WEIGHT DEPENDING DOSING OF DESMOPRESSIN (DDAVP) IN NOCTURNAL ENURESIS.

Hypothesis / aims of study
In children as well as in adults, a uniform starting dose of desmopressin is prescribed. This uniformity is based on the inability to detect a weight-dependent dose-concentration correlation as this correlation is probably blurred by the wide intra- and interindividual differences in plasma concentration for a fixed desmopressin dose. Recently, a smaller variation in plasma concentration was shown for the oral lyophilisate formulation of desmopressin (compared to tablet formulation) (1). Therefore, this study assessed a possible correlation between weight-corrected dose and plasma concentration for both formulations.

Study design, materials and methods
23 children (4 girls and 19 boys) with monosymptomatic nocturnal enuresis were recruited in a tertiary centre. Two tests were performed on two separate days (at two weeks interval) in identical, standardized conditions: on day 1 desmopressin tablet 200µg and on day 2 desmopressin oral lyophilisate 120µg was administered. Plasma concentrations were measured at one, two and six hours post dosing. Statistical evaluation was performed using statistical software SPSS version 19. The nonparametric Spearman’s rank correlation coefficient was used for assessing the correlation between weight corrected dose and plasma concentration.

Results
Mean (SD) age and body weight of the patients were respectively 12.7 (2.9) years and 50.1 (15.2) kg. A positive correlation between plasma concentration of dDAVP was found for the oral lyophilisate formulation at 2 hours and 6 hours post dosing. This is not the case for the tablet formulation (table 1). Results are shown graphically in figure 1 and 2.

Table 1: two-tailed correlation test by the Spearman’s rank correlation coefficient Rs

<table>
<thead>
<tr>
<th>Correlation</th>
<th>1h post dosing</th>
<th>2h post dosing</th>
<th>6h post dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tablet</td>
<td>Oral</td>
<td>Tablet</td>
</tr>
<tr>
<td>Tablet dose/weight</td>
<td>Rs = 0.120</td>
<td>Rs = 0.206</td>
<td>Rs = 0.117</td>
</tr>
<tr>
<td>P-value: 0.613</td>
<td></td>
<td>P-value: 0.371</td>
<td>P-value: 0.765</td>
</tr>
<tr>
<td>Oral lyophilisate dose/weight</td>
<td>Rs = 0.393</td>
<td>Rs = 0.499</td>
<td>Rs = 0.773</td>
</tr>
<tr>
<td>P-value: 0.096</td>
<td></td>
<td>P-value: 0.021</td>
<td>P-value: 0.005</td>
</tr>
</tbody>
</table>

Figure 1 and 2: correlation of dose corrected by weight to plasma concentrations at 2 and 6 hours post dosing.
**Interpretation of results**

To the best of our knowledge, this is the first pharmacokinetic study showing a significant dose (normalized for size) – concentration correlation for desmopressin. This correlation was only significant for the oral lyophilisate group. This result is clinically important as it is a strong indication for more predictable plasma concentrations for the oral lyophilisate formulation, and thus preventing elevated concentrations of desmopressin. In contrast to the oral lyophilisate formulation, no size dependency could be documented for the tablet formulation. Underlying cause might be the high variability in plasma concentration, as demonstrated in recent pharmacokinetic studies.

**Concluding message**

Our results show a significant dose concentration correlation in the oral lyophilisate group when we normalize dose for size (body weight), in contrast to the tablet group. It remains to be explored how this information can be used to develop an optimal dosage regimen of the drug in an individual patient.

**References**


**Disclosures**

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