



## De-mystifying the “Mixifusor”

**Absolam A et al. Pediatric Anesthesia, 2020; 30(12): 1292-1298**

Total Intravenous Anesthesia (TIVA) using a combination of propofol and remifentanyl in the same syringe has become a common and accepted technique in Paediatric Anaesthesia. This commentary outlines a recent publication in Pediatric Anesthesia from a group of UK paediatric anaesthetists who performed a service evaluation assessing the safety and efficacy of a propofol/remifentanyl mixing technique in around 900 cases looking at complications and adverse reactions. The commentary also discusses potential issues from a pharmaceutical, pharmacokinetic and medico-legal standpoint.

### Findings

Potential issues from a pharmaceutical perspective included physical stability of the emulsion, changes in drug concentration over time, non-uniform mixing and risk of bacterial contamination.

From a pharmacokinetic point of view when delivered as a propofol target controlled infusion (TCI), remifentanyl is not targeted and passively follow the predicted plasma or effect site concentrations of propofol. Consequences include potential rapid increase and peak in remifentanyl concentrations risking apnoea, bradycardia and hypotension particularly with concentrated doses (>10mcg/ml) and the faster decline risks inadequate analgesia and patient movement.

Medicolegal considerations include creating a new, unlicensed drug taking responsibilities of the manufacturer and thus consequences of its administration. If a critical incident or harm does occur, then the clinician’s practice may result in criticism.

### Take home messages

If you chose to mix, adverse reactions are unlikely particularly if lower concentrations of remifentanyl (5mcg/ml) are used. If using a TCI model perhaps consider a staged approach to the initial TCI target rather than achieving it in a single step to minimise the transient remifentanyl overdose at the commencement of the infusion. If an adverse event does occur, the individual must be cautious regarding liability and potential medicolegal consequences.

**Reviewed by Dr Justin Hii**

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**Ultrasound assessment of gastric emptying time after intake of clear fluids in children scheduled for general anaesthesia – A prospective observational study**  
Beck C et al. *Pediatric Anesthesia*, 2020; 30(12): 1384-1389

This is a small prospective study examining the effect of clear fluid intake on gastric antral area (GAA), which was used to represent gastric emptying. 26 children on elective surgical lists were recruited at a single university hospital site in Germany. They had an initial ultrasound to measure their gastric antral area. The children were then given either water or clear fruit juice (approximately 5ml/kg – median 4.7ml/kg, range 1.8-11.8ml/kg) and had serial ultrasounds to measure GAA. GAA increased initially before returning to pre-fluid levels between 30 and 45 minutes. After 1 hour, the GAA had returned to baseline for 20 children but not in four children with a fluid intake greater than 5ml/kg.

**Commentary**

Many paediatric centres have made changes towards a shorter fasting time for clear fluids from two hours to one hour. This study attempts to give scientific evidence towards this decision. It uses a sensible and easy to follow method.

The authors acknowledge the small number of participants would make it difficult to find any potential complications of fluid intake, so it uses GAA as a surrogate marker. The small number of participants would still allow the study authors to detect a 7.5cm<sup>2</sup> increase in GAA (to a 90% statistical power), although it is not clear the significance of this measurement. The amount of fluid taken does vary from 1.8 to 11.8ml/kg.

I feel this study does support the change that many paediatric centres have made towards a 1 hour fasting regime for clear fluids, however the initial increase in GAA may suggest that free fluids up until theatre is not the safest practice.

**Reviewed by Dr Patrick Cowie**

**Current state of noninvasive, continuous monitoring modalities in pediatric anesthesiology**

van Wijk J et al. *Current Opinion in Anaesthesiology*, 2020; 33(6): 781-787

The increase in safety in anaesthesia is at least partly attributable to the improvement of intraoperative monitoring. This review examines the literature to ascertain the status of development and evidence around continuous, non-invasive monitoring modalities used in the paediatric population undergoing anaesthesia for non-cardiac surgery. The modalities examined

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include haemodynamic monitoring (continuous non-invasive blood pressure), non-invasive cardiac output monitors, near-infrared spectrometry (NIRS) and transcutaneous blood gas analysis.

