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- Cognitive effects of perioperative pregabalin

Abbreviations used in this issue:

ASA = American Society of Anaesthesiologists; BMI = body mass index; COX-2 = cyclooxygenase-2; ICU = intensive care unit; IV = intravenous; MAC = minimum alveolar concentration; NSAID = non-steroidal anti-inflammatory drugs; NMB = neuromuscular blockade; OSA = obstructive sleep apnoea; TOF = train-of-four.

Welcome to issue 15 of Anaesthesia Research Review.

Anaesthetists work in complex high-stake and high cognitive demand environments whereby one must perform under critical conditions. There are a high number of distractions and interruptions, which may increase the risk of anaesthesia-related error. Anaesthetists are met with a variety of patients of all ages, varying medical conditions and a large range of diverse surgical and diagnostic interventions. Many problems may occur during anaesthesia, requiring fast, effective and appropriate reactions by the anaesthetist. Acuity, vigilance, alertness and constant monitoring of the patient are thereby very important aspects at all times. Therefore, it is common practice to have adequate monitoring, a range of techniques to provide general and regional anaesthesia, and a profound knowledge of diseases and pharmacology. Anaesthesia, regional blocks, and drugs administered by anaesthetists work almost instantly, requiring a good knowledge of pharmacokinetic and pharmacodynamic parameters of the drugs used.

We’re glad to offer you this edition of the Anaesthesia Research Review, whereby colleagues focused on some of these problems, in review of recent publications, e.g.:

- Whether caudal or paravertebral blocks have a better outcome despite the latter being technically more challenging.
- Supraglottic airway devices are advised as rescue devices in difficult airway management algorithms, but researchers found that they were only successful in two-thirds of the patients, underpinning the importance that anaesthetists should evaluate whether the device is in the correct position in the hypopharynx.
- The interaction of S-ketamine on the MAC of sevoflurane is not studied well, but is important as the combination is used more and more in our daily practice.
- Postoperative pain relief is often offered to patients in the form of multimodal analgesia. In obstructive sleep apnoeic patients, opioids may have adverse risks of respiratory complications. Therefore we need to substitute part of the opioids with non-opioid agents.
- It is interesting to see that 34% of anaesthetists report upper limb disorders, making ergonomic design of our medical devices, equipment and workstations a point of care.
- Reversal of neuromuscular blocking agents is part of emergence of anaesthesia. It is laudable that anaesthetists look for good alternatives to common rocuronium-sugammadex combinations to reduce side effects.
- It is interesting to see several studies focusing on the association of the use of anaesthetic agents (e.g., inhaled anaesthetics) and the incidence of the recurrence of cancer.
- Caesarean deliveries under spinal anaesthesia are complicated with postdural puncture headache. It is interesting to find out whether continuous infusions of sympathicomimetics will provide the answer to the problem.
- Postoperative delirium is a complication we realise does exist on a much larger scale than previously thought. The question is whether electroencephalography-guided anaesthesia will prevent delirium.
- Opiate-sparing effects of pregabalin are useful in anaesthesia, but the agent negatively affects cognition. How does it compare to other analgesic regimens?

I wish you an enjoyable reading experience of our selected literature.

Kind Regards,

Professor André van Zundert
andre.vanzundert@researchreview.com.au

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Comparison of caudal epidural block with paravertebral block for renal surgeries in pediatric patients: A prospective randomised, blinded clinical trial

Authors: Naraishman P et al.

Summary: This single blind RCT aimed to compare the efficacy of ultrasound-guided single-shot paravertebral block (0.2% ropivacaine plus 1:200000 adrenaline) compared to the more widely used ultrasound-guided single-shot caudal block for postoperative analgesia in 50 children (aged 2-10 years) undergoing renal surgeries. The children in the paravertebral group had longer duration of analgesia compared to the caudal group (p < 0.0004), lower postoperative FLACC (Face, Legs, Activity, Cry, Consolability scale) scores from 3 hours onwards (p < 0.005) and lower overall analgesic requirements (p < 0.0004). Paravertebral recipients also demonstrated higher parental satisfaction compared to caudal recipients (p < 0.02). Mean fentanyl requirement over 24 hours in paravertebral recipients was 0.56 versus 1.8 μg/kg in caudal recipients. No complications occurred in either group. The paravertebral approach had one failed block that required fentanyl immediately postoperatively.

