Welcome to the new combined issue of Anaesthesia and Pain Management Research Review. Notwithstanding the different specialist expertise required in the management of patients’ anaesthesia and pain therapy, many readers of these reviews maintain an active interest in both areas. Thus in this issue, papers from each discipline will be reviewed, with Dr Michal Kluger commenting on pain management and myself on anaesthesia. Henceforth, as I take a step nearer to retirement(!!!), Michal will assume responsibility for reviewing papers from both disciplines. I would therefore like to take this opportunity to thank those readers who have provided feedback on the reviews.

This issue’s anaesthesia topics include: a trial of a new dopaminergic antiemetic; papers on two ‘everyday’ topics (facemask ventilation and induction of children), both of which should give rise to some thought if not an immediate change in practice; a study of the effects of mild NMB on pharyngeal function in the elderly; and finally, a retrospective study of longer term outcomes following the use of etomidate for induction.

We hope you enjoy this new combined review – please feel free to send us your comments, feedback and suggestions.

Kind regards,
Dr Malcolm Futter
malcolmfutter@researchreview.co.nz

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**I.V. APD421 (amisulpride) prevents postoperative nausea and vomiting**

**Authors:** Kranke P et al.

**Summary:** Adults scheduled for a surgical procedure expected to last ≥1 hour under standard inhaled anaesthesia, and who had ≥2 Apfel risk factors for PONV, were randomised to receive single intravenous injections of amisulpride (APD421) 1mg (n=58), 5mg (n=50) or 20mg (n=53) or placebo (n=54) at anaesthesia induction. Compared with placebo, the amisulpride 1mg and 5mg doses, but not the 20mg dose, were associated with significantly lower incidences of PONV during the 24-hour postoperative period (48%, 40% and 57%, respectively, vs. 69%; respective p values 0.048, 0.006 and >0.1). The rates of vomiting, rescue medication use and nausea were also significantly lower. The safety findings, and no significant central nervous system or cardiac adverse events were reported.

**Comment (MF):** Further trials are likely to follow, because, as the authors point out, the safety and/or side effect profile of droperidol (probably the most frequently used antidopaminergic antiemetic) is still regarded as a potential limiting factor in its use. Apart from its activity on both dopamine-2 and -3 receptors, amisulpride is ‘interesting’ because of the reduction in efficacy with a 20mg dose – apparently a similar effect is seen when haloperidol is used in higher doses as an antipsychotic. The authors offered no explanation for this effect, which appears the converse of the duality of effect of partial opioid agonists. Hopefully future trials will use current antiemetics as controls (rather than placebo), and we can only hope that if and when available for clinical use, prices are not similar to those initially associated with serotonergic and neurokinin antagonists!

**Reference:** Br J Anaesth 2013;111(6):938-45

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**Abstract**

Prescription opioid analgesic usage in the US

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**In this issue:**

- Intravenous amisulpride prevents PONV
- Inspiratory pressure level for minimising gastric insufflation
- Propofol impairs postop short-term memory in children
- Pharyngeal function and breathing during partial NMB in the elderly
- Etomidate for induction increases mortality and cardiovascular morbidity
- Regional anaesthesia to prevent postsurgical chronic pain
- TAP block improves pain after laparoscopic surgery
- Root-cause analyses reduce adverse events
- Clinical action of pregabalin in chronic pain
- Prescription opioid analgesic usage in the US

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**Abbreviations used in this issue**

- NMB = neuromuscular block
- OR = odds ratio
- PONV = postoperative nausea and vomiting
- PPP = persistent postsurgical pain
- RCT = randomised clinical trial
- TAP = transversus abdominis plane

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**Conditions apply**
Real-time detection of gastric insufflation related to facemask pressure-controlled ventilation using ultrasonography of the antrum and epigastric auscultation in nonparalyzed patients

Authors: Bouvet L et al.

Summary: Patients requiring anesthesia induced with propofol and remifentanil (evaluable n=67) were randomly assigned to receive an inspiratory pressure of 10, 15, 20 or 25 cm H₂O during controlled-pressure ventilation. Facemask ventilation was started for 2 minutes when eyelash reflex occurred, and gastric insufflation was detected by auscultation and real-time antral ultrasonography. Auscultation demonstrated significantly increased incidences of gastric insufflation with increasing inspiratory pressure from 0% in the 10 cm H₂O group to 41% in the 25 cm H₂O group, and the respective values according to ultrasonography were 19% and 59%. Ultrasonographic detection of gastric insufflation was associated with a statistically significant increase in the antral area in the 20 and 25 cm H₂O groups. Lung ventilation was not sufficient in the 10 cm H₂O group.

