The objective of this study was to develop a method to identify NFX metabolites in human samples, and apply it to the discovery of NFX metabolites in urine from pediatric patients undergoing treatment for Chagas disease.

Methods Urine was collected from 12 pediatric patients and 8 healthy volunteers (controls), and anonymized before analysis. Informed consent was obtained from all participants. Samples were aliquoted, deproteinized with ACN (BNZ as internal standard) and centrifuged in cold. 10% of supernatant in water was injected into a 1.8 µm C18 column and chromatographed in 3.5 min under a water/ACN gradient at 0.4 mL/min in a *Shimadzu Nexera X2* UHPLC equipment. Species were positively ionized by a *Turbo IonSpray* source. Metabolites were identified and characterized by an *ABSciex 6500 QTRAP* spectrometer through Enhanced-Mass-Screening (EMS), Neutral-Loss (NL), Precursor-Ion (PREC), Enhanced-Product-Ion (EPI) and MS³ experiments. For chromatographic monitoring, parameters were optimized and the three most intense Multiple-Reaction-Monitoring (MRM) transitions were selected.

Results Denitrated NFX conjugated with cysteine (M1) and N-acetyl-cysteine (M2), as well as other phase I metabolites like saturated nitrile (M3), hydroxyamide (M4), carboxylic acid (M5) or aldehyde (M6) were identified in most samples. The final MS/MS detection method was high reproducible and sensitive for all metabolites.

Conclusions We found the main NFX metabolites in pediatric urine using a fast MS/MS method that can allow us to efficiently study the role of NFX and its metabolites in pediatric treatment response and the adverse drug reactions, and in combination with PK/PD experiments will facilitate future clinical trials, and possibly develop new therapeutic drug monitoring strategies.

REFERENCE

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Disclosure(s) Nothing to disclose

P39 ESTABLISHMENT OF THE SWISS DATABASE FOR DOSING MEDICINAL PRODUCTS IN PEDIATRICS

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Background Drug therapy in children is challenging. Due to the lack of licensed drugs for paediatric use, off-label or unlicensed prescription is frequent. To improve quality and safety of prescription of medicinal products for children in Switzerland, the requirement to create and continuously run a national database was added in the revision of the therapeutic products act (TPA Art. 67a). The task of operating the database was given to SwissPedDose, an association representing eight Swiss children's hospitals, the Swiss Society of Paediatrics (SGP) and the Swiss Association of Public Health Administration and Hospital Pharmacists (GSASA).

Methods Substances used in three therapeutic areas 'general paediatrics', 'infectious diseases' and 'neonatology' are selected according to their frequency of use in the eight participating

hospitals. Dosage data of substance-indication pairs are requested from the hospital pharmacists. Based on these data and literature review a dosage suggestion consisting of substance, indication, route of administration, dose, daily repetitions and, if applicable, additional remarks is then elaborated by a specialised pharmacist of SwissPedDose. This suggestion is then discussed by experienced physicians delegated from the eight clinics. The elaboration, discussion and agreement on a national dosage recommendation takes place and is documented in an online platform specially programmed for this structured harmonisation process. Once an agreement has been achieved, the national dosage recommendation is sent to the eight participating clinics and published in a free accessible public database.

Results As of December 31st 2018, 195 dosage recommendations for children including 87 indications and 54 substances have been harmonised and published and are available for medical professionals on <https://swisspeddose.ch/database>.

Conclusion The goal of published recommendations for 100 substances by March 2021 is feasible to reach due to interprofessional collaboration. SwissPedDose may thus contribute to a more efficient and safe use of drugs prescribed to children in Switzerland.

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P40 COMPARISON OF ANTIBIOTIC CONSUMPTION BETWEEN PEDIATRIC HOSPITALS

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Background Antibiotic exposure and reduced microbiome diversity in early childhood are associated with the incidence of inflammatory bowel disease,¹ asthma² and type-1 diabetes³ later in life. Together with the emergence of microbial resistance, those adverse effects of antibiotics impacting on the individual and population levels.

Periodic monitoring of therapeutically used antibiotics in the framework of antimicrobial stewardship is required for their effective and restricted use in hospitals.

Children's hospitals face two challenges for a meaningful quantification of antibiotic consumption:

§ Firstly, the algorithm DDD/inpatient days used in adult patients do not take into account the heterogeneity of the pediatric population. Up to date there is no global consensus on how to calculate and interpret the antibiotic consumption of wards and hospitals for children.

§ Second challenge is the relative scarcity of suitable pediatric hospitals as basis for comparison.

This study deals with the comparison and interpretation of antibiotic consumption between two similarly structured children's hospitals in Austria.

Methodology The annual use of antibiotics was assessed in two large pediatric clinical settings at geographically distinct locations in Austria, encompassing all relevant wards, such as neonatology, internal medicine, surgery, pediatric oncology and PICU's. The analysis discriminates among the wards and classes of antibiotics.