ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

https://iap-kpj.org

Karnataka Paediatric Journal

Journal Review

Journal watch

Vikram Sakaleshpur Kumar[1]

[1]Department of Paediatrics, Subbaiah Medical College, Shivamogga, Karnataka, India.

***Corresponding author:**
Vikram Sakaleshpur Kumar,
Department of Paediatrics,
Subbaiah Medical College,
Shivamogga, Karnataka, India.

vikramskumar@yahoo.co.in

Received: 30 March 2022
Accepted: 31 March 2022
EPub Ahead of Print: 10 May 2022
Published: 22 June 2022

DOI
10.25259/KPJ_4_2022

Quick Response Code:

Source: Akunne OO, Mugabo P, Argent AC. Pharmacokinetics of vancomycin in critically ill children: A systematic review. *Eur J Drug Metab Pharmacokinet*. 2022 Jan;47(1):31-48. doi: 10.1007/s13318-021-00730-z. Epub 2021 Nov 8. PMID: 34750740; PMCID: PMC8574943.

Vancomycin is often used in the ICU for the treatment of Gram-positive bacterial infection. In critically ill children, there are pathophysiologic changes that affect the pharmacokinetics of vancomycin. This is a systematic review of vancomycin pharmacokinetics and pharmacodynamics in critically ill children.

Thirteen studies were included in this systematic review. A wide variety of dosing and sampling strategies were used in the studies. Methods for estimating vancomycin pharmacokinetics, especially the area under the curve over 24 h, varied widely between the studies. Vancomycin doses of 20–60 mg/kg were given daily. This resulted in high variability in pharmacokinetic parameters. *Vancomycin trough level was less than 15 μg/mL in most of the studies.* Vancomycin clearance ranged from 0.05 to 0.38 L/h/kg. The volume of distribution ranged from 0.1 to 1.16 L/kg. Half-life was between 2.4 and 23.6 h. Patients in the study receiving continuous vancomycin infusion had AUC_{24} <400 μg·h/mL.

This systematic review shows that there is a large variability in the pharmacokinetics of vancomycin among critically ill paediatric patients. Studies to assess the factors responsible for this variability in vancomycin pharmacokinetics are needed.

Source: De Sutter AI, Eriksson L, van Driel ML. Oral antihistamine-decongestant-analgesic combinations for the common cold. *Cochrane Database Syst Rev. 2022* Jan 21;1(1): CD004976. doi: 10.1002/14651858.CD004976.pub4. PMID: 35060618; PMCID: PMC8780136.

Although combination formulas containing antihistamines, decongestants and/or analgesics are sold over-the-counter in large quantities for the common cold, the evidence for their effectiveness is limited, yet they are being used unscrupulously. This is a Cochrane review update of a review first published in 2012. Randomised controlled trials (30 studies [6304 participants] including 31 treatment comparisons) investigating the effectiveness of antihistamine-decongestant-analgesic combinations compared with placebo, other active treatment (excluding antibiotics) or no treatment in children and adults with the common cold were selected.

The authors found a lack of data on the effectiveness of antihistamine-analgesic-decongestant combinations for the common cold. Based on these scarce data, the effect on individual symptoms is probably too small to be clinically relevant. *There is no evidence of effectiveness in young children.* In 2005, the US Food and Drug Administration issued a warning about adverse effects associated with the use of over-the-counter nasal preparations containing phenylpropanolamine.

Source: Sevinc N, Bilici N, Sevinc E, Dogan E. Blood and faecal lead levels in children with various functional gastrointestinal disorders. *An Pediatr (Engl Ed). 2022* Jan;96(1):35-42. doi: 10.1016/j.anpede.2021.02.001. Epub 2021 Mar 4. PMID: 35058019.

The researchers investigate the blood lead levels (BLLs) and faecal lead levels (FLLs) in children with various functional gastrointestinal disorders (FGIDs) such as functional constipation (FC) (n = 36), functional abdominal pain (FAP) (n = 36) and functional nausea (FN) (n = 30) and compare them with controls.

The median BLLs in the FGIDs group were significantly higher than in controls (5.12 and 1.77 μg/dL, respectively). The BLLs were above 5 μg/dL in 51.9% of children with FGIDs. There was a statistically significant difference in BLLs between FC subgroup and the other subgroups (FAP and FN) (P = 0.003 and P < 0.001, respectively). The FLLs in the FGIDs group were significantly higher than in controls (28.08 and 0.01 μg/g, respectively). There was no significant difference in FLLs between FC subgroup and the other subgroups (P = 0.992 and P = 0.989, respectively). No significant relation was found between BLLs and FLLs of the FGIDs group (P = 0.123).