Comment (MF): This study is of interest, not only because of the suggested ‘safe’ pressure that can be applied during facemask ventilation, but also because of the questions both it and an accompanying editorial raise. The study’s methodology and hence the results, whilst attempting to replicate ‘clinical practice’, may not be representative of NZ – general anesthesia was induced and maintained during the period of measurement with propofol and remifentanil, whilst facemask ventilation routinely employed a two handed technique, a Guedel airway and a mechanical ventilator. Details of whether the latter was volume or pressure cycled were not provided, although it was presumably the former, with the ‘target’ pressures being applied to the airway throughout the entire inspiratory phase. Unfortunately only gastric pressure was measured; the corresponding intra-gastric and barrier pressures were not. As the editorial notes, these pressures are at least as important in determining the potential risks of gastric insufflation. Until further research is undertaken, I’ll probably be setting the circuit’s pressure relief valve at 15 cm H₂O albeit in conjunction with single-handed facemask ventilation and manual ‘bagging’ (both of which may reduce the potential of insufflation). For the future, it would be fascinating to see the same methodology, along with gastric pressure measurements, applied to ventilation via various supraglottic airway devices.

Reference: Anesthesiology 2014;120(2):326–34

The effects of general anaesthesia on memory in children: a comparison between propofol and sevoflurane

Authors: Yin J et al.

Summary: This research randomised 60 children aged 7–13 years to receive either propofol or sevoflurane for general anaesthesia during elective hernia surgery. The use of propofol was associated with significantly impaired short-term image recollection, figure recognition and visual reproduction memory 7 days postoperatively compared with preoperative levels (respective p values 0.02, 0.01 and 0.03), with baseline levels restored at 3 months. Neither anaesthetic agent was associated with impairment of immediate or long-term memory.

Comment (MF): If confirmed, the findings could have a significant impact on propofol use in paediatrics, because so much surgery is undertaken on a ‘day stay’ basis with the expectation that the child’s normal life (including schooling) is minimally disrupted. The methodology used by the authors was “unusual” (etomidate induction then sufentanil and atracurium infusions for all subjects), with either a propofol infusion (5–10 µg/kg/min not target controlled) or 1–3% end-tidal sevoflurane being given intraoperatively for 20- to 30-minute hernia repairs. No attempt was made to monitor depth of anaesthesia, although an attempt was made to prevent any cerebral blood flow variation secondary to hypotension or bradycardia. I am not able to ‘critique’ the psychometric testing employed, but it seemed well founded. The authors’ discussion provided a brief overview of what is known about postoperative cognitive impairment after ‘routine’ anaesthesia, particularly in association with these two agents. It remains to be seen whether another group is able to demonstrate short-term memory loss following total propofol doses averaging <0.9 mg/kg.

Reference: Anesthesia 2014;69(2):118–23

Pharyngeal function and breathing pattern during partial neuromuscular block in the elderly: effects on airway protection

Authors: Hårdemark Cedborg Al et al.

Summary: These researchers used manometry and videoradiography to evaluate the effects of partial NMB on pharyngeal function, co-ordination of breathing and swallowing and airway protection in 17 volunteers aged >65 years who were administered rocuronium to obtain steady-state train-of-four ratios of 0.70 and 0.80, respectively, and a greater degree of dysfunction was seen for swallowing during partial NMB. Pharyngeal dysfunction did not differ significantly from the control value after train-of-four ratio recovery. Compared with control values, resting upper oesophageal sphincter pressure was lower at all partial NMB levels. Impaired co-ordination of breathing or swallowing was not able to be demonstrated.

Comment (MF): The principle findings of this study probably come as no surprise – striated muscle function is affected by partial NMB. The ‘background’ to this discussion is closely aligned to that of the paper looking at facemask ventilation, and similarly emphasises the changes in pharyngeal function that can be associated with anaesthesia. The 37% incidence of pharyngeal dysfunction for control values was of interest, particularly when the authors contrasted it with the findings of an earlier study of young volunteers – clearly residual NMB is not the only challenge we face when anaesthetising the elderly. Whilst not the investigators’ primary goal, their quantification of the subjective effects of partial paralysis reminded me of my own experiences in very similar circumstances many years ago – subjects feel sedated and calm rather than the alarm that might be expected. As is commonly the case in the increasing number of studies examining the physiological effects of partial NMB, the clinical impact is difficult to quantitate.

Reference: Anesthesiology 2014;120(2):312–25

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Abstract

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Anesthetic induction with etomidate, rather than propofol, is associated with increased 30-day mortality and cardiovascular morbidity after noncardiac surgery

Authors: Komatsu R et al.

