Transnasal humified rapid-insufflation ventilators exchange (THRIVE) in children: a randomised controlled trial.

Humphries et al;

BJA, 118(2):232-8 (2017)

This prospective randomised controlled trial and its accompanying editorial explores the effectiveness of THRIVE in prolonging safe apnoeic oxygenation time in infants and children. The study also looked at the effectiveness of CO2 clearance using this technique.

The study involved 48 children from 0-10 years old with normal airways and cardiovascular system, presenting for elective surgery. Following standardised anaesthetic induction, the patients were divided in to the control group receiving jaw thrust only during apnoea and the THRIVE group receiving jaw thrust and age specific flow rates of oxygen with the THRIVE device. Apnoea time was calculated as time for drop of SPO2 to 92% in the control group and as time that exceeded twice the published apnoea time, at which ventilation was resumed. Transcutaneous haemoglobin, saturation and CO2 were monitored.

The use of THRIVE significantly prolonged the apnoeic time with the SPO2 recorded at an average of 99.6% during the apnoeic phase. The increase in transcutaneous CO2 was similar in both groups. The heart rate decreased during apnoea in both groups. No other complications were recorded. The study did not assess the maximum allowable apnoea time with THRIVE in infants and children.

Take home message:

This study addresses the paucity of data on the safety and efficacy of THRIVE in infants and children with respect to anaesthetic management. The use of THRIVE doubles the safe apnoeic oxygenation time and will have useful implications in safe management of difficult airways in this age group. The issues with hypercarbia may persist with prolonged apnoea and it remains to be seen whether other factors such as flow rates have a role in reducing the rate of CO2 rise during this phase with THRIVE. The role of THRIVE in airway surgery and maintenance of apnoeic ventilation is unclear and will need further studies in children.

Reviewed by: Priya Sreedharan

Patency of paediatric endotracheal tubes for airway instrumentation.

J. Elfgen, P. K. Buehler, J. Thomas, M. Kemper, S. Imach and M. Weiss

Acta Anaesthesiologica Scandinavica 61 (2017) 46–52

This is a bench top study that assess the ease of passage of fibre-optic bronchoscopes (FOB) and airway exchange catheters (AEC) through paediatric endotracheal tubes. The study examined paired cuffed and uncuffed ETTs from 12 different manufacturers and from different production runs (i.e. the same manufacturer). In total, they examined 306 FOB insertions and 600 AEC insertions in a randomised manner.

They demonstrated that if the manufacturer's recommendations are followed there is a 63.6% difficulty with FOB insertion and 23.2% difficulty with AEC insertion. They demonstrated significant differences both between manufacturers and within the same brand.

Take home message:

This article demonstrates the inaccuracy of recommendations for compatible sizes of endotracheal tubes and FOB or AEC in order to provide minimal impingement during insertion and removal. .Both the sensible conclusion of the article and the editorial comment are to test the specific equipment combinations before attempting to use them in a patient. This reinforces current practice.

Reviewed by: Rob Laing

Children and parental anxiolysis in paediatric ambulatory surgery: a randomized controlled study comparing 0.3mg kg^{-1} midazolam to tablet computer based interactive distraction.

Marechal et al.

British Journal of Anaesthesia, 118 (2): 247–53 (2017)

This is a study similar to Seiden et al.[1], that had shown that Tablet interactive distraction reduced perioperative anxiety, emergence delirium, and time-to-discharge and increased parental satisfaction when compared to midazolam in paediatric patients undergoing ambulatory surgery. In this study, Marechal et al., randomised 118 4-11 year olds to either 0.3mg kg^{-1} of midazolam or Tablet-based interactive distraction. Anxiety levels were assessed at baseline, time of parental separation and anaesthetic induction. Data for emergence delirium, nursing and parental satisfaction, and time-to-PACU discharge were also collected.

Bottom line:

Tablet-based distraction was as effective as, but "not superior" to midazolam at blunting anxiety in children undergoing ambulatory surgery based on anxiety scores. However, the subjective satisfaction with induction of anaesthesia as judged by nurses and parents was better in the tablet group.

