Welcome to issue thirteen of Anaesthesia Research Review.

Anaesthetists are confronted with an overwhelming amount of knowledge in all fields of medicine. It is virtually impossible for any anaesthetist to cope with this ever-increasing theory, which subsequently needs to be translated into clinical practice. One can only do so much, when more than one thousand new pages of anaesthesia research are published in anaesthesia journals every day of the year. Therefore, it is the aim of our Anaesthesia Research Reviews to help anaesthetists by providing summaries and comments on recently published manuscripts. It is our intent that this will enable anaesthetists globally to be updated on the latest research using a concise framework, so anaesthetists can benefit the most from it.

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

Kind Regards,

Professor André van Zundert
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A triple-blind, placebo-controlled randomised trial of the ilioinguinal-transversus abdominis plane (I-TAP) nerve block for elective caesarean section

Authors: Staker JJ et al.

Summary/Comment: (Ben Steiger) Regional anaesthesia is a well-established adjunct in post-operative multimodal analgesia across a wide range of surgeries. The ilioinguinal-iliohypogastric block and transversus abdominis plane block have been shown to reduce post-operative opioid requirements after lower abdominal surgery. Anaesthetists from the Lyell McEwin Hospital in Adelaide have been successfully using a hybrid ilioinguinal-transversus abdominis plane block (I-TAP) with subjective improvement in analgesia for the past 18 months. This triple-blind RCT aimed to assess the efficacy of the I-TAP block (as part of a multimodal analgesia regimen) in elective caesarean sections in reducing post-operative opioid consumption. One hundred patients due to undergo a planned spinal anaesthesia (hyperbaric bupivacaine, 15 μg fentanyl and 150 μg morphine, as well as 100 mg diclofenac and 1.5 g rectal paracetamol) for elective caesarean section were randomised to receive an I-TAP or sham block as part of their post-operative analgesia regimen. Both groups were identical in key characteristics and received identical pre-block and post-block treatment. The anaesthetists performing the block were blinded to patient identity but not to the procedure being performed. Patients and recording staff were blinded to the procedure received. The primary outcome assessed was total fentanyl usage at 24 hours. Secondary outcomes tested were pain scores at rest and during movement, sedation score, nausea and vomiting requiring treatment, pruritus requiring treatment, maternal satisfaction and requirement for additional analgesia. Total fentanyl used through patient-controlled analgesia (PCA) at all time points examined (4, 8, 16 and 24 hours) was significantly lower (p < 0.001) in the I-TAP block group than in the control sham block group, with a 24-hour mean cumulative dose of 71.9 μg (55.6 μg-92.7 μg) versus 179.1 μg (136.2 μg-231.4 μg), respectively. Across all time points, the reported VAS pain scores were significantly lower (p < 0.001) in the I-TAP group compared to the control group. There was no difference in minor side effects between groups (nausea and vomiting, pruritus, sedation), although in the I-TAP group, one patient received a femoral nerve block from fascial spread of local anaesthetic. This study was able to establish the efficacy of the I-TAP block in post-caesarean section multimodal analgesia regimes in reducing opioid requirements and pain scores. Further studies will be required to establish its effectiveness and applicability in other lower abdominal surgeries.

Reference: Anaesthesia 2018;73(5):594-602

Abstrakt

Independent commentary has been provided by Matthew Black, Matthew Bright, Robert Burnett, Ben Cahill, Gunjan Chawla, Andrew Lonergan, Anna Pietzsch, Michelle Roets, Ben Steiger and Angela Tognolini.
Intraoperative cell salvage with autologous transfusion in elective right or repeat hepatectomy: a propensity-score-matched case-control analysis

Authors: Zacharias T et al.

Summary: This propensity matched retrospective case-control study at a single hospital, compared the allogenic erythrocyte transfusion rate after elective right or repeat hepatectomy between patients (n = 41) who had intraoperative cell salvage (since January 2013) with a cell saver device versus patients who did not (controls; treated between 2007-2012; n = 55). The groups were balanced for demographic and clinical variables. The allogenic blood transfusion rate in the 90 days post-operatively (primary endpoint) was 20% (95% CI 12.5%-43.7%) in the cell saver group versus 72% (95% CI 56.3%-87.5%) in the control group (p < 0.001). Intraoperative transfusion triggers included haemoglobin <80 g/L (to achieve 100 g/L), blood loss and haemodynamic intolerance. There were no significant differences in overall and infectious complication rates between the two groups.