Comment: (Dr Ben Steiger) The single-shot caudal epidural block has been widely used for analgesia in paediatric operations. The paravertebral block has seen increasing use since the early 1990s. This study compared the postoperative analgesia requirements between caudal and paravertebral blocks with the primary endpoint being time to rescue analgesia and secondary endpoints being total postoperative opioid use, FLACC scores and parental satisfaction. They utilised an appropriately powered sample size of 50 patients, aged between 2 and 10 years old, undergoing elective renal surgery. They were able to achieve single blinding of the anaesthetist evaluating postoperative analgesia requirements, but it is unclear if the nursing staff administering analgesia or assessing for pain were blinded. The anaesthetic was performed by protocol to ensure both groups received identical induction/sedative agents, intra-operative opioids, anti-emetics and anti-pyretics. Fluctuations in haemodynamic parameters by >20% from baseline during the operation were deemed inadequate analgesia and a 1 μg/kg fentanyl bolus was administered in both groups. Postoperative analgesia was also conducted under a similar fentanyl protocol. The use of strict protocols and identical groups allowed appropriate comparison of the groups. There was no difference between the groups in intraoperative use of fentanyl or incidence of complications. The paravertebral block took more than double the time to perform and had the only failed block, but this was not statistically significant. The paravertebral block demonstrated a longer time to rescue analgesia, less overall opioid use, lower FLACC scores and higher overall parental satisfaction. These results provide good evidence for the use of unilateral paravertebral block in the paediatric population for renal surgeries. The paravertebral block is more technical and time consuming, but did not demonstrate a higher incidence of complications. Further studies would need to be conducted to ensure that the incidence of failure and complications are not higher in the paravertebral group, as this study was underpowered to determine this. These findings should be validated for other surgeries with similar approaches/incisions in the same population to allow generalisation of the paravertebral block over the caudal epidural block.

Reference: J Clin Anesth. 2019;52:105-10

Effect of intravenous S-ketamine on the MAC of sevoflurane: a randomised, placebo-controlled, double-blinded clinical trial

Authors: Hamp T et al.

Summary: This randomised, double-blind, placebo-controlled clinical trial examined whether IV ketamine (0.5 or 1 mg/kg S-Ketamine) influenced the minimum alveolar concentration (MAC) of sevoflurane in 60 adult patients undergoing elective surgery. Sevoflurane MAC was higher in placebo recipients (2.1%) than in low-dose (0.9%; p < 0.01) or high-dose (0.5%; p < 0.01) recipients; the sevoflurane MAC was also higher in low-dose versus high-dose ketamine recipients (p < 0.01).

Comment: (Dr Kate Taylor) This study is the first to investigate the effects of IV administration of ketamine on the MAC of inhalational anaesthetic sevoflurane in females undergoing elective surgery. Despite widespread use of ketamine in perioperative settings, there is insufficient knowledge of the interaction between ketamine and inhalational anaesthetic agents in humans. In this prospective, randomised, controlled, double-blinded study, participants were assigned by computer-generated randomisation to one of three groups and, after inhalational induction with sevoflurane, administered a bolus of either placebo, 0.5 mg/kg S-ketamine or 1 mg/kg S-ketamine followed by an infusion of the same amount per hour. Doses and preparations of ketamine actually vary more greatly in peroperative settings. Participant characteristics and morphometric data did not differ significantly between groups. Response to skin incision (movement vs non-movement) was recorded by the anaesthetist, which raises concerns of observer bias. The MAC of sevoflurane was assessed by a titration method. Results revealed low- and high-dose ketamine reduced the MAC of sevoflurane by >50% and 75%, respectively. This is consistent with results found in published studies in animals. The effect of IV ketamine in suppressing the motor response to skin incision alone should be evaluated to determine whether ketamine has a synergetic or additive effect on the MAC of sevoflurane. This study is clinically important because it creates greater understanding of the interaction between inhalational sevoflurane and IV ketamine, which are routinely used together in perioperative patient management.


