

## PRIMARY NOCTURNAL ENURESIS: A COMBINED PROPIVERINE AND DESMOPRESSIN TREATMENT REGIMEN IMPROVES OUTCOMES

### Hypothesis / aims of study

In children and adolescents with primary nocturnal enuresis only in 40 – 80 % treatment success is achieved with monotherapeutic strategies (1). Therefore, as second line therapy combined treatment strategies must be taken into consideration comprising desmopressin, enuresis alarm, antimuscarinics, behavioural interventions, psychotherapy, etc. According to results of other investigators (2,3) especially the combination of desmopressin and antimuscarinics is extremely successful. Therefore, the aim of this study was to evaluate the efficacy and tolerability of a combined treatment regimen of the antimuscarinic propiverine (Mictonetten®) and desmopressin in patients unresponsive to previous monotherapies.

### Study design, materials and methods

122 children and adolescents (4 - 21 years of age, arithmetic mean 10.8 years of age) suffering from primary nocturnal enuresis, without overt daytime symptoms, so far unresponsive to treatment at other centers, were enrolled. These patients had been allocated already to one or more successive monotherapies before being referred to our center; to a limited extent also various combination therapies, others than antimuscarinics and desmopressin, had been applied: In 12 % 1, in 23 % 2, in 31 % 3, in 18 % 4, in 16 % 5 treatment episodes without treatment success according to patients' history. These prior treatment episodes comprised enuresis alarm (78x), desmopressin (75x), antimuscarinics (65x), behavioral interventions (61x), antidepressants (59x), psychotherapy (41x), acupuncture (23x), and phytotherapeutics (11x). However, persistent treatment success had not been achieved.

Subject of this paper are 107 of 122 children and adolescents, all allocated to a combined treatment regimen comprising propiverine (0.4 mg/kg body weight b.i.d.; in some cases doses increased) and desmopressin (0.2 mg b.i.d.). Subsequent to this 3-month combination regimen stepwise successive withdrawal programs for propiverine and for desmopressin, in most cases one after the other, according to the prevalent symptoms, were performed.

### Results

The primary treatment outcome, continence at nighttime, was achieved in 104 children / adolescents (97 %). During the individual follow-up periods of 8 months up to 4 years 18 patients relapsed (17 %) following the withdrawal of propiverine, another 23 relapsed (26 %) following the withdrawal of desmopressin.

With respect to tolerability adverse events of moderate intensity, none of them inducing premature treatment withdrawal, manifested during the combination treatment: headache (17x), tiredness (14x), dryness of the mouth (12x), concentration difficulties (11x), transient accommodation disorders (1x).

### Interpretation of results

Children and adolescents with primary nocturnal enuresis, who so far have been unresponsive to a broad range of monotherapies, in many cases even unresponsive to successive monotherapies, can be treated successfully with a combined regimen of propiverine and desmopressin. Our results are consistent with results presented by other investigators (3): the combination of antimuscarinics and desmopressin in patients suffering from primary nocturnal enuresis, and unresponsive to monotherapies, achieved continence in approximately 90 %. The key issue for treatment success in primary nocturnal enuresis resistant to monotherapy obviously is to target more than one pathophysiologic mechanism: the beneficial effects of increasing bladder capacity, mediated by propiverine, and of decreasing nocturnal diuresis, mediated by desmopressin, support each other favourably.

The high rate of relapse in approximately more than 40 % of patients reflects the natural course of primary nocturnal enuresis and is a plea for extended treatment duration and a stepwise dose reduction, which has been shown to be preferable to sudden withdrawal of medication (3). Furthermore, the option of reallocating treatment failures to a treatment, which is tailored to individual symptoms, should be used.

### Concluding message

Treatment failures following various monotherapies in children suffering from primary nocturnal enuresis should be allocated to a combined treatment of propiverine and desmopressin for at least 3 months, thus achieving treatment success in 97 % of cases. However, the frequent occurrence of relapse even after stepwise withdrawal of medication might require to reallocate patients to propiverine and / or desmopressin, depending on their individual symptomatology.

### References

- (1) Enuresis – Background and treatment. Scand J Urol Nephrol Suppl 206: 1, 2000
- (2) Nocturnal Enuresis and Daytime Wetting: A Multicentric Trial with Oxybutynin and Desmopressin. Eur Urol, 31: 459, 1997
- (3) A suggested treatment algorithm in nocturnal enuresis with emphasis on partial responders. 33<sup>rd</sup> Annual Meeting of the ICS, 5-9 October 2003 Florence, Italy Neurourol Urodyn (2003) 22(5):441-442

**FUNDING: NONE**

**DISCLOSURES: NONE**

**HUMAN SUBJECTS: This study did not need ethical approval because not applicable but followed the Declaration of Helsinki Informed consent was not obtained from the patients.**