

## Intravenous paracetamol: Salvage and safety proposition

Sir,

Paracetamol is widely prescribed and recommended for neonates and young infants, primarily for analgesia and pyrexia.<sup>[1]</sup> Intravenous (IV) preparation is very commonly used in hospital settings, and it is available in India in either 50 ml (few brands) or 100 ml vials containing 1.0% w/v paracetamol. Prescribed doses for IV paracetamol are 7.5 mg/kg or 0.75 ml/kg (<10 kg), 15 mg/kg or 1.5 ml/kg (10-50 kg), 1 gm or 100 ml (>50 kg) to be administered over 15 min.<sup>[2]</sup> The dose in above vials would suffice its use in adult populations, while in neonates and small children the required volume per dose is way less, leading to reuse from opened vial, wastage, or improper dilution of the drug.

Paracetamol vial requires storage below 30°C, requires protection from light and is meant to be consumed within 30 min of opening the vial.<sup>[2,3]</sup> Paracetamol is extremely sensitive to oxygen and light. Following degradation, paracetamol is converted to 4-aminophenol, which is quickly converted to the hepatotoxic molecule N-acetyl-p-benzoquinoneimine.<sup>[2]</sup> Paracetamol, is therefore, synthesised within a tightly controlled target pH range of 5-6 to avoid conversion to 4-aminophenol. Secondly, to avoid chemical oxidation reactions, the IV preparations are packed in hermetically sealed oxygen-impermeable containers which have been bubbled with nitrogen to lessen the amount

of oxygen present and filled with a ready-to-use formulation. In addition, to achieve stable aqueous solutions of paracetamol, most IV preparations have added antioxidants (e.g., cysteine) and isotonicising or stabilising agents (e.g., mannitol). To minimise the effect on stability of this formulation of paracetamol, the dilution should not be more than 10 times its volume using normal saline or 5% dextrose and the solution should be administered over 15 min within the hour after its preparation.<sup>[2]</sup> So, prolonged, and repeated use of a single large vial is not advisable for paediatric group.

Our main concern is that due to the impracticability of discarding the large amount of left-over drug after withdrawing a miniscule amount (1.5 ml for a 2 kg child), inappropriate and potentially dangerous practices are prevailing. We conducted a telephonic survey among 10 paediatric anaesthesiologists regarding the paracetamol administration practices and received some particularly concerning responses. This included addition of paracetamol directly to the maintenance IV fluids (generally Ringers lactate or Plasmalyte) leading to inappropriately large dilution and possibility of instability of the drug (due to alteration of pH or dilution of stabilising/antioxidant agents), thereby leading to questionable effectiveness and potential harm. It was also administered directly without dilution by a syringe, which may inadvertently lead to faster injection. The same vial once opened is used multiple times for administration to subsequent cases which may take the whole day. A hypodermic needle used for drawing the drug is

left inserted in the vial cap increasing the chances of oxidation and contamination. In addition, the prescription doses mentioned in some cases were 15 mg/kg for a neonate.

Calculation errors and accidental overdose have been reported in young children in the past due to confusion between the dose prescribed in mg and volume and pose a high risk of paracetamol poisoning owing to their immature liver especially in those with liver disease or chronic malnutrition and may induce complete and irreversible hepatic necrosis.<sup>[3,4]</sup> The Medicines and Healthcare products Regulatory Agency and Safe Anaesthesia Liaison Group thereby conveyed the possibility of accidental overdose in children associated with the use of 100 ml (1 gm) vials.<sup>[4,5]</sup> This may be averted if a stable 0.1% (w/v) paracetamol formulation is introduced whereby, the need for dilution and administration in a separate container will be obviated.

Recent data on drug wastage in the paediatric emergency department found that paracetamol (100 ml vial) was the drug with the highest proportion of mean wastage.<sup>[6]</sup> Smaller vials would be more economical.

Therefore, we suggest that IV paracetamol should also be made available in economically viable smaller volume (5/10/20 ml) or lower concentration formulations (0.1%w/v) for young children. This will promote its utilisation by being user-friendly, reduce accidental overdosage/over-dilution and lead to downturn in the financial burden imposed by drug wastage.

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#### Conflicts of interest

There are no conflicts of interest.

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## REFERENCES

1. Mehrotra S. Postoperative anaesthetic concerns in children: Postoperative pain, emergence delirium and postoperative nausea and vomiting. *Indian J Anaesth* 2019;63:763-70.
2. Paracetamol 10 mg/ml Solution for Infusion. Available from: <https://www.medicines.org.uk/emc/product/2972/smhc>. [Last accessed on 2020 Jul 15].
3. In-use product safety assessment report for Intravenous paracetamol in neonates, infants and. Children- Specialist Pharmacy Service. Available from: <https://www.sps.nhs.uk/wp-content/uploads/2018/07/Paracetamol-IV-risk-assessment-Final.pdf>. [Last assessed on 2020 Jul 27].
4. MHRA Drug Safety Update. July 2010. Intravenous paracetamol (Perfalgan ▼): Risk of accidental overdose. Available from: <https://www.gov.uk/drug-safetyupdate/intravenousparacetamol-perfalgan-risk-of-accidental-overdose>. [Last accessed on 2020 Jul 27].
5. Safe Anaesthesia Liaison Group. Intravenous Paracetamol. May 2013. Available from: <https://www.aagbi.org/sites/default/files/intravenousparacetamol.pdf>. Last accessed on 2020 Jul 27].
6. Bucak IH, Almis H, Dogan CN, Turgut M. The status of drug wastage in the pediatric emergency department of a tertiary hospital. *Avicenna J Med* 2020;10:10-4.

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