Supraglottic airway devices in difficult airway management: a retrospective cohort study of 658,104 general anaesthetics registered in the Danish Anaesthesia Database

Authors: Thomsen JLD et al.

Summary: This retrospective Danish study examined the records of 658,104 general anaesthetics recorded in the Danish Anaesthesia Database from 2008 to 2012 to examine the use of supraglottic airway devices (SGA) in difficult airway management. They identified 4898 cases (0.74%; 95% CI 0.72-0.76) that had a difficult airway (>3 tracheal intubation attempts, failed tracheal intubation or difficult facemask ventilation). SGAs were used in 607 difficult airway cases (12.4%; 95% CI 11.5-13.3) and were successful in 395 (65.1%; 95% CI 61.2-68.3) ‘in cannot intubate cannot facemask ventilate’ cases, SGAs were used in 86 of 455 cases (18.9%; 95% CI 15.6-22.8) and were successful in 54 (62.8%; 95% CI 52.7-72.3).

Comment: (Dr Peter Malcomson) I was impressed by the comprehensive nature of this study in terms of its use of a registered database and the high numbers of cases in the analysis. The authors point out in the analysis that there is little existing data regarding the use of SGAs in difficult airway scenarios, and such data as exists is based on outcome measures such as leak pressure and the use of manikins simulating difficult airways. In my opinion, this evidence is little use compared to that of a retrospective look at the use and success rates of SGAs in difficult airways in a live population as exemplified by this study. The external validity of the study is improved by the broad nature of the cases in terms of patient, surgical and anaesthetic factors captured in this analysis. The success rate of all SGAs was noted as “similar”, but no other breakdown could be given. Future research would ideally look at the success rate of the particular type of SGA being used. Of interest is the breakdown of difficult airway causes; >3 tracheal intubation attempts in 3687 cases (75.3%), failed tracheal intubation in 236 cases (4.8%) and by isolated difficult facemask ventilation in 975 cases (19.9%), and that difficult airway scenarios were more common in older, male patients with higher ASA score and in elective rather than emergency scenarios. The take home message is that in 65% of difficult airway scenarios, SGA placement was successful, but the SGA was only attempted in 12% of those difficult airways cases. This study encourages the use of SGAs in difficult airway management.

Reference: Anaesthesia 2019;74(2):151-7
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IMMEDIATE RELEASE

ATYPICAL OPIOID

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*Analgesia not solely derived from opioid agonism. *S8 analgesic.
†Non-inferior efficacy (5-day sum of pain intensity difference) and significantly lower incidence of constipation, nausea and vomiting (nominal p<0.001 for all events); PALEXIA® IR 50mg vs. oxycodone IR 10mg. Secondary endpoint. Primary endpoint was met.

