



## **1. Influence of isoflurane exposure in pregnant rats on the learning and memory of offspring**

Huang W, Dong Y, Zhao G, et al .

*BMC Anesthesiology* 2018 18:5

Concerns remain about possible effects of general anaesthesia on the developing foetal central nervous system when pregnant women undergo operations. This Chinese group compared the ability of the offspring of rats exposed to varying concentrations of isoflurane during pregnancy to navigate the Morris water maze (MWM).

48 pregnant rats were exposed to 1.3% or 2% isoflurane or an oxygen control group, for 3 hours. This was the equivalent of 1 and 1.5MAC, at a time point where brain development of rats is equivalent to human foetuses at 12-16 weeks, and equivalent to 48 hours anaesthesia in humans. 316 male offspring were tested in the MWM at 28 or 90 days after birth. Expression of proteins related to learning and memory in the hippocampus was then compared.

Results: Following 5 days of training and learning to find a platform in the MWM the rats were tested for spatial learning and memory when the platform was removed. The test of spatial localisation was similar in all 3 groups but the time crossing the platform (accuracy of spatial memory) was significantly worse in the 2% isoflurane group.

After testing the rats were anaesthetized and the expression of proteins in the hippocampus compared. p-CREB expression (crucial for memory formation) was significantly lower in the 2% isoflurane group.

Discussion: Intra-uterine exposure to 2% isoflurane impaired the accuracy of spatial memory in rats but not spatial localisation. This is accompanied by changes in protein expression in the hippocampus. As with all animal trials it remains to be seen how this correlates to outcomes in humans.

## **2. Short-Term Neurodevelopmental Outcome in Congenital Diaphragmatic Hernia: The Impact of Extracorporeal Membrane Oxygenation and Timing of Repair**

Danzer E, Hoffman C, D'Agostino J, et al.

*Pediatric Critical Care Medicine* 2018; 19(1):64-74

This retrospective single centre study (The Children's Hospital of Philadelphia) aimed to identify the neurodevelopmental difference in children with congenital diaphragmatic hernia (CDH) who underwent repair on ECMO versus post-ECMO.

Methods: A retrospective review between 2004 and 2016 of CDH survivors. All patients' perinatal and postnatal care was according to their unit policy. ECMO was indicated for hypoxia, high peak inspiratory pressure or mean airway pressure, hypotension refractory to inotropic support or persistent metabolic acidosis secondary to inadequate oxygen delivery. Neonates less than 34 weeks



or <2kg were excluded. The surgeons chose when to operate based on a number of factors. Neuro developmental outcomes were determined using the Bayley Scales of Infant Development (BSID-III) and clinical evaluation.

Results: 212 children were included and assessed at a median age of 22 months. 50 children required ECMO with 4 children being repaired pre-ECMO, 25 on ECMO and 21 children post-ECMO. The entire cohort requiring CDH repair scored in the low-average range by BSID-III. Those requiring ECMO were also significantly more likely to develop neuromuscular hypotonicity and scored significantly lower for cognition and motor skills than those not requiring ECMO.

Cognition and motor scores were significantly lower when repaired on ECMO than repair pre or post-ECMO. Children repaired early on ECMO (within 8 days) did not differ in their neurodevelopmental outcome from those repaired later on ECMO.

The authors suggest delayed CDH repair, post-ECMO is associated with a lower risk of poor neurodevelopmental problems. There is a risk of selection bias with relation to timing of repair.

### **3. Cuffed vs. uncuffed tracheal tubes in children: a randomised controlled trial comparing leak, tidal volume and complications**

Chambers NA, Ramgolam A, Sommerfield D, et al.

*Anaesthesia* 2018; 73: 160–168

This single centre RCT (Princess Margaret Hospital for Children in Perth) compared differences in tidal volumes and gas leakage around randomly assigned cuffed and uncuffed endotracheal tubes (ETT) in 86 children aged 0-16 years having elective surgery 2012-2014. Exclusions included <5kg, airway malformation, upper airway surgery and post-operative ventilation.

ETTs < size 5 had low-volume cuffs and size 5 upwards had high-volume, low-pressure cuffs. Once intubated patients were commenced on volume-controlled ventilation. Leakage around the ETT was measured 5 times (inspiratory and expiratory tidal volume) and the mean calculated. Leakage was re-measured with pressure-controlled ventilation, and again after a standardised recruitment manoeuvre and at 10 and 20 minutes post-recruitment.

Results: 104 children were recruited but only 86 were included in the final analysis as 18 were excluded from the uncuffed group for tube related problems. Appropriate size ETTs were selected on first attempt in 83% of the cuffed tube group but only 33% of the uncuffed group. Leakage volumes were significantly less in the cuffed ETT group ( $p < 0.001$ ). Both inspiratory and expiratory tidal volumes were higher in the cuffed group for both volume and pressure controlled ventilation although this did not always reach significance for the inspiratory volumes. Airway complications such as persistent coughing, desaturation, sore throat and hoarse voice were more frequent in the uncuffed ETT group perhaps in part secondary to repeated intubation with different tube sizes.



This centre saw a lower leak, higher tidal volume and less adverse events in the cuffed tube group.

#### **4. The European Society of Regional Anaesthesia and Pain Therapy/American Society of Regional Anesthesia and Pain Medicine Recommendations on Local Anesthetics and Adjuvants Dosage in Pediatric Regional Anesthesia**

Suresh S, Ecoffey C, Bosenberg A, et al.

