Assessment of a multimodal analgesia protocol to allow the implementation of enhanced recovery after cardiac surgery

Authors: Markham T et al.

Summary: The impact of a multimodal analgesia protocol for enhancing recovery following cardiac surgery was explored in this retrospective analysis of perioperative patient outcomes; 25 patients enrolled in the multimodal analgesia protocol were compared with 25 controls. Compared with controls, patients who received the multimodal analgesia protocol had similar mean times for cardiac bypass time and aortic clamp, but 12 were extubated in the operating room versus one from the control group, their postoperative opioid consumption was lower (27.3 vs. 51.7 morphine equivalents [p=0.006]) and they had nonsignificant trends for shorter stays in both the ICU and the hospital.

Comment: The ERAS Society guidelines for different surgeries in 2010 did not include cardiac surgery. Recent review for enhanced recovery for cardiac surgery emphasised optimal analgesia, appropriate fluid administration, transfusion management and mobilisation. Previous study showed dexmedetomidine in coronary artery bypass graft was associated with better clinical outcomes, and intraoperative dexmedetomidine decreased mortality and reduced the incidence of delirium. Gabapentin and regional blocks were previously shown to be opioid sparing and enhance analgesia. These data support the need for a larger prospective study of ERACS within cardiac surgery.


Abstract

In this issue:

- Multimodal analgesia protocol for enhanced recovery after cardiac surgery
- Local/regional vs. conventional analgesia for preventing persistent postoperative pain
- Mechanistic pain profiling for predicting efficacy of NSAIDs/paracetamol for knee OA
- Adjunctive fulranumab for cancer-related pain
- Telehealth for chronic back pain: nurses vs. mental health professional delivery
- Long-term intrathecal drug delivery system use in CRPS
- Opioid use disorder and overdose reversals in the community
- Real-life onabotulinumtoxin A use for chronic migraine

Abbreviations used in this issue:

ACS = alternating current stimulation; CBT = cognitive-behavioural therapy; CRPS = complex regional pain syndrome; CRP = C-reactive protein; ERAS = Enhanced Recovery after Surgery; NOC = numerical oral pain scale; NRS = numerical rating scale; NSAID = nonsteroidal anti-inflammatory drug; OA = osteoarthritis; OR = odds ratio; QALY = quality-adjusted life-year; RCT = randomised clinical trial; VAS = visual analogue scale.

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Pain Management Research Review

Making Education Easy

Issue 55 - 2019

Welcome to issue 55 of Pain Management Research Review.

This issue begins with a retrospective analysis reporting decreased opioid use and increased successful extubation in the operating room when a multimodal analgesia protocol that enhances recovery after cardiac surgery was used. Other included research reports that mechanistic pain profiling was able to predict pain alleviation associated with NSAID plus paracetamol (acetaminophen) use for chronic knee OA (osteoarthritis). An internet-delivered exposure therapy programme for fibromyalgia was found to be cost effective with large societal cost savings. This issue concludes with an open-label study reporting on the real-world use of long-term onabotulinumtoxinA for managing chronic migraine.

I hope you find our latest update in pain management research informative. Please feel free to send any feedback or suggestions.

Kind Regards,

Dr Tim Ho

tim.ho@researchreview.com.au

Keep reading...
Local anesthetics and regional anesthesia versus conventional analgesia for preventing persistent postoperative pain in adults and children

Authors: Levene JL et al.

Summary: This update of a Cochrane systematic review and meta-analysis added 40 new and seven ongoing RCTs investigating local or regional anaesthesia versus any systemic analgesia for reducing the risk of persistent postoperative pain in adults or children, resulting in a total of 63 RCTs. Data from 39 studies (n=3027) were able to be synthesised in a balanced design. The data analyses revealed that regional anaesthesia was favoured for thoracotomy (OR 0.52 [95% CI 0.32–0.84]; moderate-quality evidence), breast cancer surgery (0.43 [0.28–0.68]; low-quality evidence) and caesarean section (0.46 [0.28–0.78]; moderate-quality evidence). Synthesised evidence favoured continuous local anaesthetic infusions following breast cancer surgery (OR 0.24 [95% CI 0.08–0.69]; moderate-quality evidence); evidence for efficacy following iliac crest bone graft harvesting was inconclusive (0.20 [0.04–1.09]; low-quality evidence).


