



## The implications of immunization in the daily practice of anaesthesia

Current Opinion in Anesthesiology Vol 30 No 3 June 2017

It is not unusual to be asked to vaccinate children whilst under general anaesthesia, and children occasionally present for surgery soon after their scheduled vaccinations. This review addresses the optimal timing of vaccinations in relation to surgery.

In order for immunisations to be effective they require a well-functioning immune system. Surgery and anaesthesia as well as opioid analgesia can compromise immune function, especially in neonates and infants, and this can theoretically lead to an altered response to vaccines. If vaccines are administered too soon before surgery the risk of vaccine-related side effects may increase, also there may be difficulty distinguishing vaccine side effects from side effects related to the surgery. If vaccinations are administered too soon after surgery their efficacy may be reduced as the required antibody response is not generated due to a compromised immune system. In particular the 'live vaccines' (MMR, polio, rotavirus, influenza, varicella zoster) may be more dangerous when administered prior to surgery.

### Summary of Recommendations

Vaccines require intact immunity and surgery compromises immunity.

The authors recommend:

1. The local schedule should be adhered to wherever possible and not delayed for elective surgery. Surgery should be timed so as not to coincide with vaccinations.
2. Ideally postpone elective surgery for one week post inactive vaccines and three weeks post live vaccines
3. If surgery must take place scheduled vaccinations should be delayed for a week in order to allow the immune system to recover.

*Reviewed by: Dr Amanda Dalton*

## Tramadol: keep calm and carry on (Editorial)

Pediatric Anesthesia 2017:27:785-788

This editorial contains succinct summary of Tramadol pharmacokinetics and pharmacodynamics and the issues of CYP2D6 polymorphism. The recent FDA's announcement regarding Tramadol use in children is described as a 'knee jerk reaction'. Other opioids, including hydrocodone and oxycodone, are also metabolised by the CYP2D6 enzyme system. Identifying CYP2D6 polymorphism prior to surgery may be a possibility in the future. Some sensible recommendations for limiting dose after adeno-tonsillectomy and monitoring the response to opioids before discharge from hospital are made. The comments in the editorial mirror the statement on tramadol use in paediatrics recently released by SPANZA.

*Reviewed by: Dr Nicole Anderson*

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## Ultrasound-guidance outperforms the palpation technique for peripheral venous catheterisation in anaesthetised toddlers: a randomised study

N Gopalasingam et al

Acta Anaesthesiologica Scandinavica 61 (2017) 601-608

This study looked at the first attempt success rates of peripheral venous catheterisation in anaesthetised toddlers undergoing elective low risk procedures comparing Dynamic Needle Tip Positioning (DNTP) ultrasound technique with the palpation technique. Secondary endpoints included overall success rates, number of skin perforations, needle redirections and time taken.

Patients less than 4 years of age needing a peripheral venous catheter (PVC) and general anaesthesia were included. Generally only healthy patients above 6 months of age were included. This was a prospective randomised crossover study. Each child received two PVC and were randomised to start with either the DNTP ultrasound technique or the traditional palpation technique, one on each arm. Only five paediatric anaesthetists participated and all received pre-study ultrasound training. All procedures were video recorded and timed.

### Results

Fifty patients participated in the study with a median age of 15 months and median weight of 11.3kg. First attempt success rates were 42/50 (84%) in the DNTP group and 30/50 (60%) in the traditional palpation group ( $p=0.029$ ). The overall success rate (defined as successful catheter placement within four skin punctures) was 50/50 (100%) in the DNTP group and significantly higher than the 42/50 (84%) in the traditional palpation group ( $p=0.008$ ).

In the DNTP group the median total time was 192 seconds (34-839) compared to 102 seconds (11-801) in the traditional group ( $p=0.073$ ). The needle manipulation time was also longer in the DNTP group ( $p=0.011$ ).

### Take Home Message

This study suggests that the DNTP ultrasound guided technique improved the first attempt success rate when compared to the traditional palpation technique in healthy anaesthetised toddlers. The authors commented in their discussion that even with both visible and palpable veins, DNTP showed superior success rates. Interestingly, only healthy and low BMI (median BMI 17.2 range 11.5-22) were included and children with known difficult venous access were excluded.

*Reviewed by: Dr Su May Koh*

## Pain prevalence in hospitalized children: a prospective cross-sectional survey in four Danish university hospitals

Walther-Larsen et al.

