P58 DEVELOPMENT OF JUNIORMED – THE AUSTRIAN PAEDIATRIC PHARMACOPOEIA

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Background Despite the regulatory measures to improve the availability of medicines for new-borns, infants and children, extemporaneous preparations are often necessary to cover the needs of these patients. In Austria the prescription of magistral medicines is more common (approx. 3.4% of all prescriptions) than in the European average (1.9%)¹, yet a paediatric pharmacopoeia which sets standards for the preparation and use of extemporaneous preparations was missing so far.

Methods The project was mutually conducted by the Austrian Chamber of Pharmacists, Austrian Society for Pediatric and Adolescent Medicine and the Austrian Society of General Practice/Family Medicine and funded by the Austrian Federal Ministry of Education, Science and Research (BMWFW-97.160/0001-C1/9/2015). 9,000 community and hospital pharmacists, paediatricians, dermatologists and general practitioners have been invited to submit commonly prescribed paediatric preparations. In a five step approach all submissions were assessed for completeness, pharmaceutical and medical correctness as well as level of evidence by the involved expert board (1 paediatric pharmacologist, 1 paediatrician, 4 pharmacists) and additional 10 external consultants covering 7 organ systems. Only preparations fulfilling the quality criteria for recommendation have been included in the compendium.

Results 1500 preparations have been submitted by 780 pharmacists, 227 general practitioners, 165 paediatricians and 3 dermatologists. 1175 were applicable for further assessment and 177 were recommended and included in the monograph compendium after assessment of correctness and level of evidence. These fell into 7 organ systems, namely 60 medicines for skin, 34 for the gastro intestinal tract, 20 for the respiratory system, 19 for CNS, 18 for ENT, 16 for circulation and kidneys, 10 for eyes.

Conclusion This project is an example of successful inter-professional cooperation with the aim to improve the quality of magistral formulations for children. The high number of excluded preparations underlines the need for quality control and standardisation.

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P59 MONITORING THE RECOVERY TIME OF CHILDREN AFTER ELECTIVE TONSILLECTOMIES USING COMMERCIAL ACTIVITY TRACKERS, AN PROSPECTIVE FEASIBILITY STUDY

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Introduction Wearable activity trackers are increasingly incorporated into daily life and are advancing in their technology in means of accuracy, validity and acceptability,¹⁻⁶ however there is deficient knowledge on using these devices in a paediatric setting. The objective of this pilot study was to assess the feasibility of physical activity tracking in children⁷ before and after a standardized surgical intervention and to assess the recovery time after surgery.

Methods This was a single centre, open-label, prospective feasibility study. We aimed at recruiting 24 children and adolescents 4–16 years of age undergoing elective tonsillectomy. The preoperative period was 10 days before surgery and the postoperative period was 28 days. Activity data were gathered with activity trackers.⁸ Reference activity was defined as the individual mean of daily steps preoperatively. Recovery time was defined as the number of days that the patient needed to reach reference activity postoperatively. The population was stratified according to age (4–7, 8–16 years).

Results Twelve male and twelve female patients participated (mean age 6yr, mean BMI percentile 44.7). The age group 4–7 years had a mean recovery time of 11.2 days (SD 5.0) compared to 8.3 days (SD 1.7) in the age group 8–16. The difference was 2.9 days. The tracker datasets were 58% complete. The rate of technical failures of the trackers was 29.2% for the total study period.

Conclusions Activity trackers are a potential tool viable to assess recovery time after surgery in children. Recovery time after tonsillectomy seems to be age-dependent with older children recovering faster. For future studies, we recommend using trackers as a part of assessing physical activity as a parameter of general wellbeing of child during or after an intervention. Using wearable activity trackers is a more modern and appropriate method to assess physical activity,⁹⁻¹⁴ especially in a paediatric population.

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P60

SERUM CREATININE IS SUPERIOR TO SERUM CYSTATIN C IN EXPLAINING INTER-INDIVIDUAL VARIABILITY OF VANCOMYCIN CLEARANCE IN NEONATES AND YOUNG INFANTS

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Background Serum creatinine (SCr) is used as a surrogate marker of glomerular filtration rate to guide dosing of drugs eliminated by the kidney. Serum Cystatin C (S-CysC) has been suggested as a more reliable biomarker than SCr for monitoring kidney function in adults and children. Purpose of this study was to evaluate whether S-CysC is a more useful marker for estimating vancomycin clearance in neonates and young infants.

Methods Pharmacokinetic (PK), Scr and S-CysC data were collected in patients undergoing continuous intravenous vancomycin treatment in the neonatal intensive care unit of Robert Debré Hospital - Paris. A population PK analysis was performed with the software package NONMEM, utilizing vancomycin therapeutic drug monitoring samples. S-CysC and SCr were compared in terms of usefulness to explain inter-individual variability (IIV) of vancomycin clearance. Statistical criteria were used for covariate selection.

Results A total of 58 concentrations from 47 patients (gestational age [GA] ranging from 23 to 41 weeks and postmenstrual age [PMA] ranging from 26 to 46 weeks) were modeled with an allometric one-compartment model with first-order elimination. The median (range) values for SCr and S-CysC were 41.5 (12.0 to 102.0) $\mu\text{mol/L}$ and 1.38 (0.95 to 2.32) mg/L , respectively. When tested individually, SCr and S-CysC explained 26.4% and 9.8% of IIV of vancomycin clearance, respectively. PMA was superior as a covariate on clearance, over the combination of GA and postnatal age. As such, body-weight, PMA, and SCr were retained as significant covariates on clearance in the final model.

Conclusions Serum Creatinine was found to be more useful than Serum Cystatin C to explain IIV of vancomycin clearance in this population. Further studies are needed to evaluate the utility of renal biomarkers to predict clearance and dosing of renally eliminated drugs in neonates.

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POPULATION PHARMACOKINETICS OF VANCOMYCIN IN CHINESE ICU NEONATES: INITIAL DOSAGE RECOMMENDATIONS

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The main goal of our study was to characterize the population pharmacokinetics of vancomycin in critically ill Chinese neonates to develop a pharmacokinetic model and investigate factors that have significant influences on the pharmacokinetics of vancomycin in this population.^{1 2} The study population consisted of 80 neonates in the neonatal intensive care unit (ICU) from which 165 trough and peak concentrations of vancomycin were obtained. Nonlinear mixed effect modeling was used to develop a population pharmacokinetic model for vancomycin.⁴ The stability and predictive ability of the final model were evaluated based on diagnostic plots, normalized prediction distribution errors and the bootstrap method. Serum creatinine (Scr) and body weight were significant covariates on the clearance of vancomycin.^{5 6} The average clearance was 0.309 L/h for a neonate with Scr of 23.3 mmol/L and body weight of 2.9 kg. No obvious ethnic differences in the clearance of vancomycin were found relative to the earlier studies of Caucasian neonates. Moreover, the established model indicated that in patients with a greater renal clearance status, especially Scr < 15 mmol/L , current guideline recommendations would likely not achieve therapeutic area under the concentration-time curve over 24 h/minimum inhibitory concentration ($\text{AUC}_{24\text{h}}/\text{MIC}$) ≥ 400 .³ The exceptions to this are British National Formulary (2016–2017), Blue Book (2016) and Neofax (2017). Recommended dose regimens for neonates with different Scr levels and postmenstrual ages were estimated based on Monte Carlo simulations and the established model. These findings will be valuable for developing individualized dosage regimens in the neonatal ICU setting.

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