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"DESMOPRESSIN RESPONSE IN THE TREATMENT OF PRIMARY NOCTURNAL ENURESIS" DRIP: AN OPEN-LABEL, MULTI-NATIONAL STUDY

Hypothesis / aims of study

Primary Nocturnal Enuresis (PNE) is a distressing disease that affects around 10% of children between 5 and 10 years of age (1). Patients and their families experience considerable emotional upset as well as burden arising, for example, from the need for frequent laundering of bedclothes and the potential difficulties associated with spending the night away from home (2). Desmopressin, a synthetic analogue of the antidiuretic hormone arginine vasopressin, is effective and well tolerated in treating enuresis (3). The current study represents the largest evaluation of the effect of desmopressin in previously untreated children to date, reflecting clinical practice. The aim of the study was to assess the efficacy, safety and influence of possible predictive factors for response, of long-term desmopressin treatment (up to 6 months) in a large sample of treatment-naïve children.

Study design, materials and methods

This was an open-label, multi-national, Phase IV study involving 86 centres in the UK, Canada, Germany and France. Patients included in the study were between 5 and 15 years of age (between 6 and 15 years in France), suffered from PNE with no organic pathology, and experienced a minimum of six wet nights over a 2-week period. The main exclusion criteria for patients were: previous treatment with desmopressin, or with other medication for nocturnal enuresis within the past year, or use of enuresis alarms in the past year; where the treatment duration lasted for more than 4 weeks. Patients who had diurnal symptoms such as urgency, frequency and/or day-wetting were also excluded.

Patients underwent an initial 2-week screening period, during which they received no medication. During the subsequent 2-week run-in period, all patients received 0.2 mg desmopressin (in Canada, run-in could be extended to 4 weeks, titrating to 0.4 mg). Patients then entered an initial 3-month treatment period (6 weeks in Germany), during which they were administered 0.2 or 0.4 mg desmopressin (maximum dose 0.6 mg in Canada), with the dose dependent on the number of wet nights during the run-in period. Medication (tablet formulation) was taken once daily, orally at bedtime. The first treatment period was followed by a 2-week washout period with no study medication. Patients who were dry after the washout period entered a 6-month follow-up period, during which desmopressin was no longer administered. Patients who were wet after the washout period continued to a second 3-month treatment period (6 weeks in Germany), followed by a 6-month follow-up period.

The primary objective was to evaluate the overall response to desmopressin after up to 6 months of treatment. Daily diary cards were used to record night-time voiding. The efficacy analysis was based on the percentage reduction in the mean number of wet nights/week from the 2-week screening period to the final 2 weeks of treatment. Patient response was categorised into one of three groups based on the percentage reduction in mean number of wet nights per week: 1) ≥90% reduction; 2) 50% to <90% reduction; 3) <50% reduction or no reduction calculated. Secondary objectives included investigation of the influence of possible predictive factors on response, and evaluation of the long-term safety of desmopressin treatment.

Results

In total, 936 patients were screened, of whom 744 were enrolled in the study. Percentage reduction in mean number of wet nights per week, following up to 6 months' treatment with desmopressin, is shown in Table 1.

Table 1:

Reduction in wet nights (%)	**N (%)**
≥90% reduction	124 (16.7%)
50% to <90%	177 (23.8%)
<50% or missing	443 (59.5%)
Total with ≥50% reduction	**301/744 (40.5%)**

The proportion of patients experiencing ≥50% reduction in wet nights, excluding those with missing data, was 42% (301/721). A total of 27% (203/744) patients responded by the end of the first run-in period, and 37% (276/744) responded by the end of the first treatment period. Some of those who responded during the first treatment period dropped out before the end of the second treatment period, at which time 39% (289/744) were found to have responded.

Age (odds ratio=1.09 per year, CI: 1.02;1.17) and nocturnal diuresis (odds ratio=1.34 per mL/10 min, CI:1.20; 1.50) were identified as predictive factors for response. Increased compliance was associated with a greater response rate (47% of patients with good compliance showed ≥50% reduction in wet nights, as compared with 25% of patients who took less than 50% of their tablets). Long-term desmopressin treatment was well tolerated: only 5% of patients experienced any treatment-emergent adverse events (TEAEs) related to study medication, none of which were serious, the most common complaints being abdominal pain and headache. The proportion of patients who experienced TEAEs was similar in all age groups.

Interpretation of results

This study confirms that long-term administration of desmopressin (up to 6 months) effectively helps previously untreated patients by reducing the number of wet nights experienced. Even for those who experienced <50% reduction in wet nights, it is worth noting that even small improvements in their condition may be meaningful for the child.

For those with ≥50% reduction in wet nights, efficacy began almost immediately and tended to increase with continued treatment. Age and nocturnal diuresis predicted response, Higher compliance was also associated with a greater response.

Concluding message

Oral desmopressin is an effective treatment for PNE in treatment-naïve children aged between 5 and 15 years. Continued treatment over a period of 6 months offers increasing efficacy for some patients who do not respond immediately, and is well tolerated by all age groups. Long-term desmopressin use for this distressing condition, from which even partial relief can be rewarding for patients and their families, is therefore recommended.

References

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