Summary: These researchers compared morbidity and mortality outcomes between 2144 etomidate recipients and 5233 propensity-matched propofol recipients who had received these agents during noncardiac surgery. Compared with propofol recipients, etomidate recipients had significantly greater likelihoods of death (OR 2.5 [98% CI 1.9, 3.4]) and cardiovascular morbidity (1.5 [1.2, 2.0]) and a significantly longer hospital stay (hazard ratio 0.82 [95% CI 0.78, 0.87]); infectious morbidity and intraoperative vasopressor use were not increased with etomidate (respective ORs 1.0 [98% CI 0.8, 1.2] and 0.92 [0.82, 1.0]).

Comment (MF): Both the paper’s authors and an accompanying editorial emphasise the difficulties encountered when databases are ‘mined’ and patient characteristics are subjected to propensity scoring in an attempt to simulate the randomised allocation that occurs in a prospective trial. Given the significant differences in the two groups before propensity matching and the relatively limited number of known variables that could be matched, the results must be viewed with caution. That being said, etomidate is now regarded with such suspicion by many practitioners (despite the equivocal findings of the studies referenced in the editorial) that this paper will probably be interpreted as further confirmation that it should never be used regardless of its superior cardiothoracic therapeutic index.


Regional anaesthesia to prevent chronic pain after surgery

Authors: Andreae MH & Andreae DA

Summary: This was a Cochrane systematic review and meta-analysis of RCTs comparing regional and conventional analgesia for PPP. Three trials (n=250) with 6-month outcome data showed that epidural anaesthesia was superior for preventing persistent post-thoracotomy pain (OR 0.33 [95% CI 0.20, 0.56]), while data from two RCTs (n=89) favoured paravertebral block for breast cancer surgery pain at –6 months (0.37 [0.14, 0.94]).

Comment (MK): Anaesthetists continue to focus on acute pain modulation as the major player in minimising PPP. Whilst acute pain control features as an important associative factor for the development of PPP, studies continue to show other conditions that may be even more important. Psychosocial risk factors including mood disturbance, stress, anxiety and catastrophisation are associated with PPP and these are consistently described in several studies and a variety of surgical populations. In addition, preoperative pain as well as surgical comorbidities also seem to be important risk factors. It is too naive to consider that a single specialty/intervention will modulate this complex issue, and rather than advocate reliance on single interventions (e.g. paravertebral block or epidural), addressing the patient in the wider context will probably lead to more meaningful outcomes.


Abstract

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Transversus abdominis plane block to ameliorate postoperative pain outcomes after laparoscopic surgery

Authors: De Oliveira GS et al.

Summary: This was a meta-analysis of ten RCTs (n=633) reporting postoperative pain outcomes in laparoscopic surgical procedures for TAP block versus placebo or no treatment; no publication bias was detected. Compared with the controls, TAP block was associated with favourable combined effects for pain at rest as assessed by a 10-point numerical scale at 2.5 hours (weighted mean difference –2.41 [99% CI –3.6, –1.2]) and at 24 hours (–1.93 [–2.19, –0.48]) and significantly less postoperative opioid consumption (–5.74mg morphine equivalents [–8.48, –2.99]). Furthermore, the effects of TAP block on early pain and opioid consumption were greater with preoperative than postoperative administration. A meta-regression analysis showed that local anaesthetic dose was associated with the TAP block effect on late pain at rest and postoperative opioid consumption. None of the included studies reported local anaesthetic toxicity.


Pregabalin rectifies aberrant brain chemistry, connectivity, and functional response in chronic pain patients

Authors: Harris RE et al.

Summary: These researchers undertook proton magnetic resonance spectroscopy, functional magnetic resonance imaging and functional connectivity magnetic resonance imaging to investigate the clinical action of pregabalin for chronic pain in 17 patients with fibromyalgia. Pregabalin was associated with: i) a significant reduction in combined glutamate plus glutamine levels in the posteriorinsula (p=0.016); ii) a significant association between clinical pain reductions and reductions in brain connectivity of this structure to regions within the default mode network (r=0.82 p=0.001); iii) reduced responses of default mode network regions to experimental pain (p=0.018); and iv) baseline values for all three neuroimaging markers predicting subsequent analgesic response. No such effects were seen with placebo.


Increases in the use of prescription opioid analgesics and the lack of improvement in disability metrics among users

Authors: Sites BD et al.

Summary: This analysis of data from the US Medical Expenditure Panel Survey found an estimated increase in the total number of opioid analgesic prescriptions among adults from 43.8 million in 2000 to 89.2 million in 2010. The proportion of adults who were prescription opioid users increased from 7.4% to 11.8% over the same period, with an estimated 6% increase in the likelihood of receiving an opioid prescription each year. However, no demonstrable improvements were seen in the age- or sex-adjusted disability and health status measures among recipients of opioid analgesics.


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