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Robinson D. [1], Cardozo L. [1], Akeson M. [2], Hvistendahl G. [3], Riis A. [4], Norgaard J. P. [4]
1. Department of Urogynaecology, Kings College Hospital, 2. Boras County Hospital, Boras, Sweden, 3. Skejby Hospital, Aarhus, Denmark, 4. Ferring Pharmaceuticals, Copenhagen, Denmark

# WOMEN TAKE CONTROL; DESMOPRESSIN – A DRUG FOR DAYTIME URINARY INCONTINENCE

## Aims of Study

Urinary incontinence is a common condition that adversely affects quality of life **[1]**. Current medical therapy is associated with significant adverse effects which are known to affect compliance **[2]**. Desmopressin, a synthetic analogue of ADH is effective in the management of nocturnal enuresis and nocturia due to its potent antidiuretic effect. The aim of this study was to assess the use of Desmopressin in the management of daytime urinary incontinence by allowing women to take the drug at a time of their choice when they wished to be dry. The primary aim of this observational study was to investigate the efficacy of desmopressin treatment on urinary incontinence during 4 hours after drug administration. The secondary aims included investigating the voiding pattern up to 24 hours post-dose and to evaluate safety in this patient population.

## Methods

A double-blind randomised placebo-controlled multi-centre multinational observational study of desmopressin nasal spray in the management of women with severe daytime urinary incontinence. Following a five-day run-in period, eligible patients received seven single doses of desmopressin (40 μg) and three single doses of matching placebo on 10 treatment days over one month according to one of four randomised sequences. Placebo was administered on three consecutive treatment days.

Patients used diaries to record the time of dosing, adverse events, body weights, voiding times, volume of each void, incontinence episodes and weight of incontinence pads before usage and whenever the pads were changed. Patients were allowed to take the spray during the daytime according to their own preference.

The primary efficacy endpoint was the number of periods without leakage (defined as ≤ 5g pad weight gain) for 4 hours post-dose. The secondary efficacy endpoints included: (1) time from medication to first void/incontinence episode (2) volume voided per incontinent episode (3) total volume voided [volume of voids and incontinent episodes] and (4) the number of periods without leakage at various time intervals over 24 hours post-dose. Statistical analysis was performed using a two-sided paired exact Wilcoxon signed rank test. Since this was an observational study no formal power calculation was performed.

## Results

64 women with severe urinary incontinence [stress (13), urge (16) mixed aetiology (31)] were recruited. Of these 60 received study medication. The mean (range) age was 53.3 (24.9-78.0) years. During the run-in period, the mean (SD) recorded number of incontinence episodes/24 hours was 3.7 (3.2) and the 24 hour urine volume was 1557 (526) ml.

There was a higher incidence of periods without leakage of 61.7% four hours post-desmopressin compared to 47.9% on placebo (p=0.001) **[Table 1]**. In addition, there was a lower mean total volume voided of 237 ml on desmopressin compared to 317 ml on placebo (p=0.001). 36% of patients had no leakage on virtually all (6 or 7) treatment days for 4 hours after desmopressin administration.

**TABLE 1: EFFICACY VARIABLES IN THE FIRST 4 HOURS POST DOSE**

| | DDAVP | Placebo | Change |
|---|---|---|---|
| **Incidence of Periods Without Leakage (%)** | | | |
| N | 58 | 55 | 54 |
| Mean (SD) | 61.7 (35.4) | 47.9 (40.2) | 14.4 (28.1) |
| Median | 71.4 | 50.0 | 9.5 |
| Min - Max | 0.0 - 100.0 | 0.0 - 100.0 | -42.9 - 85.7 |
| **Total volume voided** (mL) | | | |
| N | 59 | 58 | 58 |
| Mean (SD) | 237 (121) | 317 (194) | -82 (180) |
| Median | 212 | 258 | -57 |
| Min - Max | 74.3 - 642.9 | 92.5 - 1090 | -810 - 318.0 |

During the time period of 4-8 hours post-dosing, there was a smaller difference between treatments with a 67.8% incidence of periods without leakage on desmopressin compared to 62.7% on placebo. Thereafter the incidence of periods without from 8-24 hours was similar for the two treatments.

Time to first incontinence episode/void was slightly higher on desmopressin (2.3±1.0 hrs) compared to placebo (2.1±1.0 hrs). Total volume voided was consistently lower on desmopressin compared to placebo up to 12 hours and the total 24-hour volume voided was significantly lower on desmopressin (1180±582 ml) compared to placebo (1375±625 ml). There were no apparent differences according to the type of urinary incontinence.

Patients reported more adverse events on desmopressin (53%) than placebo (29%); however, none of these were classified as serious or unexpected. Only 7 (11%) of the patients did not complete the study; five did not return for a follow-up visit and two withdrew due to possibly drug-related adverse events.

## Conclusions

Desmopressin is a safe and effective treatment allowing women to choose when they need treatment. Self-motivation allows choice with regard to the management of daytime urinary incontinence thus improving compliance. This exploratory study suggests that the concept of using an antidiuretic agent in urinary incontinence should be further investigated in a larger confirmatory clinical trial.

## References

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