Acta Anaesthesiologica Scandinavica 61 (2017) 328-33

This prospective mixed-method cross-sectional survey surveyed 570 paediatric patients on a random unannounced weekday, asking them to report their pain experience and its management in the previous 24 hours.

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37% of patients responded that they had experienced pain in the last 24 hours, with 24% experiencing moderate to severe pain. Most analysis involved the group experiencing moderate to severe pain. For example, only 46% of this group had a documented pain assessment and for those who did, the staff members' median ratings of the pain was lower than the patients' (6 vs 8). There were low rates of administration of analgesia (paracetamol, NSAIDs and opioids). Parents reported use of a wide range of non-pharmacological pain management strategies although these were rarely documented.

The cause of the pain for the children was significantly weighted towards invasive procedures, with needles, other invasive procedures (e.g. IDC and NGT insertion) and surgery being the most painful procedure for 36%, 20% and 4% of the patients. The remaining causes for pain were related to the underlying disease.

The authors found that their results were similar to other published data but concluded that the high rates of moderate to severe pain with lack of documentation of this and lack of systematic pharmacological or non-pharmacological management, meant that changes were needed.

#### Take home message

It is always good to have data with which to compare one's own institution. Additionally this study serves as a reminder of how traumatic paediatric patients find invasive procedures, especially those extremely common procedures involving needles!

*Reviewed by: Dr Vanessa Rich*

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### **Aerosolised Vasodilators for the Treatment of Pulmonary Hypertension in Cardiac Surgical Patients: A Systematic Review and Meta-Analysis**

Elmi-Sarabi M et al.

Anesthesia and Analgesia. 2017. 125 (2): 375 – 377.

This systematic review and meta-analysis aims to compare the efficacy of inhaled aerosolized pulmonary vasodilators with IV agents and placebo in adult patients with pulmonary hypertension undergoing cardiac surgery with cardiopulmonary bypass. The authors cite the efficacy of inhaled nitric oxide and draw the reader's attention to the fact that other inhaled pulmonary vasodilators might be just as efficacious. One major reason for undertaking this review is the high cost of inhaled nitric oxide (approx. \$3000/day vs the alternatives at approx. \$100/day). The authors hypothesise that there will be less hypotension with inhaled vs intravenous vasodilators and that there will be "better" haemodynamics with inhaled pulmonary vasodilators than placebo. Unfortunately, they do not attempt to make a distinction between the inhaled dilators, lumping the studies that used iNO in with the studies that used alternative inhaled dilators. They then go on to make mortality their primary outcome. Secondary outcomes can be split in to two broad groups; haemodynamic variables and lengths of stay (Hospital and ICU length of stay)

There was a good search strategy and study selection process that was likely to include all major studies on this topic. The authors chose to take a single haemodynamic dataset (such as maximum MAP or data at time of entry to ICU) rather than an average or some other time weighted measure. This is unlikely to be representative of the effects of these drugs over time. Due to the large number of haemodynamic parameters studied a Bonferroni correction for multiple tests on the same dataset was applied making the actual p value for statistical significance very small ( $p < 0.0004$ ). There were only a handful of trials comparing different types of inhaled vasodilator and these trials were too heterogenous in terms of the patient populations, the treatment strategies and the data presented to be usefully compared. The authors did go on to make some comparisons but they should be taken with a very large pinch of salt.

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Of the 10 studies with a total patient number of around 400, only six actually addressed the primary outcome of mortality. No mortality benefit was found in using inhaled pulmonary vasodilators over placebo. There were insufficient studies to compare inhaled vs intravenous agents with respect to mortality. With respect to haemodynamic variables there were no differences at all in any haemodynamic variables with inhaled vs placebo. This included the finding that when compared with placebo inhaled pulmonary vasodilators did not reduce PVR! When inhaled dilators were compared with intravenous agents the results showed that inhaled agents reduced PVR, increased MAP and RV ejection fraction compared with intravenous agents. When the Bonferroni correction was applied this eliminated the results for PVR and MAP but left the increase in RVEF as significant. These results are as one would expect for selective as opposed to non-selective pulmonary vasodilators but the fact that inhaled dilators have no measurable effect against placebo is concerning for the designs of the included studies given that we already accept the efficacy of these drugs in patients whose pulmonary hypertension is dilator responsive.