Comment: (Michelle Roets) We commend the authors on a study that will add to the growing evidence to confirm the safety and cost benefit of cell salvage for cases with major blood loss, in particular during liver surgery. Even though this study included a small number of cases it confirms at a minimum, the potential to reduce allogeneic blood transfusion by using intraoperative cell salvage for patients undergoing hepatectomy. It is however not surprising that there was not a statistically significant difference in complication and wound infection occurrence between the two groups. Review articles including RCTs and large observational studies that assess the association between allogeneic blood transfusion and post-operative infection involve large numbers of cases to ensure adequate power. It is unlikely that any one hospital would be able to support a large enough number of cell salvage cases to enable such a comparison that would confirm the reduction of post-operative infection by using cell salvage instead of allogeneic blood transfusion. The authors mention various studies where attempts were previously made to confirm both the potential to reduce the incidence of allogeneic transfusion as well as the potential to reduce transfusion-associated adverse outcome by using autologous blood instead. Most authors who studied these topics identified the need for larger well-powered studies. However, several practical aspects complicate cell salvage research including the small numbers of cell salvage cases conducted within single hospital units where similar techniques and practices apply, different techniques and policies used across hospitals and varied transfusion triggers and practices.


Abstract

Comparing adductor canal block with local infiltration analgesia in total knee arthroplasty: A prospective, blinded and randomized clinical trial

Authors: Tong QJ et al.

Summary: This was a prospective, blinded and randomised clinical trial at a single hospital comparing local infiltration analgesia (LIA) and adductor canal block (ACB) for analgesia in 40 patients (ASA I to III) undergoing total knee arthroplasty (TKA) under single-dose spinal anaesthesia. LIA recipients received an intraoperative local infiltration of ropivacaine 150 mg, ketorolac 30 mg, morphine 10 mg, and adrenaline 200 mcg in a total volume of 75 mLs, administered by the surgeon, while ACB recipients were given an ACB post-operatively. Outcomes such as opioid-related side effects (PONV, sedation scores), length of hospital stay (median 5 [2-6.5] vs 3 [2-5]; p = 0.686) and 48 hours (5 [2-6] vs 3.5 [2-5]; p = 0.565), which may affect scale 0-10), there was, however, a trend to higher dynamic pain scores in the ACB group at 24 hours after TKA. Patient groups were well matched in this study, and all received a standardised single-dose spinal anaesthetic, post-operative pain regime (morphine PCA) and rehabilitation protocol. Whilst results show a significant reduction in total morphine consumption, all patients in the LIA group routinely received 10 mg of morphine in the block by protocol. Morphine consumption was used as an indication of effective analgesia and there were no significant differences in the median pain scores (numerical rating scale 0-10), there was, however, a trend to higher dynamic pain scores in the ACB group at 24 hours (5 [2-6.5] vs 3 [2-5]; p = 0.686) and 48 hours (5 [2-6] vs 3.5 [2-5]; p = 0.565), which may affect functional recovery. Despite the reduction in morphine consumption, there was no difference in secondary outcomes such as opioid-related side effects (PONV, sedation scores), length of hospital stay (median 5 days), quadriceps strength, or the ability to mobilise. However, this study may not have been adequately powered to assess these outcomes. There was also no ability to assess the effectiveness of the ACB, nor was the duration of anaesthesia of the blocks measured. Furthermore, obese patients (BMI > 32 kg/rrm) and those with chronic opioid use were excluded, therefore potentially excluding an important patient population where a significant reduction in morphine consumption may be more clinically relevant.


Abstract

Cognitive decline in the middle-aged after surgery and anaesthesia: results from the Wisconsin Registry for Alzheimer’s Prevention cohort

Authors: Bratzke LC et al.

