dependent children depends on both the type of drug and the drug levels prior to weaning. In this study, there was insufficient information to characterize midazolam withdrawal dynamics, potentially because of slow midazolam weaning with insufficiently high NRS withdrawal scores.

REFERENCES

Disclosure(s) Nothing to disclose

034 ITEM RESPONSE THEORY MODELING; OLD KID ON THE BLOCK TO IMPROVE PEDIATRIC DRUG DOING
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Background Quantification of changes in disease states or clinical conditions is essential to establish drug effects and dosing guidelines. When single endpoints for direct measurements are lacking, multi-factorial observational scales may be used, like for instance pain or sedation scales.1,2

Methods Analysis of data from multi-factorial observational scales is commonly based on total scores. This assumes each item to be equally informative, which is generally not true. Item Response Theory (IRT), a long existing method in social sciences and psychology, has only recently been recognized for its ideal applicability to the analysis of multi-factorial observational scales. In this approach a latent variable is derived from effects were evaluated based on changes in the latent variable and back calculation to the total score of the observational scales allowed for the clinical interpretation of findings.

Conclusion IRT offers a desperately needed data analysis framework that may revolutionize pharmacological studies for diseases or conditions that cannot be directly quantified in children. New techniques augmenting the performance of the classical IRT approach when assumptions are violated are currently being developed in our group.

REFERENCES

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035 MIDAZOLAM PHARMACOKINETICS IN CHILDREN WITH OBESITY
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Background Midazolam is a first-line drug for treatment of status epilepticus,1,2 both by buccal and intravenous administration. In children with obesity, the midazolam pharmacokinetics may be altered, and the current dosing guidelines may therefore be insufficient.

The aim of the study was to investigate the pharmacokinetics of midazolam, after intravenous administration, in obese and non-obese children, aged 11–18 years.

Methods Trial subjects were divided into groups by Body Mass Standard Deviation Score (SDS). All children received 1 mg midazolam administered an intravenous bolus dose. Thirteen blood samples were collected per participant at prespecified timepoints over 9 hours. Plasma concentration-time data was fitted to pharmacokinetic models using non-linear mixed effects modelling (NONMEM, 7.4).

Results Seventy-two children were enrolled in the study, of these 67 children were included in the analysis. The pharmacokinetics of midazolam was best described with a two-compartment model. The changes in pharmacokinetics in children with obesity were best described with a linear function of BMI SDS on inter-compartmental clearance and peripheral volume. Thus, the rate of distribution was faster, and the peripheral volume of distribution was larger in children with obesity as compared to non-obese children. Simulations revealed that long-term infusions based on total body weight, could lead to high plasma concentrations in children with obesity. Furthermore, simulated plasma concentrations after a fixed buccal dose showed that children with obesity may be at risk of subtherapeutic plasma concentrations.

Conclusion BMI SDS was shown to have a significant influence on the peripheral volume of distribution and the inter-compartmental clearance of midazolam. The current Danish dosing guidelines for status epilepticus (http://www.paediatri.