolality after 12 hours of water deprivation of the patients were obtained. All patients were asked to keep a calendar for dry and wet nights for two weeks. At the end of the two weeks they were randomly put on either oxybutynin (0.5 mg/kg), pseudoephedrine (2 mg/kg) or indomethacin (2 mg/kg) therapy in two or three doses for four weeks. There were nine children in the oxybutynin group (1st group), 11 in the pseudoephedrine group (2nd group) and nine in the indomethacin group (3rd group). Their ages ranged from six to 15 years. Their complaints about the medications and blood pressures were recorded during the treatment period. Treatment results were evaluated by testing the significance of the differences between the average number of dry nights in the two weeks before and after treatment, by use of the Wilcoxon Matched-Pairs Signed-Ranks test. Differences between parameters were assessed by Kruskal-Wallis analysis of variance.

Results

There were no differences between the three groups in regard to the average age of the patients, the specific gravity and osmolality of the urine, and the average number of dry nights before treatment ($p > 0.05$) (Table I).

Table I Initial Parameters of The Patients

	1. Group (n = 9)	2. Group (n = 11)	3. Group (n = 9)
Average age (years)	10.8 ± 2.8	8.6 ± 2.2	9.0 ± 2.6
Specific gravity of the urine	1021.6 ± 5.6	1023.2 ± 5.6	1019.4 ± 5.8
Osmolality of the urine (mosmol/L)	781.5 ± 171.4	808.5 ± 192.3	881.6 ± 192.0
Number of dry nights in the two weeks before treatment	2.4 ± 2.2	2.5 ± 2.2	2.0 ± 2.3

The presence of a family history of enuresis and the socioeconomic condition of the families in the three groups were also similar.

Treatment Results: The significance of the difference between the average number of dry nights before and after treatment was tested. The number of dry nights in the two-week period were found to increase from 2.4 ± 2.2 to 4.7 ± 3.9 with oxybutynin, and from 2.0 ± 2.3 to 4.3 ± 4.0 with indomethacin; however, the differences were not statistically significant ($p > 0.05$). In the pseudoephedrine group the number of dry nights increased from 2.5 ± 2.2 to 6.2 ± 3.8 and the difference was statistically significant ($p < 0.05$) (Fig. 1).