This interesting and thought-provoking study revealed that *children with FGIDs had higher BLLs and FLLs than controls and also more than half of the children with FGIDs had BLLs ≥5 μg/dL which is considered a toxic level.* These results might revive the question of whether or not clinicians need to evaluate routine BLLs in children with FGIDs.

Source: Burns JC, Roberts SC, Tremoulet AH, *et al*. Infliximab versus second intravenous immunoglobulin for the treatment of resistant Kawasaki disease in the USA (KID CARE): A randomised, multicentre comparative effectiveness trial. *Lancet Child Adolesc Health. 2021*;5(12):852-861; doi: https://doi.org/10.1016/S2352-4642(21)00270-4.

Although intravenous immunoglobulin (IVIG) is an effective therapy for Kawasaki disease, 10–20% of patients have recrudescent fever as a sign of persistent inflammation and require additional treatment. The researchers aimed to compare infliximab with a second infusion of IVIG for the treatment of resistant Kawasaki disease.

Patients were randomly assigned (1:1) to a second IVIG (2 g/kg over 8–12 h) or intravenous infliximab (10 mg/kg over 2 h without premedication), using a randomly permuted block randomisation design with a block size of two or four. Patients with fever 24 h–7 days following completion of the first study treatment crossed over to receive the other study treatment. The primary outcome measure was a resolution of fever at 24 h after initiation of study treatment with no recurrence of fever attributed to Kawasaki disease within 7 days post-discharge. The secondary outcome measures included duration of fever from enrolment, duration of hospitalisation after randomisation and changes in markers of inflammation and coronary artery Z score.

There was no difference between treatment groups for markers of inflammation or coronary artery outcome. Twenty-four (44%) of 54 patients in the infliximab group and 33 (67%) of 49 in the second IVIG group had at least one adverse event. A drop in haemoglobin concentration of at least 2 g/dL was seen in 19 (33%) of 58 patients who received IVIG as either their first or second study treatment (three of whom required transfusion) and in 3 (7%) of 43 who received only infliximab (none required transfusion; P = 0.0028). Haemolytic anaemia was the only serious adverse event deemed definitely or probably related to study treatment and was reported in 9 (15%) of 58 patients who received IVIG as either their first or second study treatment and none who received infliximab only.

They conclude *that infliximab is a safe, well-tolerated and effective treatment for patients with IVIG-resistant Kawasaki disease, and results in a shorter duration of fever, reduced need for additional therapy, less severe anaemia and shorter hospitalisation compared with a second IVIG infusion.*

Source: Letouzey M, Lorthe E, Marchand-Martin L, Kayem G, Charlier C, Butin M, Mitha A, Kaminski M, Benhammou V, Ancel PY, Boileau P, Foix-L'Hélias L; EPIPAGE-2 infectious diseases working group. Early antibiotic exposure and adverse outcomes in very preterm infants at low risk of early-onset sepsis: The EPIPAGE-2 cohort study. *J Pediatr. 2022* Apr;243:91-98.e4. doi: 10.1016/j.jpeds.2021.11.075. Epub 2021 Dec 21. PMID: 34942178.

The researchers set out to assess the association between early empirical antibiotics and neonatal adverse outcomes in very preterm infants without risk factors for early-onset sepsis (EOS). This is a secondary analysis of the EPIPAGE-2 study, a prospective national population-based cohort that included all live-born infants at 22–31 completed weeks of gestation in France in 2011. Infants at high risk of EOS (i.e., born after preterm labour or preterm premature rupture of membranes or from a mother who had clinical chorioamnionitis or had received antibiotics during the past 72 h) were excluded from the study. Early antibiotic exposure was defined as antibiotic therapy starting at day 0 or day 1 of life, irrespective of the duration and type of antibiotics.

Among 648 very preterm infants at low risk of EOS, 173 (26.2%) had received early antibiotic treatment. Early antibiotic exposure was not associated with death or late-

onset sepsis or necrotising enterocolitis; however, it was associated with higher odds of severe cerebral lesions and moderate-severe bronchopulmonary dysplasia (BPD). *Early empirical antibiotic therapy administrated in very preterm infants at low risk of EOS was associated with a higher risk of severe cerebral lesions and moderate-severe BPD.*

Source: Storm DW, Copp HL, Halverson TM, Du J, Juhr D, Wolfe AJ. A child's urine is not sterile: A pilot study evaluating the paediatric urinary microbiome. *J Pediatr Urol. 2022* Mar 4:S1477-5131(22)00092-4. doi: 10.1016/j.jpurol.2022.02.025. Epub ahead of print. PMID: 35337731.

A bladder microbiome (urobiome) exists in adults. Data support the effects of the adult urobiome on urinary tract health with associations between dysbiotic urobiomes and lower urinary tract disorders. Understanding urobiome origin is important since other microbiomes establish around birth and microbiome alterations are linked to disease development. However, the paediatric urobiome has not been well studied.