MINIMUM PRODUCT INFORMATION: PALEXIA® IR (tapentadol hydrochloride) INDICATION: Moderate to severe pain. CONTRAINDICATIONS: Known hypersensitivity to tapentadol or any component of PALEXIA IR, conditions in which mu-opioid receptor agonist activity is contraindicated e.g. significant respiratory depression and acute or severe bronchial asthma or hypoxemia, confirmed or suspected paralysis, latent or active intoxication with alcohol, hypothyroidism, centrally acting anxiogenic or psychotropic drugs; patient who are receiving MAO inhibitors or who have taken them within the last 14 days. PRECAUTIONS: Monitor for signs of abuse and addiction; repeated administration may lead to tolerance; withdrawal symptoms could occur after abrupt discontinuation, not recommended in patients with increased intracranial pressure, impaired consciousness, coma and severe renal or severe hepatic impairment, caution in patients with impaired respiratory functions, patients with head injury, brain tumours, a history of fractures or any condition that increases risk of seizures, severe renal impairment, moderate or severe hepatic impairment or biliary tract disease, including acute pancreatitis. Use in pregnancy (Category C). Should not be used during breastfeeding. Not recommended for children <18 years old. May impair ability to drive or operate machinery. INTERACTIONS: Care should be taken when combining with mixed agonist antagonist or partial mu-opioid agonist antidepressants, CNS depressants, including alcohol and illicit drugs. Reduction of dose of one or both agents should be considered; concomitantly patients who are receiving MAO inhibitors or who have taken them within the last 14 days; isolated case reports of serotonin syndrome when used in combination with serotonergic drugs (see full PI). ADVERSE EFFECTS: Very common (≥1/10): dizziness, somnolence, headache, nausea, vomiting. Common (≥1/100 to <1/10): Decreased appetite, anxiety, confusional state, hallucination, sleep disorder, dry mouth, pruritus, hyperhidrosis, rash, muscle spasms, asthenia, fatigue, feeling of body temperature change, abnormal dreams, tremor, flushing, constipation, diarrhoea, dyspepsia, dry mouth, pruritus, hypertension, rash, muscle spasms, asthenia, fatigue, feeling of body temperature change, abnormal dreams, tremor, flushing, constipation, diarrhoea, dyspepsia, dry mouth, pruritus, hypertension, rash, muscle spasms, asthenia, fatigue, feeling of body temperature change, abnormal dreams, tremor, flushing, constipation, diarrhoea, dyspepsia, dry mouth, pruritus, hypertension, rash, muscle spasms, asthenia, fatigue, feeling of body temperature change, abnormal dreams, tremor, flushing, constipation, diarrhoea, dyspepsia, dry mouth, pruritus, hypertension, rash, muscle spasms, asthenia, fatigue, feeling of body temperature change.


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Non-opioid analgesic modes of pain management are associated with reduced postoperative complications and resource utilisation: a retrospective study of obstructive sleep apnoea patients undergoing elective joint arthroplasty

Authors: Cozowicz C et al.

Summary: This online survey of 10,231 electronically accessible members of the UK Association of Anaesthetists was conducted to determine the incidence of upper limb disorders (ULDs). In total, 3884 (38%) patients with reduced postoperative complications and resource utilisation: a retrospective study of obstructive sleep apnoea patients undergoing elective joint arthroplasty were included in the study and 88.5% received multimodal analgesia. In 64,174 patients who received multimodal analgesia, opioid prescription dose reduced by 14.9% (primary outcome). There was a decrease in gastrointestinal complications (OR 0.65; CI 0.53-0.78), postoperative mechanical ventilation (OR 0.23; CI 0.16-0.32) and critical care admissions (OR 0.60; CI 0.48-0.75); all p < 0.0001.

Comment: (Dr Srey Loch) Many studies have shown that surgical patients with OSA have increased risks of respiratory complications, need for ICU services, and increased length of stay. With this in mind, preoperative guidelines often advocate for multimodal analgesia to minimise the use of opioids, fearing that its respiratory depressant effects can worsen OSA and increase adverse postoperative risks. However, studies looking at the benefits of multimodal opioid-sparing adjuncts are limited. Cozowicz et al.’s large, retrospective cohort study aimed to demonstrate the positive impact of multimodal analgesia in reducing opioid prescription and its associated complications. This study found that there was a proportional decrease in opioid prescription of up to 14.9% as patients received an increasing number of non-opioid agents such as NSAIDs, COX-2 inhibitors, gabapentin/pregabalin, ketorolac, and low-dose steroids. The biggest decreases were observed with use of NSAIDs (-11%) and COX-2 inhibitors (-12.5%). Secondary outcomes evaluating opioid-related adverse effects (respiratory, gastrointestinal, renal) and OSA-associated complications (CPAP use, critical care admission, mechanical ventilation) also favoured multimodal analgesia use. It is important to note that there was no increase in nephrotoxicity associated with multimodal analgesia. Not surprisingly, the opioids only group had the highest opioid prescription dose, adverse complications, and longer hospital stay. All in all, this study addresses an important clinical question and provides strong support for the use of non-opioid adjuncts. Although this study focused on OSA patients undergoing joint arthroplasty, the results might also be generalised to patients with similar risk factors undergoing different procedures. Considering that non-opioid adjuncts are readily available, it is worthwhile adding simple medications such as ibuprofen and celecoxib in an effort to reduce narcotic use and improve patient outcomes. The study is well powered, however, it is limited by its retrospective nature.


