Welcome to the sixth issue of Anaesthesia and Pain Management Research Review.

The research selected for this issue includes an RCT that found manual physical therapy to be as effective as surgery for CTS in women. There is also an interesting study reporting decreases in pain tolerance among patients who have sleep problems. Data pooled from 15 RCTs suggest that patients undergoing surgery benefit from the use of low tidal volumes for ventilation. Another of several meta-analyses concludes this issue, with evidence that propofol is effective for preventing emergence agitation and reducing its severity in paediatric patients.

We trust you will find the research selected for this issue interesting. We enjoy receiving your feedback, questions and suggestions, so please keep them coming.

Kind regards,
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Long-term outcome of the management of chronic neuropathic pain

Authors: Moulin DE et al.

Summary: This was a prospective observational analysis over 24 months of 789 patients with chronic neuropathic pain (mean duration 4.88 years) treated according to standard guidelines. Significant improvements were seen at 12 months for pain intensity, the Interference Scale Score of the Brief Pain Inventory, mood, quality of life and overall treatment satisfaction (p<0.001), but a clinically significant improvement in pain and function at 12 months, assessed as a ≥30% reduction in pain intensity and a 1-point decrease in the mean 10-point Interference Scale Score, was achieved by only 23.7% of patients. Univariable analyses revealed significant associations between worse outcomes and longer pain duration, greater cigarette smoking, more disability compensation and higher baseline and 12-month opioid doses.

Comment (DR): Neuropathic pain remains a challenging clinical problem that is very difficult to treat effectively. While RCTs are important, those involving people with neuropathic pain have often suffered from small sample sizes, relatively short interventions and follow-up periods and the inclusion of only specific neuropathic pain conditions such as painful diabetic neuropathy or postherpetic neuralgia, limiting their generalisability to other clinical populations. The value of this observational cohort study is that it involved patients with a range of different chronic neuropathic pain conditions across seven different multidisciplinary pain centres and included long-term follow-up. Of note, only 1 in 4 patients demonstrated a clinically important improvement after 1 year, defined as ≥30% reduction in average pain intensity and at least a 1-point decrease in average pain interference. While not directly comparable, this appears lower than is reported in many RCTs involving people with neuropathic pain, where between 2 and 5 patients are typically needed to achieve a 50% improvement in pain intensity. Perhaps of most interest though were the factors associated with poorer outcomes at 12 months, including longer duration of pain and higher opioid consumption – both at baseline and at 12 months. These findings suggest that, where possible, earlier multidisciplinary intervention is best and that opioids may not be beneficial and, in fact, may be harmful in the long-term treatment of neuropathic pain.

Reference: J Pain 2015;16(9):852–61

Abstract

Independent commentary by Dr John Barnard

Dr John Barnard works as an anaesthetist at Waikato Hospital with a part time academic component. In addition to his role in the operating theatres, four years ago he became the Clinical Director of the Hospital Pharmacy and Chairman of the hospital's Medicines and Therapeutics Committee.

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Independent commentary by Dr David Rice

Dr David Rice is a Senior Lecturer in the School of Clinical Sciences and a Senior Research Officer in the Health and Rehabilitation Research Institute at AUT University. He also has a position as a Scientific Officer in the Department of Anaesthesiology and Perioperative Medicine at Waitemata DHB.

For full bio CLICK HERE
Early increasing-intensity treadmill exercise reduces neureopathic pain by preventing nociceptor collateral sprouting and disruption of chloride cotransporters homeostasis after peripheral nerve injury

Authors: López-Álvarez VM et al.