Seventy-four children <18 years of age without recent antibiotic exposure were recruited, including 48 males and 26 females, aged 2 weeks–to 209 months of age. Transurethral catheterised urine samples and samples from the perineum, urethra, vagina and foreskin were collected. Specimens were assessed using the expanded quantitative urine culture protocol and by 16S rRNA gene sequencing. Dada2 was used to profile microbial compositions, and BLCA was used to identify microbial taxa. Bacteria were detected in 90.5% of urine samples and identified in children as young as 2 weeks of age. Microbial communities and compositions of the female bladder and other urogenital niches (urethra, perineum and vagina) differed significantly by age. Lactobacillus predominated the bladder, urethral and vaginal microbiomes in post-pubertal girls. Compared to female urinary microbiomes, those of males differed less substantially. Only perineal microbiomes differed significantly by age, whereas male urethral and foreskin microbiomes did not differ significantly.

A paediatric urobiome exists, with differences between males and females and can be detected at a young age with changes occurring throughout childhood. Similarities and differences are also seen between the paediatric urobiome and adjacent niches.

Source: Neena R, Remya S, Anantharaman G. Acute acquired comitant esotropia precipitated by excessive near work during the COVID-19-induced home confinement. *Indian J Ophthalmol. 2022* Apr;70(4):1359-1364. doi: 10.4103/ijo.IJO_2813_21. PMID: 35326055.

The authors conduct a retrospective, clinical study to evaluate the causes of acute acquired comitant esotropia (AACE) in young adults and children in the setting of COVID-19-induced home confinement, who presented to the Paediatric Ophthalmology and Strabismus services of a tertiary eye care centre in South India from August 2020 to January 2021 during the COVID-19 pandemic.

Eleven (73.3%) of the total 15 patients were students, above 10 years and with a mean age of 16.8 years. Twelve patients (80%) had more than 8 h of near activity a day with a mean duration of 8.6 h/day. The most common near activity was online classes, followed by job-related work and mobile games, and 86.7% used smartphones for near work. The average esotropia was 22.73 prism Diopter (PD) for distance and 18.73 PD for near. A majority (66.6%) had hyperopia with basic or divergence insufficiency esotropia, and the remaining 33.3% had myopia and fitted into the Bielschowsky type AACE. There was no precipitating event other than sustained near work in all, except in one patient who also had a fever before the onset of esotropia.

The authors conclude that *the habit of a long time and sustained near work, especially on smartphones, may increase the risk of inducement of AACE.*

Source: Keene JC, Morgan LA, Abend NS, Bates SV, Bauer Huang SL, Chang T, Chu CJ, Glass HC, Massey SL, Ostrander B, Pardo AC, Press CA, Soul JS, Shellhaas RA, Thomas C, Natarajan N. Treatment of neonatal seizures: Comparison of treatment pathways from 11 neonatal intensive care units. *Pediatr Neurol. 2022* Mar;128:67-74. doi: 10.1016/j.pediatrneurol.2021.10.004. Epub 2021 Oct 11. PMID: 34750046.

The authors conducted a descriptive analysis of 11 neonatal seizure management pathways from Level IV neonatal intensive care units in the United States that specialise in neonatal neurocritical care including guidelines for electroencephalography (EEG) monitoring, antiseizure medication (ASM) choice, timing and dose to highlight areas of consensus and describe aspects of variability.

All sites had 24/7 conventional EEG initiation, monitoring and review capability. Management pathways uniformly included prompt EEG confirmation of seizures. Most pathways included a provision for intravenous benzodiazepine administration if either EEG or loading of ASM was delayed. Phenobarbital 20 mg/kg IV was the first-line ASM in all pathways. Pathways included either fosphenytoin or levetiracetam as the second-line ASM with variable dosing. The third-line ASMs were most commonly fosphenytoin or levetiracetam, with alternatives including topiramate or lacosamide. All pathways provided escalation to continuous midazolam infusion with variable dosing for seizures refractory to initial medication trials. Three pathways also included lidocaine infusion. Nine pathways discussed ASM discontinuation after resolution of acute symptomatic seizures with variable timing.

The authors conclude that, despite a paucity of data from controlled trials regarding optimal neonatal seizure management, *there are areas of broad agreement among institutional pathways. However, there are also areas of substantial heterogeneity that requires further research and includes optimal second-line ASM, dosage and timing of ASM discontinuation.*

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

Dr. Vikram Sakaleshpur Kumar is in the Editorial Board of the journal.

How to cite this article: Kumar VS. Journal watch. Karnataka Paediatr J 2022;37:35-8.