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 0.33 (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

Disclosure(s) JMB declares no potential conflicts of interest. JDS declares no potential conflicts of interest. JTC declares no other potential conflicts of interest.

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

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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

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