1. Seiden, S. C., McMullan, S., Sequera-Ramos, L., De Oliveira, G. S., Roth, A., Rosenblatt, A., Jesdale, B. M. and Suresh, S. (2014), Tablet-based Interactive Distraction (TBID) vs oral midazolam to minimize perioperative anxiety in pediatric patients: a noninferiority randomized trial. Paediatr Anaesth, 24: 1217–1223.

Reviewed by: Michael Heytman

Higher risk of opioid-induced respiratory depression in children with neurodevelopmental disability: a retrospective cohort study of 12 904 patients

M. A. Jay B. M. Thomas R. Nandi R. F. Howard.

Br J Anaesthesia (2017) 118 (2): 239-246.

The study aims to quantify, examine and gain understanding of the risks of Opioid Induced Respiratory Depression (OIRD) in heterogeneous group of children with neurodevelopmental disorders.

A well designed single center retrospective analysis of prospectively gathered clinical data to rigorous, mandatory protocol. All children (12904) who underwent major surgery at Great Ormond Street Hospital requiring Morphine NCA from 1996 to 2011 were identified. They were divided in to groups with and without neurodevelopmental disabilities based on data entered, clinical diagnoses or presence of evidence of neurodevelopmental delay on examination. Data on various confounders, administration of intra operative opioids, morphine NCA dose protocol, overall morphine use, occurrence of respiratory depression, serious adverse effects and patient satisfaction for each patient were collected and analyzed. Respiratory depression was defined as a drop in respiratory rate below that stipulated by prescriber.

19 % (n=2390) of the children had neurodevelopmental disorders (NDG), they tended to be heavier, more prone to OSA, had longer duration of surgery and needed Morphine NCA for longer. The cumulative Incidence of respiratory depression in NDG *vs* control group CG was 1.09% *vs* 0.59 %(odds ratio1.65). On subgroup analysis patients with cerebral palsy, Down's syndrome or encephalopathy appear to be at most risk (1.68, 1.84 and 2.53 *vs* 0.59%). Risk of OIRD increased with increasing doses of post-operative Morphine in NDG. Cumulative incidence of serious adverse events which included instances of respiratory depression needing naloxone was 0.59 % (NDG) *vs* 0.36% (CG). Half of the serious adverse events and respiratory depression occurred on day 0 and 92% within 48 hours in both groups. Increasing Age decreased the risk of both respiratory depression and serious adverse events.

Gender, presence of renal impairment, OSA, administration of intra-operative opioids, NCA bolus size and overall post-operative morphine dose on Day 0 were all **not** significant predictors of OIRD. Overall satisfaction was very good or good in 98% patients but satisfaction in NDG was 1.2 % more likely to be rated fair or poor.

Take home message:

Despite OIRD being a predictable side effect, children with neurodevelopmental disorders are 1.65 times more likely to be affected, there is no significant increase in serious adverse events attributable to post op Morphine NCA use.

Reviewed by: Sadhish Shanmugam

Accuracy of dispersing tramadol capsules for oral administration in young children.

M Kluger et al

AnaesthIntensiveCare 2016 44(6): 742--4

While tramadol is not licensed in Australia for use in children under the age of twelve, many institutions are using preparations of tramadol as an analgesic in young children because of its lower incidence of side-effects such as respiratory depression, constipation and sedation. Due to the limited preparations, it is difficult to provide the appropriate dose to children without risk of error.

In this study, 20 volunteer nursing staff were asked to prepare a mock 15mg dose of tramadol using a 50mg tramadol capsule, their choice of syringe, water for dilution and medicine cup for mixing. The concentration of tramadol in the syringe and mixing cup was measured using high performance liquid chromatography. The mean tramadol dose prepared was 15.3mg (range 13.9-17.1mg, SD 0.8mg). The highest dose was 14% greater and the lowest was 7% lower than intended. 19/20 (95%) of the mock preparations were within 10% of the intended dose.