Mechanistic pain profiling as a tool to predict the efficacy of 3-week nonsteroidal anti-inflammatory drugs plus paracetamol in patients with painful knee osteoarthritis

Authors: Petersen KK et al.

Summary: This research sought to determine the value of mechanistic pain profiling for predicting pain outcomes associated with NSAID plus paracetamol treatment for knee OA in 132 patients treated for 3 weeks with ibuprofen 400 mg, diclofenac 150 mg and paracetamol 3 g/day and placebo 20 mg/day. Facilitated temporal summation of pain was identified at baseline among patients who failed to respond to the 3 weeks of treatment as compared with responders for both 30% and 50% pain alleviation criteria (p=0.02). A linear regression analysis revealed that poor alleviation of pain with treatment was significantly, independently predicted by facilitated temporal summation of pain and low clinical pain scores.

Comment: Paracetamol with an NSAID is often used as the first-line treatment for painful knee OA. Recent reviews suggested there is a nociceptive/neuropathic component in a subpopulation of OA patients. Previous study has suggested that preoperative facilitated temporal summation of pain, or conditioned pain modulation, predicts a poor outcome after total knee arthroplasty. This is an exploratory prospective cohort study (n=132) of mechanistic pain profiling showing facilitated temporal summation of pain as a predictor for a poor response rate to NSAID and paracetamol treatment in chronic knee OA patients at 3 weeks. A computer-controlled cuff algometer at the head of the gastrocnemius on the side most affected by OA was used for cuff pressure pain tolerance threshold. For temporal summation, 10 x 1-second cuff pressure tolerance threshold was given with 1-second breaks, and the difference between the tenth and first VAS score was used. This study adds to the growing evidence of mechanistic pain profiling and targeted treatment.

Reference: Pain 2019;160:486–92

Fulranumab as adjunctive therapy for cancer-related pain

Authors: Stalini N et al.

Summary: This phase 2 study randomised 98 terminally ill patients with cancer to receive a single subcutaneous injection of fulranumab 9mg or placebo, as an adjunct to opioids, in a 2:1 ratio in a 4-week double-blind phase, after which 71 of the participants received open-label fulranumab 9mg every 4 weeks for 48 weeks. There was no significant difference between the fulranumab and placebo recipients for change in average cancer-related pain intensity (–0.8 vs. –0.7 [p=0.592]) after the first double-blind injection, but there were benefits for the secondary endpoints of 30% response rate (p=0.020), Brief Pain Inventory-Short Form pain intensity subscale score (p=0.003) and pain interference subscale score (p=0.006). The most commonly reported treatment-emergent adverse events in the respective fulranumab and placebo arms were asthenia (16% and 10%), decreased appetite (12% and 6%), fatigue (10% and 0%) and malignant neoplasm progression (10% and 0%).

Comment: In previous rat study, anti-NGF treatment reduced cancer pain in prostate carcinoma and osteogenic sarcoma without affecting tumour growth. This is a phase 2 double-blind RCT study (n=100) of terminally ill cancer patients with refractory pain despite opioids and other adjuvant therapy, showing no significant difference between fulranumab (an anti-NGF antibody) and placebo on the primary endpoint, VAS reduction (0.8 vs. 0.7). However, for the secondary endpoints, responder rate (30% overall pain reduction) was greater in the fulranumab group (31% vs. 9.7%). This is similar to the study of tanezumab for the treatment of metastatic bone cancer pain, where the primary endpoint was not met at 6 or 8 weeks. The treatment-emergent adverse event rates were similar to previous studies. The incidence of significant adverse events leading to discontinuation was low. I note that joint-related adverse events were not seen in this trial. Further confirmation study is needed.

Reference: J Pain 2019;20:440–52

Identifying and engaging neuronal oscillations by transcranial alternating current stimulation in patients with chronic low back pain

Authors: Ahn S et al.