Abstract

Upper limb disorders in anaesthetists - a survey of Association of Anaesthetists members

Authors: Leifer S et al.

Summary: This online survey of 10,231 electronically accessible members of the UK Association of Anaesthetists was conducted to determine the incidence of upper limb disorders (ULDs). In total, 3884 (38%) responses suggested an association between upper limb disorders and years since commencing anaesthetic training, having children, and critical care admissions (OR 0.60; CI 0.48-0.75); all p < 0.0001. With right-handedness may reflect the ergonomic design of environment and/or equipment and may be a modifiable risk factor.

Comment: (Dr Stefan Saric) dNMB is favourable in certain surgical procedures. However, the reversal of dNMB is often problematic as anticholinesterases may be ineffective, and the high cost of sugammadex precludes its routine and widespread clinical use. This paper attempted to demonstrate a cheaper alternative to rocuronium- or vecuronium-sugammadex combinations, by comparing pipercuronium with moderate dose (2 mg/kg) vs standard dose (4 mg/kg) sugammadex reversal. Pipercuronium is similar in structure, onset, and duration to pancuronium, and has no cardiovascular side effects. It is also the most potent aminosteroid neuromuscular blocking agent (NMBA), and has the highest binding affinity for sugammadex. The authors were conscientious in their design of NMB monitoring in this study, acceleromyographs were calibrated prior to administration of the NMBA and quantitative definitions of recovery from deep block (T1/T0 >0.9) and re-dosing interval (T0/T1FC 1) were established. Clinically appropriate non-inferiority limit was specified in advance. However, the study suffered from two major limitations: lack of generalisability, and an unclear randomisation process. Firstly, the lack of inclusion of obese (>25 kg/m² BMI) and elderly (>65 years) patients is discordant with a significant population of surgical patients. Additionally, the mean surgical time between both arms was 83.47 minutes, and longer procedures (i.e. >2 hrs) were not assessed. Pipercuronium also appears to be available in the UK, Australia, or New Zealand, and it is not clear whether the simple randomisation process adopted was truly random; 25 cards labelled “4 mg/kg” and another 25 cards labelled “2 mg/kg” were placed in an envelope, and then picked out by an anaesthetist as patients were enrolled into the study. Combined with the small sample size, these factors limit the validity and generalisability of the results. Future studies should adopt broader inclusion criteria, and a more sophisticated randomisation process.


Abstract

Reversal of deep pipercuronium-induced neuromuscular blockade with moderate versus standard dose of sugammadex: A randomized, double-blind, noninferiority trial

Authors: Tassonyi E et al.

Summary: This small (n = 50), single-centre, Hungarian, randomised, parallel-arm non-inferiority study assessed whether moderate dose sugammadex (2 mg/kg; n = 25) was as effective as standard dose (4 mg/kg; n = 25) in the reversal of deep neuromuscular blockade (dNMB) with pipercuronium, in 18-65 year old (mean age 44.4 years), ASA I-III patients with a BMI of 18.5-25.0 kg/m² who were undergoing general anaesthesia for elective abdominal surgery with expected duration >60 minutes. The non-inferiority margin was an increase in reversal time (normalised TOF ratio of 0.9) of no greater than 10%. In the 2 mg/kg group, mean reversal time was 1.73 minutes (65% CI 1.33-2.13), and in the 4 mg/kg group reversal time was 1.42 minutes (65% CI 1.17-1.67). The mean difference in reversal times between the two groups was 0.31 minutes (95% CI -0.18 to 0.8). All patients recovered to a normalised TOF ratio of 0.9, and there were no cases of residual NMB. The authors concluded that sugammadex 2 mg/kg was non-inferior to 4 mg/kg in reversing dNMB with pipercuronium.