### Take home messages

- Non-invasive blood pressure measurements – NIBP is generally lower when taken from the leg compared to the arm in the paediatric population (converse to the adult population). Continuous measurements of blood pressure using finger clamp cuff technology generally provides accurate diastolic and mean arterial pressure but under reads the systolic blood pressure.
- Cardiac output monitoring – various techniques are available and include pulse contour analysis (from a non-invasive blood pressure finger cuff technique), bioimpedance and bioreactance. No method has currently demonstrated sufficient accuracy with up to 45% error reported compared to the gold standard of an invasive thermodilution technique.
- Near infra-red spectrometry (NIRS) – NIRS measures the regional tissue oxygenation (r-SO<sub>2</sub>) and is not a form of pulse oximetry. An absolute lowest NIRS value for safety is still yet to be defined. However, a reduction of 20% from baseline has been shown to negatively impact patient outcome. Combining NIRS with a measurement of peripheral muscle regional tissue oxygen to produce a ratio is an area of growing interest and could provide an early identification of centralisation.
- Transcutaneous blood gas analysis – this method of measuring carbon dioxide is useful for those patients without instrumented airways. It functions by heating the skin locally to enable diffusion of carbon dioxide through the skin to be measured. This method is accurate and has been shown to be more closely correlated to PaCO<sub>2</sub> than end tidal CO<sub>2</sub>.

Reviewed by Dr Gihan Ganesh

## Early Childhood General Anesthesia and Neurodevelopmental Outcomes in the Avon Longitudinal Study of Parents and Children Birth Cohort

Walkden G et al. *Anesthesiology*, 2020; 133(5): 1007-1020

Preclinical studies have demonstrated that many general anaesthetic agents cause accelerated neuronal apoptosis after extended exposure in early development. Recent evidence has however demonstrated that a brief exposure to general anaesthesia in infancy does not result in poorer childhood neurocognitive testing outcomes. Neurodevelopmental and behavioural outcomes have mixed but generally poor level evidence. The hypothesis of this study was that exposure to general anaesthesia and surgery before 4 years would be associated with adverse neurodevelopmental outcomes at ages 7 to 16 years.

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## Findings

This large longitudinal cohort study of 13 433 children in Southwest England compared children who were exposed to anaesthesia and surgery with children who were not exposed before 4 years of age. Children were grouped by none, single or multiple exposures. The paper looked at 46 neurodevelopmental outcomes including motor, cognitive, linguistic, educational, social and behavioural.

Overall, there was no evidence for a global picture of clinically nor statistically significant long term neurotoxic effects between 7 and 16 year olds. General anaesthesia and surgery were not associated with impairments in general cognitive ability, attention, working memory, reading, spelling, verbal comprehension or expression, behavioural difficulties, English, mathematics and science assessments.

In all the outcomes the only statistically significant differences were evidence of increased risk of poorer motor function and social communication. Exposed children had lower scores for heel to toe walking and peg placing tasks which corresponded to at most one step in the heel-to-toe walking test and a 2 second difference in the peg placing task. Singly exposed children had a lower word reading efficiency which corresponded to at most a two word performance difference.

The children in this cohort would have undergone anaesthesia between 1991 – 1997 and since then widespread improvements in anaesthesia techniques, levels of monitoring and training have occurred. Such changes are likely to have improved paediatric anaesthesia care providing greater reassurance.

## Take home messages

Early childhood general anaesthesia and surgery were not associated with a global picture of clinically and statistically significant neurodegenerative effects between 7 and 16 year olds, providing reassurance about the neurotoxic potential of general anaesthesia. There were some associated motor and social linguistic impairments, which although statistically significant may not be clinically significant.

**Reviewed by Dr Justin Hii**

**Edited by Dr Su May Koh**

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