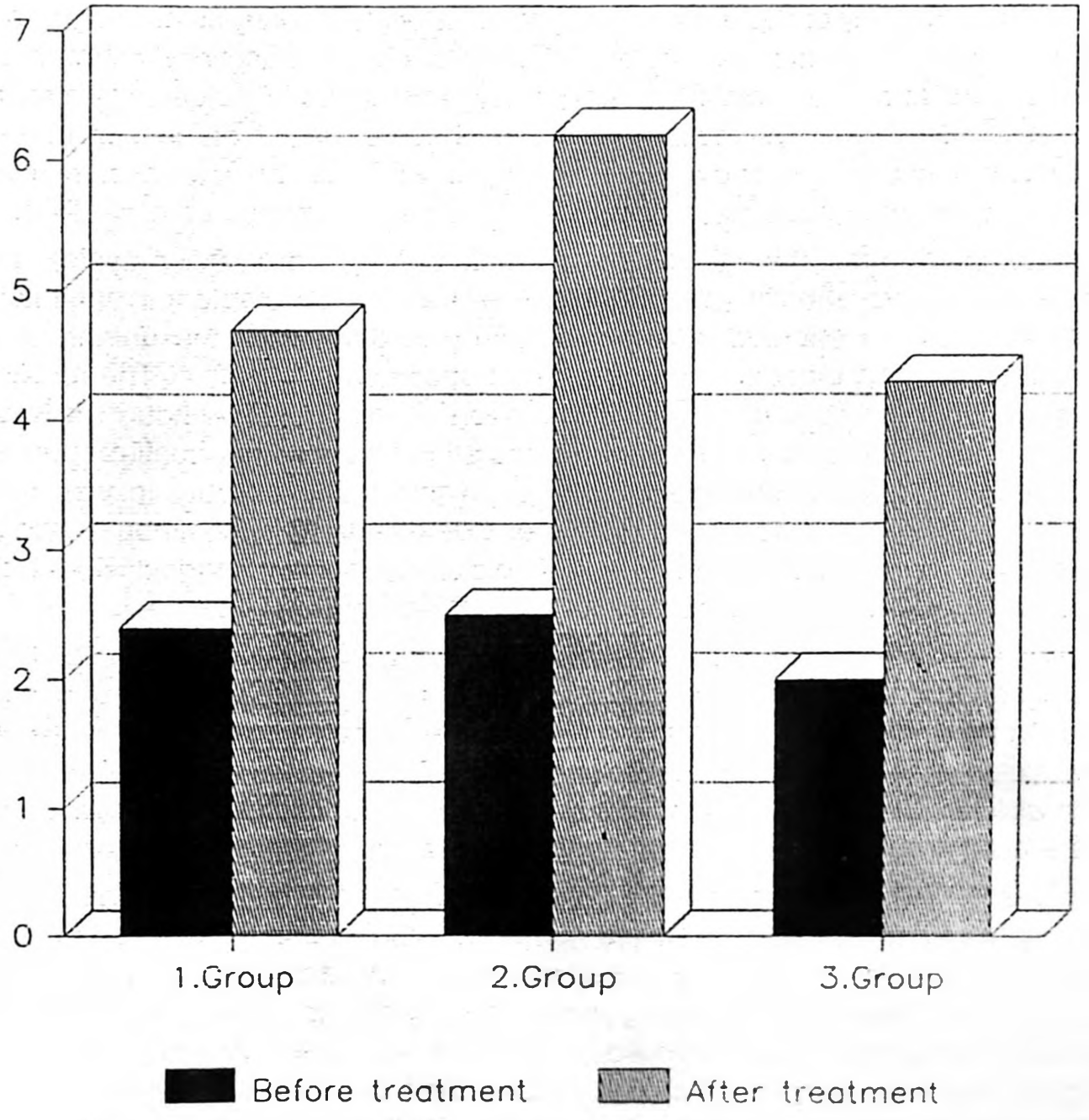

Fig. 1: Number of dry nights before and after treatment.

Side Effects: Three patients in the oxybutynin group had epistaxis that could not be explained by other causes. Epistaxis recurred in two of these patients and ceased only after the dose of oxybutynin was reduced. Another patient on oxybutynin therapy complained of flushing, vertigo and dryness of the hands and also required reduction of the dose. One patient had urinary hesitancy and incomplete evacuation of the bladder.

Indomethacin caused gastrointestinal irritation in one patient. There were no side effects in the pseudoephedrine group.

Discussion

The pathophysiology of nocturnal enuresis remains unclear. Many studies highlight the importance of urodynamic factors (bladder-urethra dysfunction)[3-6]. Enuretic children are known to void more frequently, and to have functionally small bladders[5]. Detrussor dysfunction has been observed in 82 percent of these patients with cystometric and micturition studies, whereas sphincter dysfunction has been detected in 20 percent with sphincter electromyographic studies[7].

We attempted to test the efficacies of an anticholinergic drug (oxybutynin), an alpha-adrenergic agonist (pseudoephedrine) and a prostaglandin inhibitor (indomethacin) in enuretic children. Oxybutynin decreases the uninhibited contractions of the bladder and has a direct spasmolytic effect[8-10]. The results of oxybutynin in enuretic children have been controversial. Although it was reported to be effective in 31 out of 39 enuretics, this was not confirmed in a double-blind, placebo-controlled trial[11, 12]. In this study oxybutynin was not effective in primary enuretics. Furthermore, side effects were common. Among these side effects this is the first report of epistaxis, which we suggest is related to drying of the nasal mucosa due to the anticholinergic effect.

Prostaglandin inhibitors decrease the tonus of the detrussor muscle[13]. Prostaglandins are known to inhibit secretion of antidiuretic hormone[14]. Prostaglandin inhibitors are used in partial diabetes insipidus and nephrogenic diabetes insipidus because of their potentiating effect on antidiuretic hormone[15]. On the limited number of studies with diclofenac sodium and indomethacin in patients with nocturnal enuresis, both were found to be effective[16-18]. In this study, however, indomethacin was not effective.

Alpha-adrenergic agonists relax the detrussor muscle while contracting the trigon and sphincter muscles[19]. The limited number of studies with these agents have disclosed different results[20, 21]. We used pseudoephedrine as an alpha-adrenergic agonist and obtained encouraging results in our enuretic patients with no side effects. These children experienced a significant increase in the number of dry nights. We thus suggest that pseudoephedrine can be used safely as an alternative drug in nocturnal enuretic patients. Further cystometric studies may reveal the exact mechanism of its effect.

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