Summary: This North American, longitudinal, observational study examined the relationship between cognition and anaesthesia in 964 middle-aged (mean age 54 years) adults without existing cognitive dysfunction over a 4-year period during which 312 underwent surgery. A decline in immediate memory of one point on the 30-point Rey Auditory Verbal Learning Test (RAVLT) was found in participants who had surgery during the study period (p = 0.013). Memory became abnormal in 21 of 114 (18%) patients after surgery versus 56 of 556 (10%) who had not had surgery (p = 0.02). Immediate memory was impacted more with longer cumulative operations (beta coefficient 0.08; p = 0.012). Of participants who had surgery between cognitive tests, longer anaesthesia time was associated with a decline in working memory (beta coefficient -0.01 [0.00], p = 0.028). Reduced cognitive speed and flexibility was associated with worse ASA physical status (beta coefficient 0.55 for ASA 1 vs 3; beta coefficient 0.37 for ASA 2 vs 3; p = 0.035), but a decline in working memory was associated with better ASA physical status (beta coefficient -0.48 for ASA 1 vs 3; p = 0.01).

Comment: (Ben Cahill) Short-term post-operative cognitive dysfunction is well established, and recent evidence suggests anaesthesia may also be associated with longer-term cognitive decline in the elderly. Bratzke et al. examined this association in 964 cognitively normal middle-aged adults using the Wisconsin Registry for Alzheimer’s Prevention cohort. Neuropsychological tests, including the RAVLT, were measured at baseline and repeated after 4 years to examine immediate memory, verbal learning, speed and flexibility and working memory. Number of operations and cumulative anaesthesia time in the preceding 5 and intervening 4 years was recorded. Other variables included APOE-ε4 status, family history of dementia and pre-operative ASA status. The results demonstrated a subtle but significant decline in immediate memory over 4 years in participants undergoing surgery. Of those who underwent surgery, a decline in working memory was associated with longer cumulative anaesthesia and, unexpectedly, better ASA physical status. Interestingly, these declines were independent of APOE-ε4 status and family history. However, the study design did not differentiate between type of anaesthesia (general or neuraxial/regional) or urgency of surgery (elective or emergency), which could be hypothesised to be significant variables. Future research with larger cohorts is required to clarify the impact of anaesthesia on cognition in middle age.


Abstract

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Other adverse events occurring in ≥5% of patients in any treatment group included dizziness, somnolence, headache, pruritus, diarrhoea and fatigue.

NON-INFERIOR EFFICACY (5-DAY SUM OF PAIN INTENSITY DIFFERENCE) AND SIGNIFICANTLY LOWER INCIDENCE OF CONSTIPATION, NAUSEA AND VOMITING

1,2*
Postoperative delirium in total knee and hip arthroplasty patients: a study of perioperative modifiable risk factors

Authors: Weinstein SM et al.

Summary: A single centre retrospective review examined modifiable factors for preventing delirium based on data from 41,766 patients undergoing THA/TKA between 2005 and 2014. In total, 922 (2.21%) patients experienced post-operative delirium. Neuraxial anaesthesia reduced the risk of post-operative delirium versus general anaesthesia (epidural OR 0.59; 95% CI 0.38-0.93; spinal OR 0.55; 95% CI 0.37-0.83; combined spinal/epidural OR 0.56; 95% CI 0.40-0.80), whereas an increased risk was observed in those receiving intra-operative ketamine (OR 1.27; 95% CI 1.01-1.59), opioids (OR 1.25; 95% CI 1.09-1.44), post-operative benzodiazepines (OR 2.47; 95% CI 2.04-2.97), or ketamine infusion (OR 10.59; 95% CI 5.26-19.91).