Summary: This research demonstrated significant rapid reductions in hyperalgesia in the saphenous nerve territory and later in the sciatic nerve territory after regeneration in rats that had been subjected to increasing-intensity treadmill exercise performed during the first week or during the first 2 weeks after section and suture repair of their sciatic nerves. There were also parallel reductions in sensory neuron and spinal cord expression of nerve growth factor and brain-derived neurotrophic factor. Extension of collateral sprouts of saphenous nociceptive calcitonin gene-related peptide fibres within the adjacent denervated skin was prevented by the treadmill exercise, as was reduced nerve growth factor expression in the same skin and in the L3 dorsal root ganglia. Dorsal root ganglia Na-K-2Cl cotransporter 1 upregulation and lumbar spinal cord dorsal horn K-Cl cotransporter 2 downregulation were induced by injury, and these were normalised by the treadmill exercise, along with reductions of microgliosis in L3-L5 dorsal horn and brain-derived neurotrophic factor expression in microglia in 1–2 weeks postinjury.

Comment (DR): It’s often hard to get too excited about pain studies involving rats, but this one grabbed me. Much of the difficulty in treating neureopathic pain lies in the myriad of neuroplastic changes that initiate and maintain pain after nerve damage, and our limited capacity to reverse or minimise these effectively. Some of the key changes leading to neureopathic pain include collateral sprouting of intact sensory fibres and a loss of inhibitory ‘tone’ due to chloride dysregulation in spinal neurons that prevents the normal ‘gating’ of nociceptive transmission. Chloride dysregulation is thought to arise due to nerve damage-related activation of microglia and the subsequent release of neurotoxins. This study showed that a progressive aerobic exercise intervention performed in the week after sciatic nerve transaction was able to significantly reduce the development of both mechanical and thermal hyperalgesia. Fascinatingly, the authors were also able to demonstrate that exercise reduced collateral sprouting and normalised the release of neurotoxins after nerve damage, preventing chloride dysregulation and the subsequent loss of inhibitory ‘tone’. This is an important study that adds to the increasing body of evidence supporting the role of exercise in the treatment and prevention of neureopathic pain. This study is amongst the first to provide clear mechanisms of action explaining exercise’s positive therapeutic effect and suggests that early exercise intervention may be a useful strategy to prevent neureopathic pain after nerve injury. I wonder how long it is before we see exercycles or treadmills on hospital wards in an attempt to reduce postsurgical neureopathic pain.

Reference: Pain 2015;156(9):1812–25

Abstract

Manual physical therapy versus surgery for carpal tunnel syndrome

Authors: Fernández-de-las-Peñas C et al.

Summary: Women with CTS (carpal tunnel syndrome) were randomised to interventions of three physical therapy sessions including central nervous system desensitisation manoeuvres (n=60) or surgical decompression/release of the carpal tunnel (n=60). Compared with surgery, physiotherapy was associated with superior outcomes at 1 and 3 months for the primary outcomes of mean pain score (respective differences –2.0 and –1.3 [p<0.01]) and worst pain score (–2.9 and –2.0 [p<0.01]) and the secondary outcome of function (–0.8 and –0.3 [p<0.01]), but not at 6 or 12 months; there was also no between-group difference for the secondary outcome of the Boston Carpal Tunnel Questionnaire symptoms severity subscale at any timepoint.

Comment (DR): CTS is a very common condition that often results in neureopathic pain involving the median nerve. There is no clear consensus regarding the superiority of surgical versus nonsurgical management for CTS, but the existing literature suggests surgical intervention may have superior long-term outcomes. This was a generally well-designed RCT (n=120) that included blinded outcome assessment up to 12 months after intervention. Curiously, being male was an exclusion criteria of the study. The interventions compared were open or endoscopic nerve decompression and carpal tunnel release versus three 30-minute sessions of once weekly manual physiotherapy, including techniques that specifically aimed to mobilise/glide the median nerve along its course from the cervical spine to the hand. There is evidence from a previous study that this may have a modulatory effect on central nociceptive processing. Of note, physiotherapy resulted in superior outcomes in both pain and hand function 1 and 3 months postintervention, with large between-group effect sizes. Surgery and physiotherapy were equally effective 6 and 12 months postintervention, with ~75% of patients in both groups being defined as treatment responders. The results are remarkable when one considers the relatively small treatment dose delivered in the physiotherapy intervention and that all patients had symptoms for a minimum of 12 months at baseline. Unfortunately, a cost-effectiveness analysis was not undertaken, but no doubt the physiotherapy intervention would have been several orders of magnitude superior on these measures. While these findings need to be replicated, they suggest that manual physiotherapy involving median nerve glides should be considered before surgery for CTS—at least in women!