Take home message:

This study demonstrates that the dispersion method is a safe approach for tramadol preparation by nurses. The risk associated with this method of dose preparation would be less than the use of the highly concentrated 100mg/mL oral drops and can provide a suitable analgesic option for patients discharged from hospital. Even if a child received the highest dose prepared in this study over a 24-hour period, the child would receive an extra 1mg/kg/day, which is not associated with any adverse effects.

To make it safe for discharge, appropriate training of parents is essential. The use of an information/instruction pamphlet, such as the one used at RCH Melbourne[1] can improve the understanding for parents if tramadol is required at home.

1. (www.rch.org.au/uploadedFiles/Main/Content/pharmacy/ drug_information/Tramadol%20administration%20fact%20 sheet.pdf)

Reviewed by: Scott Ma

Paravertebral block in paediatric abdominal surgery- a systematic review and meta- analysis of randomised trials

Page et al,

BJA; 118(2): 159-66 (2017)

This review of RCTs evaluating the paravertebral block in children 0-18 years of age undergoing abdominal surgery. Six trials enrolling 358 patients were identified and paravertebral blocks were compared with other analgesic regimens that were comparable.

Surgical procedures included inguinal herniorraphy, cholecystectomy and appendectomy. The local anaesthetic agents used in the block included Lignocaine, Ropivacaine and bupivacaine with or without fentanyl. There was a limited reduction in the early pain scores. VAS pain score showed a difference of 0.85 at 6 h and 0.64 at 24 hrs.

The difference in pain scores was more significant in inguinal herniorraphy as was the difference in the rate of same day discharge, in favour of the Paravertebral block. There was a small benefit of paravertebral blocks reducing rescue analgesia but not for time to first analgesic requirement. There was higher parent and surgeon satisfaction in the three trials involving paravertebral blocks in inguinal herniorraphy.

There was no reduction in the incidence of postoperative nausea and vomiting in any of the trials. There was a higher incidence of site tenderness of 8.4% in this review than other studies have suggested. No major complications were recorded in any of the included trials.

Ultrasound guided paravertebral blocks have higher success rate and appear to be effective in reducing early pain with some site tenderness.

Take home message:

Paravertebral block may be an acceptable analgesic alternative in abdominal surgery, especially with ultrasound use to improve accuracy, although the reduction in pain scores at 24 hours was minimal. Parental satisfaction may be higher as compared to caudal blocks due to absence of motor block in older children.

Reviewed by: Priya Sreedharan

Paediatric Lung Isolation

Letal et al

BJA Education 2017; 17(2): 57-62

One lung isolation can be challenging in the paediatric population especially in those <2 years. This review articles discusses indications for lung isolation and an approach using the 'ABCDs' (anatomy, bronchoscopy, chest imaging and diameter of the paediatric airway) variation of Slingers method for the paediatric patient. In addition, the age appropriate methods of lung isolation were discussed included benefits and pitfalls and displayed in a comprehensive table. The preferred methods for isolation according to age are as follows:

Age	**Method**
0-6 months	Bronchial intubation with single lumen endotracheal tube
6 months – 2 years	Bronchial blocker using parallel technique
2 – 8 years	Bronchial blocker using coaxial technique
8 – 18 years	Double lumen tube

Take home message:

It forms a useful reference article when faced with a situation requiring lung isolation.

Review by: Sorcha Evans

Oral Morphine dosing predictions based on a single dose in healthy children undergoing surgery.

Dawes J, Cooke E, Hannam J et al.

Pediatric Anesthesia 2017. 27. 28-36.

Methods: 34 children, mean age 4.1 (SD 1.2) years, undergoing elective surgery, were randomised to receive preoperative oral morphine 100mcg/kg, 200mcg/kg, or 300mcg/kg. Blood levels were measured at 30, 60, 90, 120, 180 & 240 minutes post dose. This data was then pooled with data from previous studies (n=1059) investigating the pharmacokinetics of IV morphine to enable the characterisation of the absorption parameters of oral morphine. These parameters were then used to predict plasma concentrations in children given various doses of oral morphine at different dosing intervals. Adverse drug reactions (ADR) were assessed during the 4hour study period and also reported via a 24hr follow up phone questionnaire.