Comment: (Matthew Bright) This study investigated what modifiable risk factors or anaesthetic decisions influenced the incidence of post-operative delirium. Weinstein et al. identified 41,766 patients who received either a TKA or THA over a 9-year period in a single centre based in New York, USA. Post-operative delirium was detected in 2.21% of patients and, unsurprisingly, non-modifiable risk factors, such as age and medical co-morbidities, particularly mental health issues, were associated with higher rates of delirium. Patients with post-operative delirium were 12 years older than their counterparts. Neuraxial anaesthesia, when compared to general anaesthesia, had lower rates of delirium, while the use of peri-operative ketamine, intra-operative opiates, or post-operative benzodiazepines increased the rates of delirium. The use of these medications is important to treat post-operative pain, which is another major contributor to post-operative delirium that was not included in this study. Interestingly, when accounting for age and increased co-morbidities, intra-operative benzodiazepines were associated with lower rates of delirium post-operatively.

Reference: Br J Anaesth. 2018;120(5):999-1008

Abstract

Transnasal humidified rapid-insufflation ventilatory exchange (THRIVE) vs. facemask breathing pre-oxygenation for rapid sequence induction in adults: a prospective randomised non-blinded clinical trial

Authors: Lodenius Å et al.

Summary: This prospective RCT compared transnasal humidified rapid-insufflation ventilatory exchange (THRIVE) versus facemask pre-oxygenation in 83 patients requiring a rapid sequence induction (RSI) for emergency surgery. There was no difference in the median lowest recorded peripheral oxygen saturation (\(\text{SpO}_2\)) during intubation until 1 minute after the tracheal tube was placed (99% vs 99%). Five patients desaturated below 93% in the facemask group, as compared to none in the THRIVE group (p = 0.019). There was no between group difference in median intubation time (51 vs 48 s) nor in median apnoea time (109 vs 116 s).

Comment: (Anna Pietzsch) THRIVE is now accepted as a successful method of pre-oxygenation for rapid sequence induction until 1 minute after the tracheal tube was placed (99% vs 99%). However, further investigation in the field of RSI is important to treat post-operative pain, which is another major contributor to post-operative delirium that was not included in this study. Interestingly, when accounting for age and increased co-morbidities, intra-operative benzodiazepines were associated with lower rates of delirium post-operatively.


Abstract

Incidence and risk factors of coagulation profile derangement after liver surgery: Implications for the use of epidural analgesia – A retrospective cohort study

Authors: Jacquenod P et al.

Summary: This retrospective review of a multicentre, prospective, observational database examined the incidence of coagulopathy after hepatectomy that might interfere with epidural catheter removal, and identification of risk factors related to coagulopathy. Post-operative coagulopathy was observed in 53.5% (95% CI 50.0-57.1) of 759 patients included in the analysis. The maximum derangement in the INR occurred on post-operative day one, and platelet count reached a trough on post-operative days 2 and 3. In multivariate analysis, factors associated with post-operative coagulopathy were pre-existing hepatic cirrhosis (OR 2.49; 95% CI 1.38-4.51; p = 0.003), pre-operative INR >1.3 (OR 2.39; 95% CI 1.10-5.17; p = 0.027), pre-operative platelet count <150 g/L (OR 3.03; 95% CI 1.77-5.20; p = 0.004), major hepatectomy (OR 2.96; 95% CI 2.07-4.23; p < 0.001), and estimated intra-operative blood loss ≥1000 mL (OR 1.85; 95% CI 1.08-3.18; p = 0.025).

Comment: (Matthew Black) Coagulation abnormalities are well known and described after hepatic resection. A disturbed liver parenchymal cell function may result in haemostatic disorders even in patients with a completely normal pre-operative coagulation function. A growing number of centres now routinely place epidural catheters in patients undergoing hepatic surgery with the aim to minimise parental analgesic side effects and improved analgesia. This study attempts further to define coagulation data in this population group to assist in the safe placement and removal of epidural catheters. The retrospective study of a registered observational database for multicentre French Hospitals was accessed between October 1, 2012 and September 30, 2013. The major aim was to determine, in patients undergoing hepatic resection, the incidence of post-operative coagulopathy that could interfere with epidural catheter removal whilst also identifying any factors that may be associated with post-operative coagulation profile derangement. Results noted an abnormal coagulation profile observed in 53.5% of patients in the 5-day post-operative period. Analysis showed statistically significant associations between abnormal post-operative coagulation profile and pre-existing hepatic cirrhosis, pre-operative INR >1.3, pre-operative platelet count <150 g/L, major hepatectomy (39.1% in patients with major hepatectomy versus 21.3% in patients with minor hepatectomy), estimated intra-operative blood loss ≥1000 mL, and volume of crystalloids and colloids administered during surgery ≥4000 mL. Interestingly it was noted that 17% of all patients still showed an INR ≥1.5 and/or a platelet count <80 g/L four to five days post the operation. The major limitations of this study are primarily due to its retrospective and observational design with gaps between data groups and the coagulation parameters that were used. Partial thromboplastin time, fibrinogen, ionised calcium, or thromboelastometry tests were either not collected or not available within the databases and as such, miss what may provide a global description of clot formation functionality. This is particularly true for thromboelastometry, which further studies could focus on. Anaesthetists should still refer to local neuraxial guidelines with regard to coagulation values associated with safe neuraxial blockade.

