aldehyde oxidase (AO) and is an AO inhibitor with complex pharmacokinetics. We have used favipiravir, in combination with other antivirals, in severely immunocompromised children with life-threatening RNA virus infections. As an unlicensed indication, favipiravir pharmacokinetics were routinely monitored at our institution. Population pharmacokinetic model is used to describe the favipiravir pharmacokinetic properties, drug exposure and sources of variability in these children.

Methods Routine favipiravir plasma levels of 9 patients (0.8–11yrs, mean age=5.3yrs; median weight=15kg) were analysed retrospectively (62 samples). All patients received favipiravir 200mg or 400mg tds and had at least one plasma level 45min (peak), 3h and 8h (trough) post-dose. Parameter estimation and model simulation properties (visual predictive check) were assessed using R language (v 4.1.2) and RStudio (2022.02.0+443).

Results A one-compartment model with weight as covariate best describes the data, with (1) elimination clearance=1L/h and volume of distribution=7.54L, both allometric scaled centring at median weight, and (2) estimated t1/2=5.17h with Cmax = 24µg/mL at 200mg and 41µg/mL at 400mg.

Conclusions To our knowledge this is the first report of favipiravir pharmacokinetic parameters in infants and young children. Weight significantly improves the model fit as a covariate. Reported EC50 for norovirus in vitro was 19–39µg/mL and enterovirus 71 was 23µg/mL, indicating higher favipiravir doses or combination with other antivirals are required.

23 PLASMA RENIN ACTIVITY IN YOUNG CHILDREN WITH HEART FAILURE: INFLUENCE OF AGE, DISEASE AND ACE INHIBITOR TREATMENT

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Introduction Increased plasma renin activity (PRA) levels may have various causes: PRA has gained importance as prognostic marker for patients with heart failure; age may have an influence on endogenous PRA levels; and ACE inhibitor (ACEi) treatment can also interfere with PRA levels. We aimed to investigate PRA levels in very young children with heart failure, with and without ACEi treatment.

Methods As part of a PK-PD study of enalapril for pediatric heart failure (LENA studies), blood samples were collected and analyzed for PRA levels before, 4 hours after and within the first week of enalapril treatment. In addition, a literature search was conducted according to the PRISMA concept in MEDLINE to identify studies on PRA levels in healthy children as well as in children with heart failure in the age range from 1 day up to 2 years. Comparison was performed with LENA study data and with data from 9 healthy volunteers.

Results Infants from LENA studies with heart failure (n= 35, aged 25 days – 2.1 years) had median PRA levels of 19.7 (n=35) before, 29.0 (n=34, $p>0.05$) 4 hours after enalapril dose, and 89.1 ng/mL/h (n=29, $p<0.01$) after 5 days of treatment. Literature search revealed mean PRA levels in healthy children between 2.3 to 29.8 (n= 14 studies) and 10.0 to 87.1 ng/mL/h in ACEi naïve heart failure children (n= 4 studies). PRA levels of 9 healthy adults ranged between 0.13 to 1.85 ng/mL/h.

Conclusions Very young children had higher endogenous PRA levels compared to adults. Heart failure at this age was associated with even higher PRA levels and ACEi treatment further increased PRA levels. These results indicate that patients appear to respond to ACEi treatment but question the value of PRA levels as prognostic marker in this population.

24 ANTIPSYCHOTICS USE AND WEIGHT GAIN IN CHILDREN COMPARED TO ADULTS: ANALYSIS OF SPONTANEOUS ADVERSE DRUG REACTION REPORTS

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Introduction Weight gain and obesity are common adverse effects of antipsychotics (APs). We aimed to assess AP-induced weight gain in pediatrics compared to adults.

Methods In a case-non case study using the WHO global database of individual case safety reports (ICSRs), VigiBase®, we evaluated the existence of disproportionality in weight gain reporting under antipsychotic treatment in children and adolescents compared to adults. Disproportionality of weight gain reporting was evaluated using the reporting odds ratio (ROR) with corresponding 95% confidence intervals (95%CI). Analysis was adjusted for sex, reporting country, year of notification, reporter qualification and concomitant use of antidepressants (ADs) and lithium.

Results A total of 282,224 ICSRs reported with an AP were retrieved: 6,446 (2.3%) in children, 14,112 (5%) in adolescents and 261,666 (92.7%) in adults. In children, 1,544 (24%) of ICSRs reported weight gain, 1,831 (13%) in adolescents and 13,506 (5.6%) in adults. Most weight gain cases concerned male patients (55%) and were reported by health professionals (47%) in North America (54%) and Europe (27%). Concomitant use of ADs and lithium was reported in 36% and 3.5% of weight gain cases overall. Disproportionality of weight gain reporting associated with APs was found in adolescents (adjusted ROR: 2.3 [95%CI 2.1–2.4]) and in children (aROR: 3.6 [95%CI 3.3–3.8]) compared to adults. Use of risperidone was associated with the highest increase in weight gain reporting in children (aROR 4.9, 95%CI 3.9–6.1) and adolescents (aROR 3.6, 95%CI 3.1–4.1).

Conclusions Children and adolescents are at higher risk of reporting weight gain under APs than adults.

25 POINT PREVALENCE STUDY OF PAEDIATRIC POLYPHARMACY

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