### **Take Home Messages**

Pulmonary hypertension is a serious clinical problem in a small number of paediatric patients undergoing cardiac surgery. Currently the standard of care for administering selective pulmonary vasodilators is to use inhaled nitric oxide, which is an off label indication in all but newborns and a very expensive proposition. The authors of this review are seeking to find evidence for an alternative and equally efficacious therapy, which is a very relevant and worthy quest. However this review pools together multiple very different populations and uses statistical methods of moulding the data into sets that can be compared together resulting in a comparison between apples and oranges and then fails to identify that they are different! The idea that a strong mortality benefit signal would shine through in a heterogenous group of only 400 patients exposed to significantly different study designs is laughable when taken at face value. It also doesn't really address the question at hand, which is whether there is an equally efficacious and more cost effective solution to achieving pulmonary vasodilation. This is an adult study with limited applicability to paediatric practice. However, it serves to highlight the major issues faced by researchers and clinicians looking for the most efficacious and yet cost effective way of caring for our complex and sick patients.

*Reviewed by: Dr Paul Davies*

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### **The association between caudal anesthesia and increased risk of postoperative surgical complications in boys undergoing hypospadias repair.**

B Taicher et al.

Paediatric Anesthesia 27(2017) 688-694

In this retrospective observational study, all single-stage hypospadias repairs performed by a single surgeon, at a single centre between 2001 and 2014 were reviewed. The study looked for postoperative surgical complications defined as urethrocutaneous fistula or glanular dehiscence. A minimum of six months follow-up was required.

395 patients were included in the study with a mean age of 15.6 months. Of these 230 (58%) received a caudal block. Postoperative surgical complications occurred in 22 (5.6%) patients. 21 of these patients received a caudal anaesthetics. Initial data showed that postoperative surgical complications were associated with severity of hypospadias, duration of surgery, earlier year of practice and caudal block (OR 16.5, 95% CI 2.2 -123.8, P = 0.007). After adjusting for confounding variables, proximal hypospadias repair (OR 6.8, 95% CI 2.7 – 16.9 p < 0.01) and use of caudal anaesthetic (OR 13.4, 95% CI 1.1-101.8 P = 0.01) remained highly associated with postoperative surgical complications.

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This is the largest study to date to review this association and the increase in postoperative complications was significant. There has been one other study that has seen this association as an incidental finding while comparing penile block efficacy to caudal anaesthesia. Other studies have shown the severity of the hypospadias to be the only causal factor in an increased postoperative complication rate. One small study showed the use of subcutaneous epinephrine was associated with an increased incidence of fistula formation. One suggested mechanism is a change in blood flow. This mechanism is likely to be debated as vasodilation, from regional techniques, usually improves wound healing. The authors suggest a multicentre randomized controlled trial to further evaluate this association and potential mechanisms.

#### Take Home Message

I thought this study addressed a relevant question as caudal anaesthesia is commonly used for hypospadias repair. If the association is proven to be true it may result in a significant change to practice. Using only one surgeon may be a strength of this study as their practice is consistent. However the findings are only retrospective, from only one surgeon at one medical centre so may not be generalizable to other centres. As suggested in the accompanying editorial in the same issue, we probably should not abandon a safe and effective form of analgesia at this stage. Further randomised studies are already underway. Watch this space!

*Reviewed by: Dr Kim Fuller*

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#### **The American College of Surgeons Children's Surgery Verification and Quality Improvement Program: Implications for Anesthesiologists.**

Houck C, Deshpande JK & Flick RP.

Current Opinion in Anesthesiology. June 2017, 30:376-382

This review showcases an American College of Surgeons initiative conceived in 2012. The multidisciplinary standards specific to children's surgery were piloted and eventually finalized in 2015. So far 5 children's surgical programs have been verified to meet these standards. A further 125 have expressed an interest in being verified.

The review starts by confirming there is still a problem that needs to be solved. Although dropping compared to the 1960s, paediatric deaths attributable to anaesthesia remain somewhere between 0.5 and 1 per 10,000 cases. The rate is particularly high in neonates receiving surgery - 69 times greater when compared to children aged over 10 years of age in one U.S study.

The authors go on to show that outcomes are improved for children receiving surgical care in a specialized environment for children. The aim of this project is clearly to replicate this improved care for all children receiving surgery across the U.S and Canada. The guidelines are extensive. A 98 page PDF file outlines how centres can be stratified into 3 levels. Each level has a different scope of practice, staffing requirements and caseload expectations. The relationship between centres is defined, including transfer between them. Finally the ongoing quality assurance process is described, including incident reporting.