Reference: J Pain; Published online Aug 14, 2015

Abstract


BRIDION® (sugammadex) is a Prescription Medicine, fully funded under Section II of the Pharmaceutical Schedule from 1 June 2013. Indications: Reversal of neuromuscular block induced by rocuronium or vecuronium. Dosage & Administration: Immediate reversal of intense block: 10.0 mg/kg IV, three minutes following administration of rocuronium (1.2 mg/kg) in adults, (including: elderly; obese patients; patients with mild and moderate renal impairment and patients with hepatic impairment), Routine reversal of profound block: 4.0 mg/kg IV following rocuronium- or vecuronium-induced block when recovery has reached 1–2 post-tetanic counts; in adults, Routine reversal of shallow block: 2.0 mg/kg IV following rocuronium or vecuronium-induced block when recovery has occurred up to reappearance of T2; in adults: 2.0 mg/kg IV following rocuronium in children and adolescents (2–17 years).

Contraindications: Hypersensitivity to sugammadex or to any of the excipients. Precautions: Repeated exposure in patients: respiratory function monitoring during recovery; use for reversal of neuromuscular blocking agents other than rocuronium or vecuronium: coagulopathy; severe renal impairment; severe hepatic impairment; marked bradycardia, use in ICU; hypersensitivity reactions (including anaphylactic reactions); pregnancy (Category B2); lactation: Infants less than 2 years of age including neonates; prolonged neuromuscular blockade (sub-optimally and/or too prolonged), Potentially identified with tachyphylaxis, hormonal contraceptives. Could interfere with prothrombin time and some coagulation parameters.


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Efficacy and safety of duloxetine on osteoarthritis knee pain
Authors: Wang ZY et al.
Summary: This was a meta-analysis of three RCTs (n=1011) reporting efficacy and safety data on the use of duloxetine for treating OA knee pain. Compared with placebo control, duloxetine was associated with significant improvements for reduction in pain intensity (mean difference –0.88 [95% CI –1.11, –0.65]), Patient Global Impression of Improvement score (–0.47 [–0.63, –0.30]), WOMAC (Western Ontario and McMaster Osteoarthritis Index) physical function subscale score (–4.25 [–5.82, –2.68]) and >30% and >50% improvements in pain intensity (relative risk ratios 1.49 [1.31, 1.70] and 1.69 [1.27, 2.25]). However, duloxetine was also associated with more adverse events (risk ratio 2.15 [95% CI 1.48, 3.11]), treatment-emergent adverse events (1.32 [1.16, 1.49]) and discontinuations for any reason (1.43 [1.14, 1.76]) than placebo, but no serious adverse events; no deaths were recorded in these RCTs.

Comment (DR): Traditionally, serotonin-noradrenaline (norepinephrine) reuptake inhibitors such as duloxetine have been recommended primarily for neuropathic pain and conditions such as fibromyalgia, where sensitisation of central nociceptive pathways is thought to be a major driver of the pain experience. However, there is increasing evidence that, at least in a subgroup of patients, central sensitisation may also play an important role in OA-related pain. It is therefore not surprising that centrally acting medications such as duloxetine are being trialled in this group of patients. While a meta-analysis of three RCTs is not huge, the results suggest that duloxetine may have some promise in the treatment of OA-related knee pain, with more patients achieving a moderate and substantial improvement in pain compared with placebo. As with any medications, this needs to be balanced against the potential increased risk of adverse events which, not surprisingly, was higher in the duloxetine groups. It should be emphasised that, across all patients, the mean difference in pain intensity compared with placebo was 0.88 points, which is of questionable clinical importance. The between-group difference in WOMAC physical function scores was also small. Taken together, these findings suggest notable variability in the individual treatment response. It would be interesting to see whether potential treatment responders to duloxetine could be better identified with the use of relatively simple quantitative sensory testing procedures, as has been shown in a study of painful diabetic neuropathy. This may lead to more rational prescribing, maximising the potential therapeutic effect while reducing potential harm in patients less likely to benefit. Until then, the jury appears out on this one.

