Author(s): Arendsen HJ[1], Stijnen Th[2]

Institution, city, country: [1]Diaconessenhuis, Department of Urology, Leiden, the Netherlands

[2]Erasmus University, Dept of Epidemiology and Biostatistics, Medical Centre, Rotterdam, the Netherlands

LONG-TERM EFFICACY AND SAFETY OF DESMOPRESSIN TABLETS (MINRIN®) IN ADOLESCENTS AND ADULTS WITH ENURESIS NOCTURNA

Aims of Study

The aim of this study was to investigate the efficacy and safety of desmopressin tablets during *long-term* treatment in adolescents and adults with nocturnal enuresis.

Methods

In this open, prospective, multicentre study 101 subjects were treated (APT-population) and used for safety analysis; 89 of them (aged 11-39 years) fulfilled all inclusion criteria and were used for analysis of efficacy. They had primary nocturnal enuresis with a minimum bedwetting frequency of 3 wet nights per week.

After an observation period of 2 weeks a dose titration of 200 up to 600 µg was done during a period of 1-3 weeks. Non-responders (reduction of wet nights < 50%) were excluded. The rest continued treatment with their individually titrated optimal dosage for 3 months (period I). After this period treatment was stopped for 1-2 weeks (wash-out period). If subjects were completely dry during 2 treatment-free weeks, they left the study. If they did not achieve complete dryness they restarted treatment after 1-2 weeks for 6 months (period II). The optimal dosage could be adjusted if necessary. This 6-month treatment was repeated for up to 3 periods (period II-IV), each followed by a 1-2 week wash-out period. The actual treatment period thus varied from 3 months (period I) to 21 months (period I-IV). Subjects who left the study after achieving 2 dry weeks without treatment were followed for a period of 1 year.

be attributed to a selection effect (dropping-out of non-responders). Since after period II hardly any dose adjustments were made (n=1), the improving efficacy could not be attributed to dose increases either
In 11 subjects (11%) adverse events (AEs) occurred that were possibly or probably related to study medication. Headache occurred most frequently. One of the events, i.e. fluid retention, was considered to be serious. This subject had a history of hypertension and was treated with atenolol prior to and during the study. The incidence of all AEs ranged from 16 to 17% during periods I and II and from 8 to 10% during periods II and IV and was lowest in the highest dose group (600 µg). Trend tests (Poisson regression) showed borderline statistical evidence (p=0,05) for this decreased incidence of AEs over time and no significant difference for the doses (p=0,61). A selection effect, however, may partly explain this decrease of AEs over time.

Blood chemistry (including serum sodium and osmolality), urinalysis and blood pressure did not show any clinically significant changes during treatment. Mean body weight and BMI was slightly increased.

Conclusion

These results indicate that long-term use of desmopressin tablets offers an effective and safe method in the management of enuresis nocturna in adolescents and adults. The efficacy did not decrease over time, but increased. In addition, the incidence of adverse events decreased over time, which, however, may partly be explained by a selection effect.

Author(s): Arendsen HJ[1], Stijnen Th[2]

Results:

Before the end of period I 19 out of 89 evaluable subjects dropped out. Of these, 16 (18%) appeared to be " non-reponders" during the dose-titration period and thus did not enter period I. The remaining 70 completed period I and were evaluated by " last observation carried forward" analyses. After period I a total number of 19 (21%) subjects left the study because of achieving 2 dry weeks during one of the treatment interruptions and 24 subjects dropped out because of other reasons.

Fig. 1 and 2 present the efficacy of treatment in all subjects who were evaluated at the end of period I according to the " last observation carried forward" method. The individual rate of response was based on the percentage reduction of wet nights: complete responders: >90% reduction; partial responders: 50-90% reduction; non-responders <50% reduction of wet nights. Mean percentage of wet nights and response rate appeared to remain similar or become better in the course of treatment.

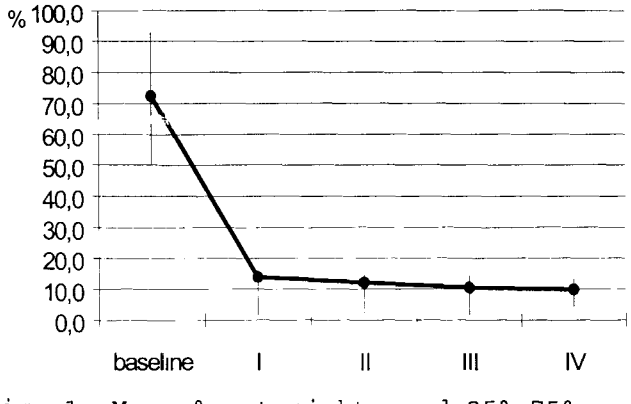

Fig. 1 Mean % wet nights and 25%-75% percentile

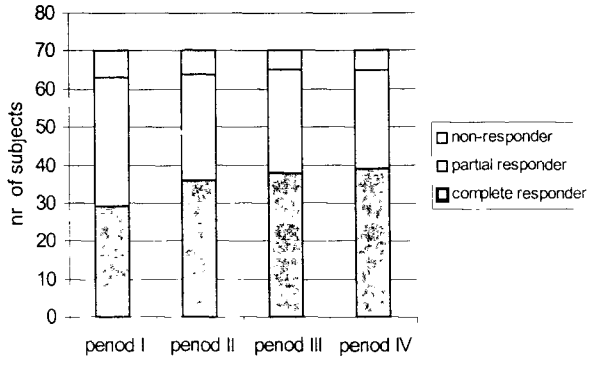

Fig. 2 Number of responders (n=70)

The repeated measurements ANOVA yielded a p-value of 0,0003 on differences between treatment periods. This indicates that the improved response may hardly