*Regional Anesthesia and Pain Medicine* 2018; 43(2): 211-216

A collaborative practice advisory to establish best evidence for doses of local anaesthetics (LA) and adjuvants for paediatric regional anaesthesia.

Methods: A systematic literature review was performed and the strength of evidence systematically evaluated by an expert committee. Expert opinion was considered when the evidence was insufficient. (See full article for specific doses and strength of evidence)

- LA metabolism is slower than in adults meaning increased risk of accumulation with infusions or repeat injections
- Higher volume of distribution of LAs in neonates and infants means lower peak plasma concentrations after a single injection
- Increased cardiac output in children means accelerated vascular absorption from tissues producing high plasma concentrations and potential toxicity (lower the dose under 2yrs)
- Toxicity risk also higher <1yr secondary to reduced protein binding and higher free fraction
- Shorter duration of spinal block in infants due to larger CSF volume
- Greater blood flow to spinal cord especially preterm also reduces LA duration
- Spinal: drugs include tetracaine, bupivacaine (hyperbaric or isobaric) and ropivacaine with dose according to weight
- Caudal: dosing should be according to the Armitage scale within the toxic limits. Ropivacaine / bupivacaine / levobupivacaine can all be used
- Epidural: maximum 1.7ml/kg for ropivacaine / bupivacaine / levobupivacaine
- Continuous infusion epidural: doses by weight are modified according to age with bupivacaine / levobupivacaine, ropivacaine and chloroprocaine
- Upper limb, lower limb and fascial plane blocks are performed successfully with ultrasound. Single injection or continuous infusion
- Adjuvants: Clonidine and preservative-free morphine are registered for epidural and spinal administration. None are registered for injection close to peripheral nerves. Ketamine should be avoided intrathecally in neonates/infants due to neuronal apoptosis. Dexmedetomidine toxicity data very limited, used in caudal blocks and peripheral blocks with minimum doses. There is a lack of evidence for synthetic opioids and corticosteroids are not recommended.

#### **5. The effect of pre-operative gastric ultrasound examination on the choice of general anaesthetic induction technique for non-elective paediatric surgery. A prospective cohort study**



Cagey A-C, de Queiroz Siqueira M, Monard C, et al.

*Anaesthesia* 2018; 73: 304–312

This single centre French study looked at pre-operative ultrasound assessment of gastric contents in children undergoing urgent or emergency surgery 2014-2015.

144 children aged 2 months to 16 years were included. The anaesthetist made an induction plan based on clinical pre-operative assessment. Gastric ultrasound was performed by a blinded operator in a 45° semirecumbent and right lateral decubitus position. Stomach contents were quantified using the Perlas grading system (0-2). Post-intubation, a nasogastric tube was inserted and gastric contents aspirated and measured. Contents were considered above 'risk threshold' if >0.8ml/kg, or containing thick fluid or solids.

Gastric ultrasound was not conclusive in 13 (9%). The anaesthetic plan was altered in 67 (47%) following ultrasound results (37 downgraded to routine induction, 30 upgraded to RSI). Appropriate induction technique was significantly higher after ultrasound compared to clinical assessment alone (85% vs 49%  $p < 0.00001$ ). Ultrasound had a sensitivity of 94% (84-98 95% CI) and specificity of 83% (71-91 95% CI) for detecting contents above risk threshold.

Pre-operative pain and vomiting were associated with clinical assessment of increased risk, but fasting time for solids <6 hours was the sole clinical factor associated with appropriate use of RSI. However, time is not a sufficient marker, 47/66 children with contents above the risk threshold had fasted >6hrs. Main factors associated with high risk gastric volumes were orthopaedic surgery and shorter fasting times.

Results suggest gastric ultrasound is a simple technique that improves decision making for induction technique. Limitations are use of NG tube to estimate gastric contents and non-evidence based cut off for risk threshold.

## **6. Deep or awake removal of laryngeal mask airway in children at risk of respiratory adverse events undergoing tonsillectomy - a randomised controlled trial**

Ramgolam A, Hall GL, Zhang G, et al.

*British Journal of Anaesthesia* 2018; 120 (3): 571-580

Current evidence suggests that in healthy children without risk factors, rates of respiratory adverse events are independent of deep or awake laryngeal mask airway (LMA) removal. This study hypothesised that in children with risk factors, deep removal would reduce the incidence of adverse respiratory events during emergence and recovery by 15% or more. 283 patients at a tertiary referral hospital in Australia with one or more risk factors were identified between 2009 and 2014.

Anaesthetists were aware of the study aim but not the hypothesis. Anaesthetic technique was to the discretion of the anaesthetist and timing of LMA removal was randomly assigned. Inclusion criteria



included one parentally reported risk factor for perioperative adverse events. Exclusions included premedication. Awake removal was performed either by the anaesthetist in theatre or the PACU nurse. Deep removal was performed by the anaesthetist in theatre.

10% more adverse events were noted in the awake group during the emergence and PACU phase, but this was not statistically significant (45% vs 35%, OR 1.5, 95% CI: 0.9-2.5, P=0.09). In the PACU phase only, there was a statistically significant increase in adverse events in the awake group compared to the deep group (39% vs 26%, OR 1.85, 95% CI: 1.1-3, P=0.02). Considering respiratory risk factors separately (not powered for this), children in the awake group saw more perioperative respiratory adverse events compared to the deep LMA removal group (55% vs 32%, OR 2.69, 95% CI: 1.43-5.08, P=0.002). The authors acknowledged that varying definitions in deep and awake removal and investigator bias may have accounted for differing results compared to previous studies. Of note, the children who experienced respiratory adverse events did not require increased PACU or recovery time.

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