Summary: This randomised, crossover, sham-controlled pilot study in patients with chronic lower back pain investigated the relationship between a oscillations and pain symptoms for target identification, and whether this target can be engaged by transcranial ACS (alternating current stimulation), thereby inducing pain relief. High-density EEG, used to measure the α oscillations, showed that prestimulation oscillation strength in the somatosensory region negatively correlated with pain symptoms. Compared with sham stimulation, stimulation with α-transcranial ACS was associated with significant enhancement of a oscillations in the somatosensory region, which correlated with pain relief.

Comment: Previous EEG/MEG study has shown pathological 8 oscillations (4–8Hz)/impaired a oscillations or thalamocortical dysrhythmia (i.e. decreased thalamic inhibition) in chronic pain. This is a double-blind RCT of chronic lower back pain patients (n=20) using 10Hz transcranial ACS modulation of a oscillations at bilateral fronto-frontal montages (somatosensory region) showing change of endogenous a oscillation (EEG correlates with pain reduction (DVPRS and ODI)). The electrode delivers in-phase sinusoidal waveforms with 1mA amplitude for 40 minutes. This target-specific approach with EEG closed-loop feedback may provide better mechanistic based neuromodulation. I look forward to follow-up study with individualised stimulation parameters and multisession stimulation.

Reference: J Pain 2019;20:2776–11

Cost-effectiveness and cost-utility of internet-delivered exposure therapy for fibromyalgia

Authors: Hedman-Lagerfeld M et al.

Summary: This was a cost-effectiveness analysis of health economic data from a trial that randomised participants with fibromyalgia to internet-delivered exposure therapy or waitlist control. The ICER (incremental cost-effectiveness ratio) was $15,295, indicating that the internet-delivered exposure therapy was highly cost-effective with each successfully treated case associated with substantially reduced net costs. The internet-delivered exposure therapy remained cost effective in two sensitivity analyses, even with willingness to pay of $0.

Comment: Exposure therapy is a form of CBT that has shown efficacy in fibromyalgia in previous study. Internet-delivered CBT requires <20% of therapists’ time. This internet-based CBT can be a cost-effective treatment. This is a cost-effectiveness analysis of internet-delivered exposure therapy (10 weeks; total therapist time of 175 minutes) versus waitlist control for fibromyalgia (n=140) showing high cost effectiveness. The ICER of one additional responder was $15,295 (for one additional responder, there was a societal cost saving of $15,295). The ICER of one additional QALY was $67,345 (for one additional QALY, there was a societal saving of $67,345). The study findings are consistent with previous health economy studies regarding CBT for fibromyalgia. It will be interesting to see the cost effectiveness of internet-delivered exposure therapy compared with face-to-face treatment.


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¹*Analgesia not solely derived from opioid agonism. †S8 analgesic.
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Telehealth therapy effects of nurses and mental health professionals from 2 randomized controlled trials for chronic back pain

Authors: Gannon J et al.

Summary: Data for study participants with chronic low back pain who had been randomised in two trials to supportive care telehealth or 8-week CBT delivered by mental health professionals (n=66) or primary care nurses (n=61) were included in this analysis. Intent-to-treat analyses showed significant improvements in RMDQ, SF-12, GHQ, NRS, PCS (Pain Catastrophizing Scale) and GSI (Global Clinical Impressions) scores for treatment in both trial arms and in both studies, but changes in BDI-2 (Beck Depression Inventory 2) scores were inconsistent. No significant differences in treatment efficacy were detected for RMDQ, NRS, PCS or GCI scores between the two study treatments.

Comment: This study compared two RCTs (n=66, n=61) of an 8-week telephone-delivered, home-based intervention with CBT versus supportive care. The telehealth therapy delivered in study 1 was by a mental health professional and in study 2 by a primary-care nurse. The study showed significant improvements in the primary outcome (disability, RMDQ) and secondary outcomes (NRS, BDI-2, PCS) in both treatments (CBT and supportive care) and both disciplines without significant differences. Depressive symptoms (BDI-2) decreased more with CBT when delivered by mental health professionals. These findings suggest that greater access to these evidence-based therapies for selected chronic back pain patients can be improved by extending the disciplines to deliver treatment without loss of treatment efficacy.