Reference: Anesthesia 2018;73(5):564-71

Abstract
Should continuous rather than single-injection interscalene block be routinely offered for major shoulder surgery? A meta-analysis of the analgesic and side-effects profiles

Authors: Vorobeichik L et al.

Summary/Comment: (Ganju Chawla) Major shoulder surgery is associated with moderate-to-severe pain. This meta-analysis evaluated 15 randomised controlled trials comparing continuous catheter-based interscalene block (CISB) versus single-injection interscalene block (SISB) in patients undergoing major shoulder surgery. Compared with SISB, CISB reduced 24- and 48-hour oral morphine consumption (primary outcome) by a weighted mean difference of 50.9 mg (95% CI -81.6 to -20.2; p < 0.001) and 44.7 mg (95% CI -90.9 to -8.7; p < 0.0001), respectively. CISB also reduced post-operative rest and dynamic pain scores up to 72 hours after surgery, delayed time-to-first analgesic, increased patient satisfaction, reduced PONV, and decreased respiratory indices by 11.0-11.7%. SISB of the brachial plexus is a popular and relatively easy technique for effective pain control after shoulder surgery. CISB, by comparison, requires more time, skill and resources and is therefore limited in clinical use. The patient benefit in maintaining a CISB infusion for at least 48 hours makes it worthwhile in patients with pre-existing pain, opioid tolerance and other risk factors for severe post-operative pain. Whether this relates to a cost-benefit in terms of hospital stay and analgesic use has not been explored. The respiratory changes noted might not be clinically significant except in patients with poor pre-operative respiratory function. Only one of the trials included in this meta-analysis used a perineural adjuvant with none mentioning i.v. adjuvants or liposomal preparations, which might prolong the analgesia from the SISB to an extent.


Effect of epidural infusion bolus delivery rate on the duration of labor analgesia: A randomized clinical trial

Authors: Lage EMS et al.

Summary: This North American, double-blinded, randomised, controlled superiority trial examined the relationship between the rate of epidural bolus infusion and adequacy of analgesia (initiated with intrathecal fentanyl 25 μg, maintenance epidural bupivacaine 0.625 mg/mL plus fentanyl 1.95 μg/mL), in nulliparous women labouring with a singleton pregnancy. Programmed (every 60 min) intermittent epidural boluses (10 mL) and patient-controlled boluses (5 mL, lockout interval 10 min) were delivered at a rate of either 100 mL/h (n = 108) or 300 mL/h (n = 102) mL/h. The primary outcome, percentage of patients requesting provider-administered supplemental bolus analgesia did not differ between the low- and high-rate groups (40.7% vs 36.3%; difference -4.4%; 95% CI 18.5 to 9.1). Secondary outcomes, bupivacaine consumption per hour, and the ratio of requests to deliveries of patient-controlled epidural analgesia, were not different between groups.

