Background The broad-spectrum antiparasitic drug ivermectin is widely used in children, and its use in children weighing < 15 kg is off-label, as little data is available to inform the use of ivermectin in this young age group. Pediatric doses associated with consistent exposure across age are still unknown. Therefore, we aim to identify a dosing strategy for ivermectin treatment in both pre-school-aged children (2–5 years of age) and school-aged children (6–12 years of age) that achieves equivalent exposure coverage in children and adults.

Methods A population pharmacokinetic model for ivermectin was developed based on data collected in 80 pre-school-aged children (2–5 years), 120 school-aged children (6–12 years),¹ and eleven adults,² receiving an oral dose of 100–600 µg/kg ivermectin. Model-based simulations were performed to optimize pediatric dosing to achieve consistent exposure across various age groups.

Results Clearance per kilogram was higher in children than in adults, with a median (90% confidence interval) of 0.35 (0.12–0.73) L/h/kg in children compared to 0.20 (0.10–0.31) L/h/kg in adults. As a result, ivermectin exposure in children following a 200 µg/kg dose is ~30% lower than in adults. An increased dose of 250 and 300 µg/kg would be needed in school-aged children (6–12 years) and pre-school-aged children (2–5 years), respectively, to achieve equivalent exposure coverage in children and adults. Alternatively, we propose a height-based dosing schedule with a stepwise increase in number of administered 3-mg-tablets from 1 to 5 for children in sub-Saharan Africa with a height of 75–90 cm, 90–130 cm, 130–150 cm, 150–165 cm, and 165–175 cm.

Conclusion We report the first dosing strategy for the widely-used drug ivermectin that is associated with equivalent exposure coverage in children and adults. Further studies are necessary to establish the safety and efficacy of appropriate doses in the pediatric population.

REFERENCES

- Wimmersberger D, Coulibaly JT, Schulz JD, Puchkow M, Huwyler J, N'Gbeso Y, et al. Efficacy and Safety of Ivermectin Against *Trichuris trichiura* in Preschool-aged and School-aged Children: A Randomized Controlled Dose-finding Trial. *Clin Infect Dis*. 2018; **67**(8):1247–55.
- Schulz JD, Neodo A, Coulibaly JT, Keiser J. Development and validation of a LC-MS/MS method for ivermectin quantification in dried blood spots: application to a pharmacokinetic study in *Trichuris trichiura*-infected adults. *Anal. Methods*, 2018, **10**, 2901–9.

Disclosure(s) JMB declares no potential conflicts of interest. JDS declares no potential conflicts of interest. JTC declares no potential conflicts of interest. JK was financially supported by the Bill and Melinda Gates Foundation (OPP1153928) and an ERC grant (CoG 614739 A-HERO), and declares no other potential conflicts of interest. MP has a part-time employment with the consulting company Certara LP (USA), and declares no other potential conflicts of interest.

025

CLAVULANATE STABILITY IN CHILD-APPROPRIATE FORMULATIONS IS INADEQUATE FOR USE IN TREATING YOUNG CHILDREN IN ASIA

¹I Mack*, ²M Sharland, ³S Rehm, ³K Rentsch, ⁴J Bielicki. ¹University Children's Hospital Basel (UKBB), Basel, Switzerland; ²St George's University of London, London, UK; ³University Hospital of Basel; ⁴University Children's Hospital Basel (UKBB), Basel, Switzerland

10.1136/archdischild-2019-esdppp.25

Background Amoxicillin-clavulanate (AMC) is among the most frequently used antibiotic for paediatric infections globally. AMC child-appropriate formulations are largely limited to dry powder suspensions, which have to be stored refrigerated once reconstituted due to stability limitations of clavulanate.

Methods Oral Amoxicillin (AMX) and AMC formulations were identified from IQVIA-MIDAS wholesale data, and 2015 antibiotic consumption in courses/1000 child-years was estimated in Bangladesh, India, Indonesia, Pakistan, Philippines and Vietnam with an assumed average treatment of 7 days. Costs per course in US-\$ standardised to 2015 were estimated from the same dataset. Nationally representative data on access to a refrigerator was extracted from the Demographic & Health Surveys Program. Degradation under different temperature conditions of two different AMC suspensions commercially available in Switzerland was tested. Average degradation (three bottles of each product) was measured during 8 days with ambient temperatures of 8°C versus 28°C.

Results In India and Pakistan more AMC than AMX courses were sold. In all countries AMC was at least twice and up to 10 times as expensive as AMX. Access to refrigeration was below 45%, even in countries with a high number of sold AMC courses (compared with AMX). In the evaluated co-formulated products, clavulanate showed a maximum degradation of 34% at 8°C, and 73% at 28°C after 8 days. AMX was largely stable at 8°C but 13% degraded at 28°C after 8 days.

Conclusions Oral amoxicillin-clavulanate suspensions are widely used in six Asian countries classified as middle-income countries by the World Bank. In reconstituted liquid AMC formulations, neither component is satisfactorily stable at room temperature. Storage conditions for stability are likely inadequate for AMC in many households in the six Asian countries of interest.

Disclosure(s) Nothing to disclose

026

POPULATION PHARMACOKINETIC META-ANALYSIS OF INDIVIDUAL DATA TO DESIGN THE FIRST RANDOMIZED EFFICACY TRIAL OF VANCOMYCIN IN NEONATES AND YOUNG INFANTS

¹E Jacqz-Aigrain, ²S Leroux, ³AH Thomson, ⁴K Allegaert, ⁵EV Capparelli, ^{1V} Biran, ^{6N} Simon, ^{7B} Meibohm, ⁸Lo Y-L, ^{9R} Marqués, ^{10J-E} Peris, ^{11I} Lutsar, ^{12J} Saito, ^{12H} Nayamura, ^{13JN} van den Anker, ^{14M} Sharland, ^{15W} Zhao*. ¹Hôpital Robert Debré, Paris; ²CHU de Rennes, Rennes, France; ³University of Strathclyde, Glasgow, UK; ⁴Erasmus MC – Sophia Children's Hospital, Rotterdam, The Netherlands; ⁵University of California, San Diego, CA, USA; ⁶Hôpital de la Timone, Marseille, France; ⁷University of Tennessee Health Science Center, Memphis, TN, USA; ⁸University of Malaya, Malaysia, Malaysia; ⁹La Fe Hospital; ¹⁰University of Valencia, Valencia, Spain; ¹¹University of Tartu, Tartu, Estonia; ¹²National Children's Hospital National Center for Child Health and Development, Tokyo, Japan; ¹³University Children's Hospital Basel, Basel, Switzerland; ¹⁴St. George's Hospital, London, UK; ¹⁵Shandong University, Jinan, China

10.1136/archdischild-2019-esdppp.26

Background In the absence of consensus, the present meta-analysis was performed to determine an optimal dosing regimen of vancomycin for neonates.

Methods A 'meta-model' using NONMEM with 4894 concentrations from 1631 neonates was built and Monte Carlo simulations were performed to design an optimal intermittent infusion, aiming at reaching a target AUC₀₋₂₄ of 400 mg*h/L at steady state in at least 80% of neonates.