Results & discussion: A serum concentration between 10 -20 mcg/L has been associated with good analgesia following intravenous morphine administration. Oral morphine 100cg/kg was consistently associated with serum values below 10mcg/L at 60min and a mean Cmax of 6.8mcg/L. Children given 200mcg/kg or 300mcg/kg achieved higher mean Cmax of 16.4 and 24.1 mcg/L respectively. There were no significant ADR during the 4hr study period. ADR were reported in 18/31 cases (58%) at the 24hr follow up. 10 of the 18 had received IV opiates after the 4hr study period and the majority of these were in the 300mcg/kg dose group.

Dosing predictions showed that a target concentration of 10-20mcg/L can be achieved using an oral loading dose of 200mcg/kg followed by a maintenance of 100mcg/kg 4hrly. However there is still considerable variability between individuals receiving the same dose and simulation demonstrates large variation in serum concentration with age. This is probably due to an age dependent decrease in clearance with age resulting in higher serum concentrations in older children for the same dose.

Comments: The perioperative use of opiates varies considerably around the world based on availability, custom and legal restrictions. Our increasing knowledge of pharmacogenetics coupled with the unfortunate cases of mortality and morbidity reported with codeine has rightly led to the widespread recommendation that it is not used for analgesia in children, particularly in “high risk” groups such as Sleep Disordered Breathing (SDB). Non opiate, multimodal analgesia is rightly advocated in perioperative care but may not provide sufficient analgesia in some cases. Alternative opiate analgesics to codeine do exist but some, like codeine, are subject to genetic polymorphism and there is a paucity of current knowledge to guide their safe and effective use in children.

This study contributes significantly to our knowledge about the safe and effective clinical use of oral morphine for perioperative analgesia in children and goes a long way in guiding the clinician in its use. However the finding of considerable variation in serum concentrations for any given dose (both between individuals given the same dose and across ages) should promote caution in prescribing oral morphine in potentially high risk cases, such as SDB, where significant sensitivity to opiate induced respiratory depression may exist.

Reviewed by: Henrik Hack

Codeine use among children in the United States: a nationally representative study from 1996 to 2013.

Livingstone et al.

Pediatric Anesthesia 2017.27.19-27.

The aim of this study is to examine the patterns of codeine prescribing to children in the US. Data was extracted from the Medical Expenditure Panel Survey (MEPS) relating to children aged 0-17yrs between 1996 and 2013. These surveys are performed by governmental agencies biannually on non-hospitalised patients (including post-operative children). Data collected included sociodemographic, health status, & medical, conditions.

Results

Data was collected from over 150,000 children within the assigned time period. Important and relevant findings included:

- Codeine use has fallen only slightly but statistically significantly ($p<0.001$) over the study period: 1.6% v 1.46% (1.08 million v 1.03 million prescriptions).
- As a percentage of total opioid use, codeine use has fallen from 52.7% to 44.3%, with a corresponding increase in oxycodone and hydrocodone use.
- Codeine was more likely to be used by older children aged 12-17 yrs. than those<6yrs.
- Emergency physicians (18%) & dentists (14%) were the most frequent prescribers of codeine. However ENT surgeons (9%), orthopaedic surgeons (6%) and general paediatricians (6%) also featured significantly.
- The commonest indications were trauma related pain and post procedural pain.

Discussion / Comments

The frequency of use of codeine in children is perhaps disappointing but it must be remembered that the widespread knowledge of the genetic polymorphism in metabolism of codeine is relatively recent, as are the multiple, national and international recommendations regarding the cessation of codeine use in children. A follow up study analysing more modern data is essential to discover whether the widespread prescription of codeine in children, particularly by surgeons and physicians who may be caring for high risk groups such as those with sleep disordered breathing, has diminished further.

Reviewed by: Henrik Hack

Codeine: an old drug with new precautions
Editorial
Paedtrc Anaesth 2017.27.7.