Comment: (Dr Stefan Saric) dNMB is favourable in certain surgical procedures. However, the reversal of dNMB is often problematic as anticholinesterases may be ineffective, and the high cost of sugammadex precludes its routine and widespread clinical use. This paper attempted to demonstrate a cheaper alternative to rocuronium- or vecuronium-sugammadex combinations, by comparing pipercuronium with moderate dose (2 mg/kg) vs standard dose (4 mg/kg) sugammadex reversal. Pipercuronium is similar in structure, onset, and duration to pancuronium, and has no cardiovascular side effects. It is also the most potent aminosteroid neuromuscular blocking agent (NMBA), and has the highest binding affinity for sugammadex. The authors were conscientious in their design of NMB monitoring in this study, acceleromyographs were calibrated prior to administration of the NMBA and quantitative definitions of recovery from deep block (T1/T0 >0.9) and re-dosing interval (T0/T1FC 1) were established. Clinically appropriate non-inferiority limit was specified in advance. However, the study suffered from two major limitations: lack of generalisability, and an unclear randomisation process. Firstly, the lack of inclusion of obese (>25 kg/m² BMI) and elderly (>65 years) patients is discordant with a significant population of surgical patients. Additionally, the mean surgical time between both arms was 83.47 minutes, and longer procedures (i.e. >2 hrs) were not assessed. Pipercuronium also appears to be available in the UK, Australia, or New Zealand, and it is not clear whether the simple randomisation process adopted was truly random; 25 cards labelled “4 mg/kg” and another 25 cards labelled “2 mg/kg” were placed in an envelope, and then picked out by an anaesthetist as patients were enrolled into the study. Combined with the small sample size, these factors limit the validity and generalisability of the results. Future studies should adopt broader inclusion criteria, and a more sophisticated randomisation process.


Abstract
Total intravenous anesthesia versus inhalation anesthesia for breast cancer surgery: A retrospective cohort study

Authors: Yoo S et al.

Summary: This Korean, single-centre, retrospective study (2005-13) compared total IV anaesthesia (TIVA; propofol plus remifentanil) versus inhaled anaesthesia (enflurane, isoflurane, sevoflurane, or desflurane) for breast cancer surgery and its impact on 5-year breast cancer recurrence rate and 5-year overall survival rate. Individual patient characteristics were accounted for by propensity score matching. Patients were excluded if they were male, had benign or in situ carcinoma, ASA score ≥2, did not receive recommended adjuvant therapy or if they had missing data. Of the 7678 patients who underwent breast cancer surgery, 5331 patient records were analysed, with 3085 patients in the TIVA group and 2246 patients in the inhaled anaesthesia group. No differences in recurrence-free survival or overall survival rates were found between the two groups. The 5-year recurrence-free survival rates were 93.2% (95% CI 91.9-94.5) for the TIVA group and 93.8% (95% CI 92.6-95.1) for the inhalation group. The 5-year overall survival rate was 94.2% (95% CI 92.9-95.5) for the TIVA group and 94.5% (95% CI 93.9-95.8) for the inhaled anaesthesia group. Furthermore, when compared with the TIVA group, inhalation anaesthesia had no impact on either recurrence-free survival (HR 0.96; 95% CI 0.89-1.32) or overall survival (HR 0.96; 95% CI 0.69-1.33).

Comment: (Dr Gabriela Kelly) Research to date has suggested that an association may exist between anaesthetic agents used for cancer treatment surgery, and the incidence of cancer recurrence. All anaesthetic agents are thought to suppress cell-mediated immunity and increase angiogenesis, which in turn may promote proliferation and metastasis of existing cancer cells. It has been hypothesised that inhalational anaesthesia for cancer-related surgery, compared with IV agents, may be associated with higher rates of cancer recurrence. Yoo et al., aimed to address this hypothesis, specifically in relation to patients with breast cancer. Women included in this study were matched for background patient information such as age, breast cancer subtype, ASA physical status, type of surgery, and use of adjuvant treatment where recommended. Patient factors not accounted for included specific patient comorbidities and cases where adjuvant cancer therapy was delayed. This research has some limitations that should be considered when interpreting the results. Firstly, 5-year mortality due to any cause was measured, and the study does not measure what proportion of these patients died from or as a consequence of breast cancer. Also, the results could be subject to bias as a number of patients recruited were ineligible for analysis due to the exclusion criteria and missing patient data. No statistical power calculation was provided for the sample size that was analysed. In addition, the authors noted that over the 9-year timeframe of the study, adjuvant therapies were updated and it is possible that this could have affected patient outcomes. Another assumption of the study was that all types of inhalational agents had equal effects on cancer recurrence. There are some in vitro studies suggesting that individual inhalational agents may differ in their actions on the immune system and cancer cell proliferation. Overall, this study provides some insight into whether mode of anaesthesia affects 5-year breast cancer recurrence; however, the authors do not recommend altering practice as a result of their research and anticipate that future studies might better answer this question.

