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De Guchtenaere A[1], Hoebeke P[1], Van herzeele C[1], Dehoorne J[1], Raes A[1], Van Laecke E[1], De Bruyne P[1], Vande Walle J[1]

1. *University Hospital Ghent*

PHARMACOKINETIC CHARACTERISTICS OF DESMOPRESSIN ORAL LYOPHILISATE (MELT) AND TABLET FORMULATION IN CHILDREN

Hypothesis / aims of study

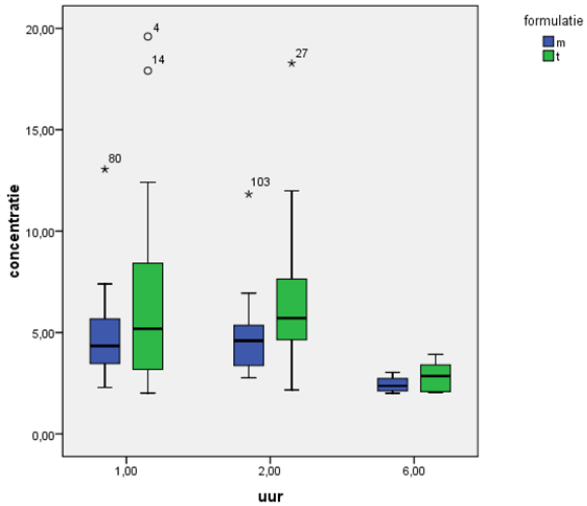
Desmopressin 120 µg oral lyophilisate and 200µg tablet are considered bioequivalent, based on extrapolation of stdies in a limited number of healthy volunteers, and one dose finding study with the melt in children. However, no comparative pharmacokinetic studies have been execute, confirming this statement.. No data are available on the influence of food-intake on bio-availability of desmopressin tablet or MELT in a pediatric setting, although studies in adults documented that food-intake resulted in significant lower desmopressin plasma-concentration. In this study, we analyzed PK-plasma concentrations of desmopressin tablet and MELT with concomitant food-intake, hypothesizing that mean differences and/or variability in PK-plasma concentrations could only be due to different localizations of mucosal absorption (buccal in MELT, gastro-intestinal with tablet), since only the latter will be influenced by food-intake.

Study design, materials and methods

23 children with MNE (4F/19M), mean age 12.7y were recruited. Two tests were performed on separate days under identical, standardized conditions with a standardized meal and fluid-intake. The drug wa administered as desmopressin tablet (T-test) or desmopressin lyophilisate /MELT (M-test) was administered immediately after the meal. Desmopressin plasma concentration was measured at hour +1, hour +2 and hour +6 (C1-C2-C6 respectively)

Results

No significant difference in plasma-concentration of the lower dosage 120µg desmopressin MELT, in comparison with 200µg tablet, establishing the proposed bioequivalence, even with concomitant food-intake. A significant difference in variability was found, with desmopressin MELT having significantly smaller variance at all C1-C2-C6 (p 0.013, p=0.037 and p=0.008 respectively) .



Interpretation of results

This study demonstrates that desmopressin MELT has comparable plasma levels, despite the lower dose, but with a significantly smaller variance, making dosage more predictable in comparison with the tablet. Therefore desmopressin MELT seems more suitable, especially in the younger age group where time- interval in the night between meal and drug administration is limited.

Concluding message

This study demonstrates that desmopressin MELT has comparable plasma levels, despite the lower dose, but with a significantly smaller variance, making dosage more predictable in comparison with the tablet. Therefore desmopressin MELT seems more suitable, especially in the younger age group where time- interval in the night between meal and drug administration is limited.

Specify source of funding or grant	**investigator driven study funded by unrestricted grant of Ferring International**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**Yes**
Specify Name of Public Registry, Registration Number	**Eudract number: 2009-017365-33**
Is this a Randomised Controlled Trial (RCT)?	**No**
What were the subjects in the study?	**HUMAN**

Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**university hospital Ghent**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**