Abstract

Sleep and pain sensitivity in adults
Authors: Svivertsen B et al.
Summary: Associations between a range of self-reported sleep measures and experimental increased pain sensitivity were explored in this cross-sectional population-based study with data from 10,412 participants. Sleep onset latency, sleep efficiency and insomnia frequency and severity, but not sleep duration, were found to be significantly associated with reduced pain tolerance and also with pain sensitivity in a dose-response manner. The relationships were attenuated when adjusted for demographics and psychological distress, but most remained statistically significant in fully adjusted models. A synergistic interaction effect was also seen on pain tolerance when insomnia and chronic pain were combined.

Comment (DR): The bidirectional relationship between sleep and pain is well established. Pain not only disturbs our sleep, but disrupted sleep can reduce the function of our own ‘in built’ pain inhibitory pathways and increase clinical pain intensity. In fact, a recent review of the evidence concluded that sleep disturbances exacerbate existing chronic pain conditions and increase the risk that pain-free individuals will go on to develop a new chronic pain condition. The strength of this paper is its large population-based sample and comprehensive range of sleep-related measures. Experimental pain sensitivity was assessed using the cold pressor test, where the hand is submerged in ice cold water and the time to withdrawal is taken as a measure of pain tolerance. A number of sleep-related factors were found to be related to pain tolerance in a dose-response manner, including the frequency and severity of insomnia, sleep onset latency (the time it usually takes to fall asleep) and sleep efficiency (the proportion of time in bed actually spent asleep). The presence of chronic pain and sleep disturbances had additive adverse effects on pain tolerance. Interestingly the actual amount of sleep, in terms of hours of sleep per night, was not associated with reduced pain tolerance. The findings of this paper should remind us that sleep is an important and multidimensional factor that deserves to be formally assessed in chronic pain patients and that, wherever possible, treatment of sleep disorders should form part of an overall patient management plan. Importantly, improving sleep is likely to reduce pain as well as enhance an individual’s quality of life.

Reference: Pain 2015;159(1):1433–9
Abstract

Naloxone added to bupivacaine or bupivacaine–fentanyl prolongs motor and sensory block during supraclavicular brachial plexus blockade
Authors: Marashi SM et al.
Summary: Patients scheduled for surgery under supraclavicular brachial plexus block were randomised to receive bupivacaine 30ml on its own or with fentanyl 100µg, naloxone 100ng or both. There were no between-group differences for sensory and motor onset times, whereas the durations of both sensory and motor blocks were significantly longer in the naloxone-containing arms than the two arms without naloxone (p<0.0001).

Comment (JB): This is another study that likely will stimulate more questions rather than provide definitive answers. If you wanted to prolong the postoperative analgesia related to a single-shot brachial plexus block by adding a drug to the local anaesthetic used for the block, what would you choose? On the basis of this study you could cross off fentanyl and you could consider naloxone (0.1microg = 100 nanogram naloxone). The opioid antagonist prolonged the sensory block by 30–50%. It would be useful to see naloxone compared with morphine or clonidine using the same experimental model. The expectation would be that naloxone would not cause as much sedation as clonidine and none of the opioid side effects related to unconsciousness or respiratory depression, but that what is the ideal dose, does naloxone work as well if given systemically, and what is the mechanism and site of action? The study includes a brief discussion about putative mechanisms – for example, the naloxone blocks opioid-mediated release of excitatory neurotransmitters from spinal glial cells.