A False comfort with codeine-
Editorial
Paedtrc Anaesth 2017.27.8-9.

These two brief editorials concisely discuss the problems associated with the use of codeine in children, the problems relating to currently available alternatives and the need for further research in this area.

Henrik Hack

Apnoeic oxygenation during intubation: a systematic review and meta-analysis.

White LD, Melhuish TM, White LK, Wallace LA.

Anaesth Intensive Care 2017; 45: 1.

Why would I read this?

Apnoeic oxygenation is a much talked about technique promoted by some to extend the time to desaturation during laryngoscopy and intubation. Arising principally from the emergency medicine field, it is timely to examine its role in anaesthesia care.

Methodology and Results:

Studies that compared apneic oxygenation during intubation to a control group were included in the review. No study design was excluded from consideration. The exclusion pathways are clearly stated. Of 1808 citations identified by electronic and manual search (!) 11 articles were included. The methodology is clear enough that it appears a keen person could replicate the process. There is significant variation in what was included as apneic oxygenation with nasal prong oxygen rates varying from 5 L/minute to 60 L/minute. No studies of children are in this meta-analysis.

The authors found strong evidence that apnoeic oxygenation prevented desaturation. Strong evidence was found for increased safe apnoea time. Strong evidence was found that the minimum recorded SpO_2 was higher.

Discussion

This meta-analysis did not assess if there were any complications or risks associated with this technique. Of particular note it is not clear to me the method by which the nasal prongs were utilised (under the mask or after the mask was removed) nor how pre-oxygenation was undertaken. There is evidence in the adult literature that applying nasal prongs under a mask during pre-oxygenation compromises expired oxygen levels, suggesting inferior pre-oxygenation(1,2). This effect is likely to be more pronounced in children. There would be a stark difference between pre-oxygenation without gentle ventilation as muscle relaxation took effect and no such efforts. There is no reason to think apnoeic oxygenation cannot fix poor pre-oxygenation. This paper also does not look at THRIVE techniques.

If apnoeic oxygenation is designed to extend apnoeic time or maintain oxygen saturations during intubation then the patients I would most like to support oxygenation in would be the critically ill patient. This meta-analysis suggested that patients with respiratory failure were the least likely to benefit, most likely because they exhibit shunting within the lungs. For the paediatric anaesthetist is there value in extending apnoeic time in healthy patients rather than ill patients, particularly in a patient population where it is generally known if airway management is likely to be difficult?

Bottom Line:

While it appears to be well conducted, this meta-analysis does not convince me to change my practice and undertake apnoeic oxygenation during induction and intubation of all of my patients. It is unclear to me if it even supports doing this for unwell patients. Even allowing for it being solely based on adult research, without a sense of how preoxygenation was undertaken it is hard to know what would be the best way to implement it. A far more useful paper for the paediatric anaesthetist is that by Humphreys et al. which begins to explore this topic in healthy paediatric patients(3). This study does suggest significantly longer times to desaturation during apnoea after effective preoxygenation. Looking at that paper I wonder if it suggests there may be a role for apnoeic oxygenation techniques during predicted difficult intubation or after reoxygenation in an unanticipated difficult intubation.

Suggested Other Reading:

1. Groombridge C, Chin CW, Hanrahan B, Holdgate A. Assessment of Common Preoxygenation Strategies Outside of the Operating Room Environment. Reardon R, editor. Academic Emergency Medicine. 2016 Feb 17;23(3):342–6.

2. MBBS CH-BB, PhD ALM, MSc BBM, MBChB MM. Efficacy of Nasal Cannula Oxygen as a Preoxygenation Adjunct in Emergency Airway Management. Annals of Emergency Medicine. Elsevier; 2016 Aug 1;68(2):174–80.

3. Humphreys S, Lee-Archer P, Reyne G, Long D, Williams T, Schibler A. Transnasal humidified rapid-insufflation ventilatory exchange (THRIVE) in children: a randomized controlled trial. Br J Anaesth. Oxford University Press; 2017 Jan 18;118(2):232–8.

Reviewed by: Andrew Weatherall