Comment: (Robert Burnett) It has been theorised that an increase in pressure at the catheter tip promotes improved distribution of local anaesthetic into the epidural space. Kumpern et al. (2016) previously established that higher flow rates increased catheter-tip pressure in multi-orifice, and, to a lesser degree, single-orifice catheters, in an in vitro study. The authors of this study hypothesised that these increased catheter pressures would lead to improved anesthetic distribution and therefore improved analgesia. The design of the study reflected this presumption, but would potentially have benefited from data supporting improved drug distribution in vivo. There were several confounding factors, including the use of a highly subjective pain scale and delivery of intrathecal analgesia to all participants. All measured outcomes demonstrated wide 95% confidence intervals. While the study found no superiority with high-rate delivery, the design of the study was limited for a variety of reasons and future research with larger cohorts or more objective endpoints would be beneficial.


The cardiopulmonary exercise test grey zone: optimising fitness stratification by application of critical difference

Authors: Rose GA et al.

Summary: A retrospective analysis of the natural variation in cardiopulmonary exercise test (CPET) metrics was conducted in 213 colorectal surgery patients. A model of natural variation identified a critical difference (analytical imprecision and biological variation) for oxygen uptake (V\text{O}_2) at the anaerobic threshold (AT) of 11 mL/kg/min, peak oxygen uptake (V\text{O}_2\text{peak}) of 16 mL/kg/min, and the ventilatory equivalent for carbon dioxide at AT (VE/V\text{CO}_2\text{AT}) of 36. When applied to patient data, these critical differences of 19%, 13% and 10%, resulted in false negative and false positive rates for unfit patients of <28% and <32%. Boundaries for unfit and fit patients were established as V\text{O}_2< AT-9.2 and ≥13.6 mL/kg/min, V\text{O}_2\text{peak} <14.2 and ≥18.3 mL/kg/min and VE/V\text{CO}_2 AT- <40.1 and ≥32.7. Between these values, fitness level stratification was indeterminate.

Comment: (Andrew Lonergan) Rose et al. conducted a laboratory study to calculate critical difference in CPET. Critical difference is defined as the combined variability that occurs in a test-derived value secondary to both (1) analytical variability (test imprecision), and (2) the natural biological variation that occurs in a test’s subject population. This is a two-armed study. In the first arm, analytical and biological variability in CPET were calculated in a laboratory, then critical difference was calculated from these results. The second arm of the study then applied this calculated critical difference to CPET results from 213 patients from a single centre in Wales. With this data Rose et al. created three zones for CPET indices; (1) fit for surgery (the zone in which patients’ CPET results confer minimal peri-operative complication risk), (2) unfit for surgery (the zone in which patients’ CPET results confer excessive peri-operative complication risk), and (3) indeterminate fitness (the zone in which patients’ CPET results confer indeterminate risk of peri-operative complications because of critical difference for CPET). Rose et al. then calculated the false-negative and false-positive rates when single-value cut-offs were used. They demonstrated that without accounting for critical difference that there is the potential for CPET results to incorrectly influence surgical planning decisions, including withholding essential surgery for patients incorrectly stratified as too high risk by CPET. The study by Rose et al. is limited by a number of factors, which the authors recognise. These limitations include (1) low subject numbers for both arms of the study, and (2) all subjects in the “calculating critical difference arm” were male, young and healthy individuals. These factors potentially bias the calculations of critical difference by minimising the potential effect of increased natural variation that occurs with increasing age, in the presence of pathology and comorbidities, and between sexes. To account for this, Rose et al. do not propose that the values they have calculated for critical difference (and the corresponding ranges for the new classification zones) in the study should represent new guidelines for CPET. Rather they suggest that their study represents proof that the existing concept of a single-value cut-off is flawed and invalid. Indeed they recognise that further large patient cohort studies are required to determine more accurate values to represent the new classification zones. In addition, the new category of “indeterminate fitness for surgery” accounted for a large proportion of the 213 patients tested with CPET. This greatly diminishes the value of CPET in being able to discriminate patients into high-risk and low-risk groups peri-operatively. What it does do, however, is more accurately identify high-risk and low-risk patients with more externally valid cut-offs for “unfit” and “fit” for surgery. Additionally it reinforces that there is a patient cohort (that is the “indeterminate fitness for surgery” classification) in which single indices alone cannot be used to make surgical planning decisions, and further supports that single-test results should not be interpreted in isolation to other patients and surgical factors.


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