Abstract

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Reversal of neuromuscular block with sugammadex: a comparison of the corrugator supercilii and adductor pollicis muscles in a randomized dose-response study

Authors: Yamamoto S et al.

Summary: These researchers recorded corrugator supercilii and adductor pollicis muscle responses to facial nerve stimulation and adductor pollicis muscle responses to ulnar nerve stimulation in 40 patients aged 20–60 years and 40 patients aged ≥70 years, who received rocuronium 1 mg/kg initiated to maintain the first twitch of a TOF (train-of-four) at 10% of the control value, once this was achieved. The participants received sugammadex 2 or 4 mg/kg immediately after rocuronium was discontinued. When corrugator supercilii block was maintained at a first twitch of 10% of the control value, adductor pollicis block was deep, with a post-tetanic count ≤5. Complete antagonism of the neuromuscular block at both muscles was achieved within 5 minutes of sugammadex 4 mg/kg administration. The older participant group had a significantly longer mean time to achieve a TOF ratio of 1.0 at the adductor pollicis (178 vs. 120 sec; p<0.0001). Sugammadex 2 mg/kg achieved reversal of neuromuscular blockade at the corrugator supercilii but not at the adductor pollicis; ten and eight participants from the 20- to 60-year and >70-year aged groups, respectively, needed additional sugammadex, significantly more than after the 4 mg/kg dose.

Comment (JB): The authors developed a study protocol that maximised the likelihood of getting ‘clean’ twitches by inducing anaesthesia, placing a laryngeal mask airway, and establishing baseline TOF values before giving the loading dose of rocuronium, and maintaining a steady level of block with a rocuronium infusion. Ideally a muscle physiologist would be helping me write the commentary for this paper because I suspect they would find it straightforward to explain the time course of neuromuscular block for each of the two studied muscles. Without a clear understanding of the physiology though, there are still important lessons for the clinician. This study commends a cautious approach when using neuromuscular function monitoring at the corrugator supercilii (or by inference other facial muscles around the eye) to measure block depth or recovery. In essence, at the end of the case, moderate intensity block (TOF1 = 10% of control) measured at the corrugator supercilii muscle corresponded to deep block (post-tetanic count ≤5) at the adductor pollicis, and at this level of block, a 2 mg/kg dose of sugammadex was reliably adequate to reverse the block as measured at the former site, but not at the latter. If your principle concern is to guarantee a moderate or deep level of blockade, then measuring function at the corrugator supercilii may be advantageous. In contrast if your principle concern is to guarantee recovery of neuromuscular function, then the adductor pollicis may be preferable. There are a couple of other gems, e.g. the need to limit the currents used when stimulating facial muscles in order to avoid direct muscle stimulation.


A systematic review and meta-analysis of ultrasound versus electrical stimulation for peripheral nerve location and blockade

Authors: Munirama S & McLeod G

Summary: This systematic review of ultrasound-guided peripheral nerve blockade versus electrical stimulation included 26 comparisons from 23 RCTs (n=2125). Ultrasound guidance was associated with less procedural pain (relative risk 0.60 [95% CI 0.41, 0.89]) and reduced rates of analgesic or anaesthetic rescue when used with or without electrical stimulation compared with electrical stimulation alone (0.40 [0.29, 0.54] and 0.29 [0.16, 0.52], respectively). Adding electrical stimulation to ultrasound did not affect the rate of rescue. Ultrasound guidance, with or without electrical stimulation, was also associated with a lower pooled rate of vascular puncture (relative risk 0.23 [95% CI 0.15, 0.37]), but did not significantly affect postoperative neurological side effects.