Abstract

An open-label prospective study of the real-life use of onabotulinumtoxin A for the treatment of chronic migraine

Authors: Ahmed F et al., on behalf of the REPOSE Principal Investigators

Summary: In the prospective open-label REPOSE study, 633 participants (85.3% women) received ≥1 treatment session that was ≥1 week after the recommended dosing interval of 12 weeks. Treatments led to a reduction in mean headache-day frequency from 20.6 days at baseline to 7.4 at administration visit 8 (p<0.001), as well as significant reductions from baseline in the Migraine-Specific Quality-of-Life Questionnaire domain scores (restrictive, preventive and emotional) and significant improvements from baseline in median EuroQol 5-Dimension Questionnaire total and health state scores. The overall and serious adverse drug reaction rates were 18.3% and 1.3%, respectively; the most frequently reported adverse drug reactions were eye oedema (5.4%), neck pain (2.8%) and musculoskeletal stiffness (2.7%).

Comment: The PREEMPT study showed safety and efficacy of onabotulinumtoxin A over 56 weeks. Data on real-world clinical utilisation, safety and efficacy are still needed. This is a European prospective multicentre observational cohort study (n=641) of patients receiving onabotulinumtoxin A for chronic migraine preventative treatment, showing sustained significant reductions in headache-day frequency and improved quality of life at 2 years. The findings are consistent with other studies on the use in the routine clinical setting. The incidence and nature of adverse drug reactions were similar to the PREEMPT study, e.g. eyelid oedema in 5.4% and neck pain in 2.8%. I note that 22.7% discontinued treatment, mostly due to lack of efficacy. Despite the inherent limitation of an observational study, the consistency of the data with the PREEMPT study is reassuring.

Reference: J Headache Pain 2019;20:26

Abstract

Characteristics of patients with opioid use disorder associated with performing overdose reversals in the community

Authors: Katzman JG et al.

Summary: Individuals with opioid use disorder (n=287) were provided with take-home naloxone and opioid overdose education in this 6-month prospective cohort study. Compared with participants who did not use the take-home naloxone to perform opioid overdoses, those who did were more likely to: i) receive emergency room care for opioid overdose (OR 4.89 [95% CI 1.54–15.52]); ii) previously witness someone else who experienced an opioid overdose (5.67 [1.24–25.87]); iii) test positive for ≥2 illicit substances in their urine at 6 months (5.26 [1.58–17.54]) or miss their 6-month urine analysis (3.46 [1.42–8.43]); iv) be aged <30 years (2.80 [1.02–7.66]), and v) be of Hispanic ethnicity (9.38 [1.41–11.21]).

Comment: Previous study by Katzman et al. showed providing opioid overdose education and take-home naloxone to patients on opioid treatment programmes can increase overdose reversal in the community. This is a US 6-month prospective cohort study of take-home naloxone and opioid overdose education (n=287) for patients with opioid use disorder showing younger age, previously witnessing an opioid overdose, receiving emergency care for an opioid overdose and having positive urine toxicology screen increased the odds of performing naloxone reversal. It will be interesting to see further local data on take-home naloxone and opioid overdose education programmes.


Abstract

Long-term outcomes using intrathecal drug delivery systems in complex regional pain syndrome

Authors: Herring EZ et al.

Summary: These researchers reported on 26 patients with CRPS who had an intrathecal drug delivery system implanted ≥4 years of continuous follow-up. Pain scores for these patients did not decrease significantly over time, and no correlation was detected between pain intensity and any intrathecal medication use. A decrease in oral opioid intake was seen over time, but intrathecal opioid dose had no significant impact on oral opioid consumption. Ziconotide use sped up the decrease in oral opioid intake, whereas a paradoxical increase was seen with bupivacaine use.

Comment: Only 29% of patients diagnosed with CRPS report improvement in pain over the disease course, and after 1 year of symptoms, regression is rare. This is a retrospective cohort study (n=26, 2000–2013) of intrathecal drug delivery systems for patients with CRPS at a Cleveland clinic showing no significant reduction in pain, and intrathecal opioid dose did not significantly impact on oral opioid consumption at 4 years or more. Interestingly, whereas ziconotide hastened the decrease in oral opioid intake, bupivacaine paradoxically increased oral opioid use. However, I note limitations of the study with a limited number of patients and the retrospective nature. Overall, the data suggest that initiating intrathecal opioid therapy in patients failing opioids may not be an effective long-term strategy in this cohort.


Abstract