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**Take Home Message:**

This review provides a link to a comprehensive set of guidelines showing how surgical care for children may be more formally prescribed in the future. What are the implications for Australasia? - Read on if you want a glimpse into that brave new world.

*Reviewed by: Dr Chris Smit*

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**Codeine and Opioid metabolism: implications and alternatives for paediatric pain management.**

Chidambaran V, Sadhasivam & Mahmoud M.

Current Opinion in Anesthesiology 2017. 30.3.350-356.

This article reviews the pharmacological and clinical basis for the recent concerns regarding serious opioid related side effects in children undergoing surgery, particularly those with Sleep Disordered Breathing (SDB) undergoing adeno-tonsillectomy. It then follows with some clinical recommendations relating to the provision of an opiate sparing, multimodal analgesic regime in such patients. The article focuses on the pharmacogenetic and physiological basis for codeine related respiratory side effects in children. The same concise and clearly written approach is then applied to alternative analgesic agents including non- opioid agents, tramadol, oxycodone, hydrocodone and oral morphine. The concluding comments to this section suggest that all of the above opioids, with the exception of oral morphine, are subject to varying metabolism and so may be as dangerous as codeine in similar clinical circumstances. They suggest that oral morphine needs further study regarding safe and effective prescribing.

The ideal approach to managing these cases would include preoperative CYP2D6 genotyping to allow a rational choice of opioid and safe dosing for individual patients. Clearly such an approach is unattainable for most of us for the foreseeable future! Acknowledging this, the authors recommend the age based analgesic regime for home care used in their institution. Under the age of 6 years they utilize a combination of paracetamol, ibuprofen and dexamethasone with no opioids. Over the age of 6years they add oral oxycodone to this regime. They state that they have had satisfactory results with this regime.

**Take Home Message**

The paper is well written with a clear assessment of the background science and potential clinical problems. Of particular interest for SPANZA members is their stated concern with the use of tramadol in such patients. Their recommendation to avoid its use until further evidence of its safety is at variance with SPANZA's recent advisory statement. In addition the routine use of NSAID's in their analgesic regime might be unacceptable to some clinicians based in North America and Australasia?

*Reviewed by: Dr Henrik Hack*

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### **Pediatric Sleep-disordered breathing (SDB): an update on diagnostic testing.**

McGrath B & Lerman J.

Current Opinion in Anesthesiology 2017. 30.3.357-361.

This well written article revisits the difficult issue of how we diagnose and attempt to stratify anaesthetic risk in children with SDB undergoing adeno-tonsillectomy. Whilst the formal Polysomnogram (PSG) remains the gold standard its cost and scarce availability for most clinicians has forced us to investigate the feasibility of other diagnostic tools. This article then considers the accuracy and feasibility of using various other diagnostic tests including internationally agreed “high risk” patient categories, various questionnaires (adult and paediatric based), overnight oximetry, drug induced sleep endoscopy and perhaps most interestingly new diagnostic biomarkers.

The relative strengths and weaknesses of most of the tests will be well known to most paediatric anaesthetists dealing regularly with this common disease. Most institutions will already have locally adopted some form of screening tool, most probably based upon local resources, and this is unlikely to change significantly in the short term.

The most interesting section of this paper discusses the recent findings of significant biomarkers present in urine, saliva, exhaled breath etc. present in children with SDB. In particular various individual and mixtures of urinary proteins and glycosaminoglycans have been shown in small studies to be sensitive markers of SDB. Although these small exciting studies are still at an early investigative stage they appear to offer real hope for the development of a simple diagnostic biochemical test for SDB in children.

*Reviewed by: Dr Henrik Hack*

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### **Neuromuscular disorders: relevance to anaesthesia and intensive care**

Joanna Roberts, Ugan Reddy

Anaesthesia and Intensive Care Medicine, 2017, 18:6, 292-295

Although a review of the adult literature, this paper reminds one of the various neuromuscular disorders that we may encounter occasionally in paediatric anaesthesia. The information presented is adequate, although mention of newer agents with substantial relevance to this field, such as sugammadex, is not made. The section probably most relevant to paediatric anaesthesia is that on muscular dystrophies but disorders seen at tertiary paediatric centres such as spinal muscular atrophy get limited mention.

*Reviewed by: Dr Justin Skowno*

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### **Videolaryngoscopy in Neonates, Infants, and Children.**

Balaban O & Tobias JD.