Comment (JB): This review provides clear evidence of the superiority of ultrasound as compared with nerve stimulation for peripheral nerve regional anaesthesia. There are a variety of ways to express the data but one of the most approachable is found in the last paragraph of the results section — “Ultrasound compared with electrical stimulation would increase the number of successful peripheral nerve blocks per 1000 patients from 828 to 918 and would reduce the rate of rescue analgesia, sedation or anaesthesia from 172 to 82 per 1000 patients.” There was no demonstrable added benefit for adding nerve stimulation to an ultrasound technique. Perhaps predictably, ultrasound techniques caused less pain during placement of the needle. The studies selected encompassed a range of blocks (sciatric >7, axillary >6, infratrochlear >6, interscalene >3 and one using median and ulnar nerve block). There was no time-based (year of publication) influence found in this review. It would be interesting to repeat the study in 5–10 years time, as the ultrasound skills of the profession improve and the quality of the ultrasound technology improves. Perhaps the finding that will raise readers’ eyebrows is the 9% of transient neurological symptoms 24 hours to 4 weeks after blockade. Understanding the causes and finding ways to improve this rate of symptoms must be a priority for regional anaesthesia researchers.

Reference: Anaesthesia 2015;70(9):1084–91

The effect of adding a background infusion to patient-controlled epidural labor analgesia on labor, maternal, and neonatal outcomes

Authors: Heesen M et al.

Summary: This was a systematic review and meta-analysis of seven trials with a low risk of bias (n=891) comparing PCEA on its own versus combined with a continuous infusion in parturients. Compared with PCEA alone, PCEA plus continuous infusion was associated with a greater rate of instrumental vaginal delivery (risk ratio 1.66 [95% CI 1.08, 2.56]), with no significant impact on caesarean delivery (0.63 [0.61, 1.13]). PCEA with continuous infusion was also associated with prolonged second stage of labour (WMD 12.3 min [p=0.0003]) and reduced requirement for physician-administered boluses (risk ratio 0.35 [95% CI 0.25, 0.47]). There were no between-group differences for maternal adverse events or neonatal outcomes.

Comment (JB): The largest and most certain effect found was the greater need for physician assisted top-ups in the PCEA only group compared with PCEA plus continuous infusion’. Given the lack of certainty regarding the other statistically significant differences, it is probably reasonable to let this resource-related benefit drive clinical practice. The greater rate of instrumental delivery in the PCEA plus continuous infusion group (favouring PCEA) and the possibly lower rate of lower-segment caesarean section in the PCEA plus continuous infusion group (favouring PCEA plus continuous infusion) would be clinically significant if either were proven in a large RCT. For the researcher planning a meta-analysis in the obstetric anaesthesia setting, this paper has a well-written methods section and an interesting discussion. The effort and precision required to complete a systematic review and meta-analysis comes through clearly, as does the value of spending some time becoming familiar with the Cochrane Collaboration technical papers.


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A RESEARCH REVIEW publication
Protective versus conventional ventilation for surgery

Authors: Neto AS et al., for the PROVE Network Investigators

Summary: This systematic review and individual patient data meta-analysis of fifteen RCTs found a significantly lower postoperative pulmonary complication rate among 1118 general surgery patients assigned to protective ventilation compared with 1009 assigned to conventional ventilation (8.7% vs. 14.7%; adjusted relative risk 0.64 [95% CI 0.46, 0.88]). Postoperative pulmonary complications did not differ significantly between patients assigned to ventilation with low tidal volumes and high PEEP levels (n=597) versus those assigned to ventilation with low tidal volumes and low PEEP levels (n=525; 8.9% vs. 12% [p=0.72]). Postoperative pulmonary complications were related to tidal volume in a dose-dependent manner (R²=0.39) but not PEEP level (R²=0.08).