Reference: Anesthesiology 2019;130(1):31-40

Norepinephrine infusion for preventing postspinal anesthesia hypotension during cesarean delivery: A randomized dose-finding trial

Authors: Hasanin AM et al.

Summary: This Egyptian single centre, double-blinded, randomised dose-finding trial was designed to assess the ideal infusion rate of noradrenaline for prevention of hypotension during cesarean delivery under spinal anesthesia. The authors studied 284 cases split into three treatment groups, which received noradrenaline infusions with different starting rates of 0.025, 0.050, and 0.075 μg/kg/min. The primary outcome was frequency of post-spinal hypotension, defined for each patient as systolic BP under 80% of their baseline non-invasive BP measurement. Secondary outcomes were intraoperative hypotension, incidence of bradycardia, and neonatal outcomes. When compared to the 0.025 μg/kg/min rate, patients receiving higher rates experienced significantly fewer hypotensive episodes. Compared to 0.025 μg/kg/min recipients (40/95 42.1%), post-spinal hypotension rates were lower in 0.050 μg/kg/min (23/93, 24.7%; OR 0.45; 95% CI 0.24-0.82; p = 0.014) and 0.075 μg/kg/min (25/96, 26.0%; OR 0.48; 95% CI 0.26-0.89; p = 0.022) recipients. The two higher-dose groups had higher systolic BP and lower HR than the 0.025 μg/kg/min group.

Comment: (Dr Robert Burnett) This was an atypical study, which was aimed at the determination of a "best" dose for use in clinical practice and perhaps future research. Maternal hypotension during spinal anaesthesia is a commonly encountered major complication, with implications for utero-placental blood flow and foetal outcomes. Peripheral noradrenaline infusion for maintenance of BP during spinal anaesthesia was first reported by Ngan Kee et al., in 2015. Metaraminol is used in Australia, which has alpha-1 effects, but also mimics noradrenaline weakly as a neurotransmitter. However the NCBI International consensus statement on the management of hypotension with vasopressors during caesarean section under spinal anaesthesia (Kinsella et al., 2018) cites a lack of good evidence for routine use of treatments outside of phenylephrine and ephedrine. The authors of this study designed a simple, elegant methodology that yielded a clear and unbiased result, which should be interpreted with caution in its context. While a 0.050 μg/kg/min dose was considered the best of the three tested, this was not actually compared to a control sample (either the established practice, phenylephrine, nor placebo). Confounders such as oxytocic administration were not described, and it is not clear whether a weight-based dosing regime is ideal in a cohort who’s median BMI was 29. Future trials in this area may benefit from assessment of variable rather than fixed-dose infusions of noradrenaline, given this is the way other vasopressor infusions are commonly used in practice. In summary, watch this research space if you aren’t satisfied with phenylephrine, ephedrine and metaraminol in your arsenal of caesarean vasopressors. Otherwise, this research has limited applicability to clinical anaesthesia without more studies.

Reference: Anesthesiology 2019;130(1):55-62
Effect of electroencephalography-guided anaesthetic administration on postoperative delirium among older adults undergoing major surgery: The ENGAGES randomized clinical trial

Authors: Wildef TS et al.

