

PAEDIATRIC UPDATE – A PROBLEM BASED APPROACH

Dr Ben van der Griend

Christchurch Hospital
Christchurch

Running late for your afternoon private list at St Elsewhere's, you meet little Johnny, a snotty-nosed three year old scheduled for an adenotonsillectomy for treatment of his snoring. His mother is very anxious and dad is outside having a cigarette. He weighs 12 kg.

Discussion Points:

1. Notes on obstructive sleep apnoea
2. Consent – Is anaesthesia safe?
 - a. Risk of death
 - b. Risk of neurotoxicity
3. ETT cuffed vs uncuffed
4. Intraoperative management
5. Fluids
6. Post operative analgesia – What's up with codeine?

1. Obstructive Sleep Apnoea (OSA)

OSA has incidence of 1-3% and in young children presentation differs compared to adults. Adenotonsillectomy improves >75% (cases with severe OSA or obesity are less likely to improve).¹

Looking at this case, risk factors include a history of snoring and the fact that he is a somewhat underweight for his age. Forty percent of snorers have OSA but OSA cannot be reliably diagnosed on history. Other risk factors (not present here) include congenital syndromes and cranial facial abnormalities, obesity, allergic rhinitis, etc.

On history, some good questions to ask include – does your child have difficulty breathing during sleep and are you worried about your child's breathing at night? Have you observed pauses in their breathing? Does your child have a restless sleep? Have you observed sweating? Does your child have behavioural problems?¹

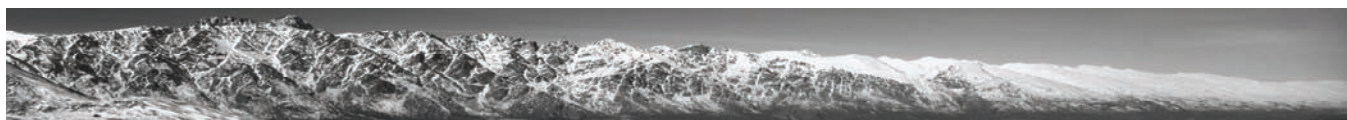
The gold standard for diagnosis is polysomnography (sleep study). However, practically very few children get a sleep study. It maybe useful for risk stratification or to rule out those with central apnoeas vs obstructive apnoeas (eg syndromic children). Echocardiography is reserved for children with signs of RV dysfunction.¹

Consider booking a HDU bed for children younger than 24 months, those that are very underweight (<3rd centile) or with morbid obesity and those with significant neuromuscular disease, syndromes prone to airway obstruction, complex congenital heart disease, or cor pulmonale / pulmonary hypertension.²

2. Consent – Is Anaesthesia Safe?

2a. Risk of Death

ANZCA produces a triennial report on anaesthesia-related mortality. Inevitably, there are a number of problems encountered with mortality estimation but despite limitations, ANZCA "guesstimates" the anaesthesia related mortality rate was 1:55,490 or 0.18 per 10,000 anaesthetics. Looking specifically at paediatric anaesthesia-related mortality there is very little data provided.³



A recent audit from the RCH, Melbourne (shameless plug for my own paper) looked at mortality from 101,899 anaesthetics administered to 56,277 individuals. This provided good data that did not rely on voluntary reporting.⁴

Overall 24 hour mortality was 14.7 per 10,000 anaesthetics delivered and mortality within 30 days was 34.5 per 10,000. Cardiac surgery had a higher incidence of 24 hour (131.5 per 10,000 anaesthetics) compared with non cardiac surgery (9.4 per 10,000 anaesthetics). The group of patients with the highest 24 hour mortality were neonates undergoing cardiac surgery (≤ 30 days old) with a 24 hour mortality of 194 per 10,000 anaesthetics.

There were 10 cases from 101,899 anaesthetics of anaesthesia-related death identified, ie those cases whereby anaesthesia or factors under the control of the anaesthetist, influenced the timing of death. Therefore, in this audit, the incidence of anaesthetic-related death is 1 in 10,190 or 0.98 cases per 10,000 anaesthetics performed. This is much higher than the ANZCA data and other data from overseas.

In all 10 cases, pre-existing medical conditions were identified as being a significant factor in the patients' deaths. Five of these had severe pulmonary hypertension (top of my list for patients to avoid). Importantly, this demonstrated that anaesthesia is safe in children with no or minor medical problems. Interestingly there were no airway-related anaesthetic deaths.

2b. Risk of Neurotoxicity

This whole debate was sparked by a discovery in 1999 that 7 day-old neonatal rats brains exposed to NMDA receptor antagonists (including ketamine) for some hours undergo apoptosis.⁵

Apoptosis is simply programmed cell death as opposed to necrosis which is cell death from some sort of injury. In the brain, redundant neurons undergo apoptosis. During the brain's 'growth spurt' period neurons undergo synaptogenesis - the neurons are trying to connect with each other. It is thought that those that don't make connections, the redundant neurons, undergo apoptosis. However, the apoptosis seen following exposure to ketamine is by far more prolific than what is normal.