Comment (JB): Research based on the intensive care environment provides strong evidence for the use of protective ventilation strategies. While the rates of severe pulmonary outcomes are lower in the theatre setting, this recent meta-analysis suggests a similar pattern of beneficial responses exists when lung protection strategies are used during surgery. As the technology of anaesthesia ventilators and monitoring has improved, clinicians have a range of ventilation modes to select from, better control of the parameter settings, and can optimise to various intra-operative target endpoints. In essence, lower tidal volumes (6–8 ml/kg of predicted bodyweight) are better than larger tidal volumes. Some PEEP is probably good. Regular recruitment manoeuvres may be good. The other side of the coin is the potential for PEEP to alter cardiovascular parameters, fluid requirements, blood loss and operative conditions. Much remains unknown about the mechanism of ventilator-induced lung injury. Volume stress, atelectasis, repeated closure and reopening of small alveoli are all thought to be important. Given the number of adjustable variables and relevant endpoints, this is a difficult area to study using an RCT model. The longer the operation (e.g. >2 hours) and the heavier the patient, the more likely it is that time spent optimising the ventilation strategy will be time well spent. If there is a provisional fellow/senior registrar in your department looking for a subject to write and present as a critically appraised topic, this would be a worthy choice.


A randomized, double-blinded trial of a ‘rule of threes’ algorithm versus continuous infusion of oxytocin during elective cesarean delivery

Authors: Kovacheva VP et al.

Summary: These researchers randomised 60 women scheduled for elective caesarean delivery to receive oxytocin as a low-dose IV bolus 3 IU/3ml or a continuous infusion 30IU in 0.9% saline 500ml., with steps taken to ensure blinding. Adequate uterine tone was achieved with a lower bolus oxytocin mean dose compared with infusions (4.0 vs. 8.4IU [p<0.0001]), with no further oxytocin or other uterotonic agents required after 6 minutes in the bolus group. There was no between-group difference for uterine tone, maternal haemodynamics, side effects or blood loss.

Comment (JB): Consistent with the introduction of this article, the practice regarding the use of uterotonics following lower-segment caesarean section delivery varies around NZ. A recent correspondent writing to the HQSC (Health Quality and Safety Commission) highlighted the dangers of oxytocin boluses and recommended that the HQSC promotes only giving this medicine as an infusion. There is added danger and no added benefit from large boluses of oxytocin makes it an unattractive alternative for Pharmac.


Does a prophylactic dose of propofol reduce emergence agitation in children receiving anesthesia?

Authors: van Hoff SL et al.

Summary: This systematic review and meta-analysis included nine trials, all with low risk of bias, comparing propofol 1 mg/kg with placebo following inhalational anaesthesia for preventing emergence agitation in a total of 997 paediatric patients. Compared with placebo, prophylactic propofol was associated with decreases in the incidence of emergence agitation (29% vs. 58%, relative risk 0.50 [95% CI 0.41, 0.61]) and its severity assessed with mean PAED (Pediatric Anesthesia Emergence Delirium) scale score (WMD –2.08 points [-3.20, –0.96]). Propylolical propofol was also associated with longer time to awakening (WMD 4.07 min [95% CI 2.22, 5.91]), but did not significantly increase recovery time (2.91 min [-0.59, 6.41]). There were no significant adverse events reported with propofol or placebo.

Comment (JB): The authors’ decision to use the PAED scale as the primary endpoint limited the number of studies that could be included, but at the same time it guaranteed that the data would combine well for the meta-analysis. The PAED scale looks to be an easy instrument to use in the clinical setting (designed and validated at the Toronto Hospital for Sick Children; published in Anesthesiology). The propofol dose given at emergence was 1 mg/kg in all the nine studies included. As noted above, there is little downside to this practice and the upside is a 50% reduction in emergence delirium. The authors note the need for further efforts to define if other agents or combinations of agents would work better than propofol. Not knowing the underlying mechanism of emergence delirium is an inherent problem. Previous work has debunked the idea that a slow sevoflurane washout is better than the more usual high-flow technique. If you are anaesthetising a patient who is at very high risk of emergence, e.g. has had prolonged and distressing periods of agitation previously or the agitation may cause harm postoperatively, then avoiding a volatile anaesthetic entirely may be the best way to increase the chances of a smooth wake up.


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