Potentially life-threatening intravenous acetaminophen overdose in a 3-month-old (40 weeks’ post-menstrual age), 2.3 kg baby girl

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ABSTRACT

A case is presented of a serious, potentially life-threatening intravenous acetaminophen overdose in a 3-month-old (40 weeks’ post-menstrual age), 2.3 kg baby girl. The neonate was scheduled for urgent laser therapy for retinopathy of prematurity. Instead of an intended intravenous Hartmann’s solution bolus of 10 ml·kg⁻¹, the neonate received a 17 ml bolus of correctly labelled intravenous 1% acetaminophen. The National Poisons Bureau was immediately contacted for advice and in the absence of data suggested a treatment with N-acetylcysteine for a 24-hour period. Baseline blood samples for clotting, liver function, urea and electrolytes, full blood count and plasma acetaminophen concentration were taken 30 min, 8.25 h, 12.5 h, 18.5 h and 120 h after the overdose. Acetaminophen concentration was 78 mg·L⁻¹ at 30 min but was undetectable at any other time. All other parameters were

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within normal limits throughout. There were no clinical sequelae.

Until recently, only limited information of the pharmacokinetics (PK) and pharmacodynamics (PD) in the neonate were available and universally known [1]. Using this recent and most complete PK-PD dataset we are able to show that the measured plasma acetaminophen concentration fits well on PK estimates for acetaminophen in this neonate (Figure 1). The non-detectable (low) plasma acetaminophen concentrations at >8 h are also consistent with this model, especially if clearance is slightly increased in the premature nursery graduate.

Several publications in the literature report the acetaminophen PK in neonates, albeit mostly for non-intravenous routes of administration. The volume of distribution of acetaminophen at birth is 174% in that of older children [2] and the CYP2E1 is immature in neonates and unable to produce the toxic metabolite N-acetyl-p-benzoquinone-imine (NAPQI). Although theoretically possible, hepatotoxicity is, therefore, rarely seen clinically in neonates [3,4].

Although specific data on the likely toxicity of intravenous paracetamol overdose in the neonate are sparse, it is known that the clearance of acetaminophen is reduced in older infants, which in overdose may mean that any treatment with N-acetylcysteine may have to be extended until acetaminophen levels are below toxic concentrations [5].

A study of the developmental pharmacokinetics in premature neonates through to infancy has suggested the following age-appropriate dosing to maintain a mean steady state target concentration >10 mg·L⁻¹ at trough ~25 mg·kg⁻¹·d⁻¹ in premature neonates at 30 weeks’ post-conceptual age, 45 mg·kg⁻¹·d⁻¹ at 34 weeks’, 60 mg·kg⁻¹·d⁻¹ at term and 90 mg·kg⁻¹·d⁻¹ at 6 months of age [6]. The potential for hepatotoxicity may exist in some patients if it’s used for longer than 2 - 3 days. In the presented patient, the lack of changes in liver function and clotting could be attributed to her likely immaturity of oxidative clearance pathways.

Medical errors are rarely the fault of an individual and they are often due to a combination of factors. Contributing factors, in this case, can be described under the following headings: Catalyst event, system fault, loss of situational awareness, of course human error. Safety barriers, which could potentially trap and mitigate such medical error, would need to be multifaceted in the approach and acted synergistically. Area of interest would come from technology, proficiency, standard operating procedures, and judgment.

The final barrier of patients’ harm, with respect to this child i.e. the early recognition of the error, was not breached. Had the error been recognized much later, or not recognized at all, it can only be speculated that the clinical outcome could have been very different.

REFERENCES


Figure 1. Simulated acetaminophen plasma concentration in this 3 months old, 2.3 kg, 40 weeks post menstrual age baby girl based on the PK dataset [1].