Most of the anaesthetic agents have now been implicated including midazolam, isoflurane and propofol.⁶ There appears to be a synergistic effect when multiple agents are given together. Interestingly, there is not only histological evidence of neurodegeneration, neonatal rats subjected to anaesthesia displayed learning / memory disabilities that persists into their adolescence and adulthood.⁷ There may be some evidence that alpha-2 receptor agonists (clonidine, dexmetatomidine) have some protective effect.⁸

Human studies rely on retrospective cohort studies, which unfortunately have a number of limitations and therefore it is difficult to draw any definitive conclusions. A few large studies have suggested some association between prolonged accumulative / multiple exposure and learning difficulties or behavioural problems.⁹ Of course association does not prove causation. Other studies, typically looking at single brief exposure, are negative. Therefore, it is possible that there is association between anaesthesia exposure and adverse outcome, but this cannot be definitely confirmed or ruled out.⁸

3. ETT: Cuffed vs Uncuffed Tubes

My practice is to intubate kids for tonsillectomies although LMAs are used very commonly and very successfully. Historically, in paediatric anaesthesia, we have used uncuffed tubes. The rule being in children the correct sized tube should pass without resistance through the larynx and should have a slight leak at an inflation pressure of 20 to 25 cm of water.

However the disadvantages of an uncuffed tube include difficulties in ventilation with the presence of leak (especially with changing lung compliance), the need for higher gas flows, the difficulty in estimating the right tube size and subjecting patients to tube changes and, even in the presence of a leak, there is no guarantee against pressure lesions.

Microcuff have improved the design of paediatric ETTs by utilising a high volume / low pressure polyurethane cuff which is designed to sit below the level of the cricoid ring. The thin polyurethane cuff creates a seal at a lower cuff pressure and thus there is a low incidence of post intubation stridor.¹⁰



However, there are disadvantages. For example, a smaller internal diameter tube is required (increased resistance), there is no Murphy eye and they tend to kink when warm and humid. They are also more expensive but this is potentially off-set by cost savings from low-flow anaesthesia.

4. Miscellaneous Aspects of Intraoperative Management

Do I spray the cords? – No, because it probably leads to more problems than what it's worth with an increased incidence of desaturation during anaesthesia.¹¹

Dexamethasone is associated with reduced incidence of PONV and pain¹² and not associated with an increased incidence of bleeding.¹³

5. Fluids

“Super-hydration” with 30ml / kg Hartmanns during the case helps reduce the incidence of post-operative nausea and vomiting.¹⁴

If post-operative fluids are required (very rare), it is important to use a solution with an adequate amount of sodium.

The debate around post-operative fluids began following the publication of a number of cases of children dying or suffering from permanent brain damage as a result of hyponatraemia, primarily caused by a presumed increase in ADH activity followed by the administration of hypotonic fluids.¹⁵

As a reaction to deaths from hospital acquired hyponatraemia in the United Kingdom, The National Patient Safety Agency recommends that 0.18% saline solutions be removed from stock in areas that treat children.¹⁶ The minimum concentration of sodium to be used for maintenance infusions is 0.45% saline. However, there is increasing evidence that isotonic fluids reduces the risk of hyponatraemia^{17,18} and should therefore be used in the postoperative setting.

6. Post-Operative Analgesia (with a focus on Codeine)

A recent case series¹⁹ reported on 2 deaths and one case of life threatening respiratory depression following the administration of codeine to children after adenotonsillectomy. Subsequent to this the FDA initiated an evaluation of the safety of codeine and identified 13 cases (including 10 deaths) associated with therapeutic codeine.²⁰ This has led to the FDA (in the USA) requiring manufacturers to add a boxed warning on the packaging (“black box”) describing the risk posed by codeine following adenotonsillectomy. A contraindication will also be added to restrict codeine use in these patients.

In the UK, the MHRA (UK) published a press release in June this year stating that codeine-containing medicines should not be used in children under 18 years with OSA post tonsillectomy and altogether in children under 12 years for any indication.

Here in NZ, Medsafe have taken a less dramatic approach and urged prescribers to “educate parents and caregivers of young patients about possible adverse effects associated with codeine use.”

Codeine is a prodrug – the activity of which depends on its conversion to morphine by the highly polymorphic CYP2D6 pathway. Poor metabolisers represent 5-10% of the population. Ultra-rapid metabolisers, represent roughly 1-10% of Caucasians and 15-30% of North African descendants. These patients are at risk of morphine toxicity, particularly dangerous in the setting of OSA and opioid sensitivity.

It is interesting to see that the US, UK and European regulatory bodies come out so strongly against codeine when the denominator (number of prescriptions) is huge compared to the handful of complications reported. It is unknown whether the alternatives (morphine, oxycodone) will prove any safer. My practice is to ensure regular paracetamol and non-steroidal analgesia is charted. I don't routinely chart an opioid but if I do, I chart oral morphine elixir.