Paediatric Critical Care Med May 2017 18(5) 477-485.

This article is a comprehensive and objective review of videolaryngoscope (VL) options. It is well-referenced with photos of the devices included. A framework for classifying the VL is made; for example the VLs are divided into direct and indirect types which is useful for emphasizing which may prove to be more useful in the anatomically difficult airway. After an overview, each scope is reviewed including those that lack a full range of paediatric sizes. The C-Mac, Glidescope, McGrath, Truphatek, Airtraq, Pentax Airway Scope and Kingvision VL are all covered. The hazards of VLs are also outlined.

The review is more than a simple product guide. It includes a discussion about the evolving place of VL in our practice. Although the literature has not demonstrated a significant advantage of the VL over traditional laryngoscopy in the *normal airway*, the ability for the instructor to finally see the airway, glottis, and tube position is proving invaluable during intubation of small infants by trainees. This advantage will be magnified in the intensive care environment where very few intubations will be truly elective.

The only caveat of a review of this scope (no pun intended) is that it will rapidly become out of date. This is a reflection of the rapid commercial evolution of devices. The C-mac manufacturer for example will be dismayed that the paediatric D-blade, Mac size 0 blade and new display for the pocket monitor all fail to rate a mention.

#### **Take Home Message**

Is the review worth reading? - Yes. Will the VL play a greater role in the everyday practice of paediatric anaesthetists? - Almost certainly. This article may prove useful to those trying to decide which VL to trial in their department. Be sure to read the editorial that accompanies the review (pg. 491).

*Reviewed by: Dr Chris Smit*

### **Effects of intraoperative liberal fluid therapy on postoperative nausea and vomiting in children - A randomised controlled trial.**

Ashok V et al.

Pediatric Anesthesia. 2017; 27: 810-815.

Perioperative liberal fluid therapy might be an inexpensive and safer alternative to pharmacological prophylaxis of PONV.

This was a randomised, double-blind study in India of 145 ASA I and II children aged 3-7 years undergoing lower abdominal and penile surgery (<60mins) under GA. The children were randomly assigned to either a restricted group or a liberal group and received an intraoperative infusion of 10ml/kg/hr and 30ml/kg/hr of Ringer's lactate respectively. Children with high risk of PONV (previous PONV or motion sickness) were excluded. All patients received sevoflurane with a caudal block and intravenous paracetamol. No intraoperative opioids, anti-emetics or muscle relaxants were given. All episodes of nausea, vomiting and rescue anti-emetics were assessed for 24 hours.

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The incidence of PONV was significantly less in the liberal group with 20 (27%) children vomiting versus 33 (46%) children in restricted group ( $p=0.021$ ). The time to first rescue antiemetic was longer in the liberal group but not statistically significant ( $p=0.337$ ). Also 60 (83%) children in the restricted group complained of thirst in the first 6 hours postoperatively compared to 12 (17%) in the liberal group.

#### Take Home Message

This study supports the more liberal use of fluids intraoperatively to prevent PONV and thirst. Obviously these results may not apply to different clinical settings such as longer surgeries or when opioids or anti-emetics are given. Whilst 30ml/kg is unlikely to cause problems for children in this setting having short procedures, potential complications of liberal fluid therapy would have to be considered for longer surgeries and in children with co-morbidities.

*Reviewed by: Dr Naomi Pearson*

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#### Should patients be advised not to drive for 4 days after isoflurane anaesthesia?

Powell and Molyneux

Anaesthesia 2017 June, 72(6): 682–685

This review article investigates the evidence behind a recent change to the Abbvie product information for isoflurane which states that performance of activities requiring mental alertness, such as driving, may be impaired for 2-4 days after isoflurane anaesthesia. The Royal College of Anaesthetists updated its advice but the update has since been removed and is currently under review. Baxter's product information remains unchanged – to avoid driving for 24 hours.

The authors found insufficient good quality evidence to draw definitive conclusions on the effect of isoflurane on driving safety after the 24 hour mark. Most studies to date have used neuropsychological testing which may not reflect reaction times or driving ability. This article does suggest however that to apply extra caution with the advice we offer our patients may be prudent.

Most of our paediatric patients are not driving. They are however going to the park on their bikes and scooters and playing on climbing equipment in the days following anaesthesia. So while the jury is still out, is there any good reason to choose isoflurane over other agents?

*Reviewed by: Dr Stephanie Aplin*

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