Paediatric Anaesthesia Update

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Hypotension in Neonates Under Anaesthesia

What we know

- Up until recently, the observation that 'the infant woke up fine after my anaesthetic' has been the standard by which we have assessed neurocognitive outcomes.
- There is little evidence to support our definitions of hypotension of infants/neonates in common practice. Blood pressure can be a poor surrogate for perfusion.
- Infants have less cerebral auto regulatory reserve and are at higher risk for inadequate cerebral perfusion.

What this update adds

- Hypotension is not uncommon during neonatal anaesthesia.
- Intraoperative hypotension has been linked to poor postoperative neurological outcomes.
- While 'neurotoxicity of anaesthesia' grabs the headlines, cerebral oxygenation and perfusion changes associated with anaesthesia may also be a contributing factor to the neurological outcome. Indeed, hypotension and hypocapnia may be the most common avoidable complications occurring during anaesthesia in neonates.
- Cerebral desaturation detected by Near Infrared Spectroscopy (NIRS) is linked to neurological damage in humans for both extent of desaturation and duration.
- The association between blood pressure changes in infants having anaesthesia and changes in regional cerebral oxygen saturation (rScO2) using (NIRS) is described, with cerebral desaturation occurring in more than 90% of whose BP drops by more than 35% of baseline.

Management recommendations

- Anaesthetic management should focus on optimising organ perfusion and not merely on maintaining a particular blood pressure.
- Paediatric anaesthetists need to be vigilant in managing blood pressure variability in neonates, limiting substantial reductions in all neonates to no more than 20% lower than baseline.
- NIRS is a simple addition to intraoperative monitoring to estimate cerebral perfusion, especially when looking at within-patient trends.
- Though not necessary for all infants, NIRS is helpful is monitoring at-risk patients like the premature neonate, infants with cardiac abnormality or having cardiac surgery, those having extensive or prolonged surgeries like diaphragmatic hernia or tracheooesophageal repair, and severely sick infants like those with necrotising enterocolitis.

Fasting

What we know

- Due to the concern regarding aspiration, most fasting guidelines suggest a 6, 4, 2 rule (6 hours of starvation for food, 4 hours for breast milk, and 2 hours for clear fluids).
- Fasting for prolonged periods in children has been shown to increase thirst and irritability, result in greater reductions in systolic blood pressure on induction and to induce a catabolic state.
- Shortened fasting times for clear fluids improves patient perioperative experience and comfort with regards behaviour, anxiety, hunger, thirst, haemodynamic conditions and vascular access.

What is new in this review

- A 2-hour clear fluid fasting policy, even when proactively managed, results in an actual fasting time of between 4 and 13 hours.
- More paediatric hospitals are considering a liberal clear fluid regime for children not at risk for aspiration, allowing free clear □uids until called to the operating suite.
- Incidence of pulmonary aspiration is no higher with a liberal fluid regimen the than with a 2-hour rule.
- Institutional Quality Improvement (QI) processes has shown to be effective in improving fasting times.

Management recommendations

- Suggestion for a more liberal fasting regime (6-4-0 fasting regime) for low aspiration-risk cases.
- Fasting in children is an important patient-focused quality factor for care and should be incorporated into a QI process. A liberal fasting time for fluids needs to be married with other QI methodology, measuring times, targeting specific key drivers and interventions, educating and empowering ward staff, reducing confusion over procedure start times, giving parents accurate information, and reducing variation.

Tramadol and Codeine

What we know

- Children with known respiratory disease have increased opioid sensitivity. Of particular concern are those with obstructive sleep apnoea secondary to tonsillar hypertrophy or obesity.

Codeine

- Codeine is a prodrug with no analgesic effect. It must □rst be metabolised in the liver to its active metabolite, morphine.
- There genetic variability in its hepatic conversion, some children being poor metabolisers who will have less analgesic bene□t, and others who are extensive or “ultra-rapid” metabolisers who will produce higher levels of morphine.
- Within the past several years, an increasing number of case reports have illustrated clinically important respiratory depression, anoxic brain injuries and death among children receiving appropriate weight-based dosages of codeine for analgesia at home, particularly following tonsillectomy.
- Several national and international organizations (WHO, EMA, FDA) have issued advisories on the use of codeine in paediatrics, based on CYP2D6 pharmacogenetics.