Summary: The ENGAGES trial, a single-centre, double-blinded, stratified block RCT, was conducted across 48 operating theatres in three facilities of Barnes-Jewish Hospital, St Louis, Missouri. Subjects were patients older than 60 undergoing a general anaesthetic (GA) for major surgery, blocked into four groups based on surgery (cardiac vs non-cardiac) and falls history (positive vs negative). All subjects were fitted with a Bispectral Index Quatro (Medtronic) frontal electroencephalogram (EEG) and computer-randomised into a guided group, which had all EEG data displayed to the anaesthetist, who was encouraged to reduce volatile anaesthetic agent use based on EEG and clinical findings, or a control group that only had the EEG signal quality index data displayed to the clinicians. Both guided and control group anaesthetists were discouraged from the use of nitrous oxide or IV hypnotic agents during the maintenance phase of the anaesthetic. The primary outcome of postoperative day 1-5 delirium was measured using the Confusion Assessment Method (CAM) and chart reviews. The guided group (n = 604) had a 26% incidence of delirium compared to 23% in the control group (n = 609); this difference of 3% was not significant (95% CI -2.0 to 8.0) despite the guided group receiving a lower dose of volatile agent with a MAC difference of -0.11 (95% CI -0.13 to -0.10). Undesirable intraoperative movement (the only non-blinded secondary outcome measure) was 6.9% higher (95% CI 2.5-11.4) in the guided group. There was no significant difference in intraoperative opioid dosage, NMB usage and dosage, anaesthetic duration, and intraoperative MAP and hypotension between the groups. 30-day mortality was lower in the guided group versus the control group (0.7% vs 3.1%; p = 0.004). Pregabalin also increased the number of errors in the stop-signal task stop-go test versus placebo (median 3 vs 1; RR 2.14; 95% CI 1.13-4.07; p = 0.020). Paired associated learning, reaction time, rapid visual processing, and spatial working memory strategy tests did not differ between groups.

Comment: (Dr Rafid Karim) NMB has a demonstrated effect in prevention of delirium. The trial concludes that EIN usage and dosage, anaesthetic duration, and intraoperative MAP and hypotension between the groups. 30-day mortality was lower in the guided group versus the control group (0.7% vs 3.1%; p = 0.004). The trial concludes that EIN-guided anaesthesia is not supported for prevention of delirium.


Cognitive effects of perioperative pregabalin: Secondary exploratory analysis of a randomized placebo-controlled study

Authors: Myhre M et al.

Summary: This report on a secondary exploratory analysis of data from a randomised, parallel group, placebo-controlled investigation in 80 donor nephrectomy patients, examined whether pregabalin 150 mg twice daily altered cognitive function (inhibition, sustained attention, psychomotor speed, visual memory, strategy; Cambridge Neuropsychological Test Automated Battery) versus placebo. The number of errors in the spatial working memory with errors test increased with pregabalin versus placebo 24 hours after surgery (median 1 vs 0; RR 3.20; 95% CI 1.55-6.62; p = 0.002). Pregabalin also increased the number of errors in the stop-signal task stop-go test versus placebo (median 3 vs 1; RR 2.14; 95% CI 1.13-4.07; p = 0.020). Paired associated learning, reaction time, rapid visual processing, and spatial working memory strategy tests did not differ between groups.

Comment: (Dr Sachin Hansrajh) Pregabalin is commonly utilised for its opiate-sparing effects; however, it is not without its own drawbacks. In a 2012 study by the Oslo University Hospital, pregabalin’s use in the perioperative setting was shown to negatively affect cognition. Looking at several domains of executive function, they specifically found that pregabalin decreased stop-signal-task abilities and spatial working memory for up to 24 hours postoperatively. These areas of executive function are responsible for inhibitory control and recording information about one’s environment and spatial orientation. Analysis of patients in the 3-5-day postoperative setting showed a complete resolution of the ill effects on these domains. Whilst the results of this study would suggest pregabalin does indeed affect cognitive function, it does not explore nor mention the clinical consequences of a temporary reduction in certain executive function domains. It is not clear as to the impact of the decrease and no tangible links are made to poorer outcomes or effects on morbidity/mortality. Although the study does an excellent job in analysing and providing data on pregabalin’s use in the perioperative setting, it does not venture on to make suggestions or recommendations. The inevitable question that this study raises is how pregabalin compares to other analgesia with its impact on executive function in the postoperative setting.

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Abstract