References

1. Schwengel DA, Sterni LM, Tunkel DE, Heitmiller ES. Perioperative management of children with obstructive sleep apnea. *Anesth Analg*. 2009 Jul;109(1):60-75.
2. Squire, Peter. Obstructive Sleep Apnea *in Clinical Pediatric Anesthesia, A Case-Based Handbook*. Oxford University Press 2012.
3. Gibbs, N (Ed.): Safety of Anaesthesia. A Review of Anaesthesia-related Mortality Reporting in Australia and New Zealand 2003-2005. Melbourne, Australian and New Zealand College of Anaesthetists, 2009.
4. van der Griend BF, Lister NA, McKenzie IM, Martin N, Ragg PG, Sheppard SJ, Davidson AJ. Postoperative mortality in children after 101,885 anesthetics at a tertiary pediatric hospital. *Anesth Analg*. 2011 Jun;112(6):1440-7.
5. Ikonomidou C, Bosch F, Miksa M, Bittigau P, Vöckler J, Dikranian K, Tenkova TI, Stefovskva V, Turski L, Olney JW. Blockade of NMDA receptors and apoptotic neurodegeneration in the developing brain. *Science*. 1999 Jan 1;283(5398):70-4.
6. Gleich S, Nemergut M, Flick R. Anesthetic-related neurotoxicity in young children: an update. *Curr Opin Anaesthesiol*. 2013 Jun;26(3):340-7
7. Jevtovic-Todorovic V, Hartman RE, Izumi Y, et al. Early exposure to common & anesthetic agents causes widespread neurodegeneration in the developing rat brain and persistent learning deficits. *J Neurosci* 2003; 23:876 – 882.
8. Sanders A, Hassell J, Davidson A et al. Impact of anaesthetics and surgery on neurodevelopment: an update. *British Journal of Anaesthesia* 110 (S1): i53–i72 (2013).
9. DiMaggio C, Sun LS, Li G. Early childhood exposure to anesthesia and risk of developmental and behavioral disorders in a sibling birth cohort. *Anesth Analg* 2011; 113:1143 – 1151.
10. Weiss M, Dullenkopf A, Fischer JE, Keller C, Gerber AC et al. Prospective randomized controlled multi-centre trial of cuffed or uncuffed endotracheal tubes in small children. *Br J Anaesth*. 2009 Dec;103(6):867-73.
11. Hamilton N, Hegarty M, Calder A, Erb T, von Ungern-Sternberg B. Does topical lidocaine before tracheal intubation attenuate airway responses in children? An observational audit. *Pediatric Anesthesia* 22 (2012) 345–350.
12. Hermans V, De Pooter F, De Groote F, De Hert S, Van der Linden P Effect of dexamethasone on nausea, vomiting, and pain in paediatric tonsillectomy *Br J Anaesth*. 2012 Sep;109(3):427-31.
13. Gallagher TQ, Hill C, Ojha S, Ference E, Keamy DG, Williams M, Hansen M, Maurer R, Collins C, Setlur J, Capra GG, Brigger MT, Hartnick CJ. Perioperative dexamethasone administration and risk of bleeding following tonsillectomy in children: a randomized controlled trial. *JAMA*. 2012 Sep 26;308(12):1221-6.
14. Elgueta MF, Echevarría GC, De la Fuente N, Cabrera F, Valderrama A, Cabezón R, Muñoz HR, Cortinez LI. Effect of intravenous fluid therapy on postoperative vomiting in children undergoing tonsillectomy. *Br J Anaesth*. 2013 Apr;110(4):607-14.
15. Arieff AI, Ayus J, Fraser C. Hyponatremia and death or permanent brain damage in healthy children. *BMJ* 1992;304: 1218 –22
16. National Patient Safety Agency. Reducing the Risk of Hyponatraemia when administering intravenous infusions to children. Patient safety alert 22. Ref. NPSA/2007/22.
17. Choong K, Arora S, Cheng J et al. Hypotonic Versus Isotonic Maintenance Fluids After Surgery for Children: A Randomized Controlled Trial. *Pediatrics* 2011;128:857
18. Neville KA, Sandeman DJ, Rubinstein A, Henry GM, McGlynn M, Walker JL. Prevention of hyponatremia during maintenance intravenous fluid administration: a prospective randomized study of fluid type versus fluid rate. *J Pediatr*. 2010 Feb;156(2):313-9
19. Kelly LE, Rieder M, van den Anker J, et al. More codeine fatalities after tonsillectomy in North American children. *Pediatrics* 2012; 129(5):e1343-e1347.
20. Racoosin JA, Roberson DW, Pacanowski MA, Nielsen DR. New evidence about an old drug--risk with codeine after adenotonsillectomy. *N Engl J Med*. 2013 Jun 6;368(23):2155-7.