Tramadol

- Tramadol is a weak opioid agonist with active analgesic activity.
- Tramadol is mainly metabolised to an inactive metabolite, and minimally through CYP2D6 to O-desmethyltrama-dol, which has a 200-fold greater affinity for opioid receptors than the parent drug.
- FDA has issued advisories on the use of tramadol in children.

What this update adds

- The warnings on the use of codeine in paediatrics are justified.
- Tramadol is not codeine and, despite the FDA warning, tramadol still a reasonable choice of analgesia for children.
- Tramadol overdose is a greater danger than CYP2D6 variants. None of the reported tramadol deaths were related to the metabolites, but rather over dosage itself, OSA and obesity.
- The droplet formulation of tramadol should no longer be available in New Zealand and has been replaced with a more preferable tramadol 10 mg/ml elixir.
- One drug that could replace tramadol is tapentadol, a drug with similar mechanism of action to tramadol but analgesic activity that is independent of enzyme systems and that has no active metabolites.

– Pharmacogenetics is an exciting and rapidly expanding □eld. The clinical availability, affordability, and practicality of personalised pharmacogenetics and prescribing remains to be seen.

Management recommendations

- Codeine offers no unique benefits over other opioids and has several well-documented negatives. It should not be used in children under 12 years old.
- A multimodal opioid-sparing analgesia strategy reduces the need for perioperative opioid use.
- Tramadol is still a reasonable choice of analgesia.
- Tramadol dose should be limited for acute pain after tonsillectomy (e.g. dose 1 mg/kg 6-8 hourly, max 400 mg/day). Children with OSA who have undergone tonsillectomy should be monitored in hospital overnight.

Anaesthesia-Induced Developmental Neurotoxicity

What we know

– There is compelling evidence from animal and laboratory studies suggesting that early exposure to general anaesthesia is detrimental to normal brain development, leading to structural and functional impairments of neurons and long-lasting impairments in normal emotional and cognitive development.
– The evidence from human studies is inconsistent and not conclusive at present. Up until recently, the vast majority of human studies were retrospective cohort studies. The findings were mixed but generally show weak evidence for an association though all have major weaknesses of confounding factors.
– In December 2016, the FDA issued a warning statement regarding the use of anaesthesia or sedation in young children highlighting potential risk of anaesthetic procedures that last longer than 3 hours or multiple procedures required in children less than 3 years of age. Evidence to support such warning is currently insuf□cient and incomplete.

What this update adds

– Some of the most important studies have appeared recently. Discussion focuses on new developments in translationally relevant NHP animal studies of anaesthesia-induced developmental neurotoxicity and summary of five recent human clinical studies: three large population-based studies; and two prospective human trials, the General Anaesthesia compared to Spinal anaesthesia (GAS) trial and The Paediatric Anaesthesia Neurodevelopment Assessment (PANDA) trial.
– These studies do allow us to draw some cautious conclusions: that short-term single exposure of 60 minutes or less to surgery and anaesthesia is not associated with measurable long-term neurodevelopmental problems.

Management recommendations

– Neurotoxicity of anaesthetic agents is an important issue for anaesthetists, but we need to place it into context of other confounding stresses on brain development and how the potential risk of anaesthesia could change practice. Should we modify the anaesthetic technique, delay surgery until older, or treat with drugs that may attenuate any harmful effects?
– The ESA/ESPA/EACTA/EuroSTAR consensus statement amount to a pragmatic and sensible two statements:

1. No child or pregnant woman should ever undergo any medical procedure that is not necessary or done for trivial reasons.

2. Established safe anaesthetic techniques delivered by trained and experienced staff in a paediatric environment supported by the necessary clinical organisation are essential factors for the delivery of safe anaesthesia and sedation in children.

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