Animal research on a diet-induced obesity model has shown increased pain in inflammatory and neuropathic pain models. This is an animal study showing a correlation of high-fat diet (40% calories from butter fat for 6 weeks) and increased animal pain behaviour as compared with low-fat normal chow. Interestingly there was a male preponderance. Mechanistic study showed that the high-fat diet was associated with increased macrophage density (in L4/5 dorsal root ganglion), increased GAP43 (associated with active nerve regeneration) and delayed wound healing. It will be interesting to see if there is a correlation between a high-fat diet and increased postoperative pain in humans in an observational study.

Reference: Pain 2018;159:1731–41

Abstract

Effectiveness of lumbar facet joint blocks and predictive value before radiofrequency denervation

Authors: Cohen SP et al.

Summary: The Facet Treatment Study randomised 229 participants to intra-articular facet bupivacaine and steroid injections, medial branch block or saline in a 2:2:1 ratio. Participants with a positive outcome (≥2-point reduction in average pain score) and a satisfaction score of ≥3 on a 5-point scale were followed for 6 months. Participants from the intra-articular and medial branch block arms with a positive diagnostic block (≥50% relief) and a negative outcome proceeded to RFA, and all participants from the saline group underwent RFA; RFA was performed in 45, 48 and 42 participants from the intra-articular, medial branch block and saline groups, respectively. The 1-month decrease in mean NRS score was 0.7 in each group (p=0.993), and higher proportions of the intra-articular and medial branch block versus saline group had positive blocks (64% and 55% vs. 30% [p=0.01]). At 3 months, there were no significant differences in average NRS score between the intra-articular, medial branch block and saline arms (3.0, 3.2 and 3.5, respectively), whereas the proportions of positive responders were greater in the intra-articular and medial branch block arms compared with the placebo arm (51% and 56% vs. 24% [p=0.005]).

Comment: Recently, RFA has come under scrutiny. This is an RCT (n=229) suggesting prognostic value of facet joint block and medial branch block before RFA, and showing increased RF responses in patients with positive facet joint block (51%) and medial branch block (56%) compared with saline placebo (24%) at 3 months. A positive diagnostic block was defined as a ≥50% reduction of pain. This study responds to a previous study by Juch et al., which concluded evidence against RFA, and noted differences in study methodology; e.g. patient selection (higher positive diagnostic block rate) and difference in electrode placement. Further RCTs on patient selection are warranted.

Reference: Anesthesiology 2018;129:517–35

Abstract

High-fat diet exacerbates postoperative pain and inflammation in a sex-dependent manner

Authors: Song Z et al.

Summary: These researchers fed Long-Evans rats high- or low-fat diets to examine the impact of obesity in a postoperative pain model. Compared with the low-fat diet, the high-fat diet was associated with prolonged mechanical hypensensitivity and an overall increase in spontaneous pain in response to paw incision in male rats, with only minor effects seen in the female rats. The effects on pain behaviours were reversed when the high-fat diet was stopped 2 weeks before evaluation, although weight gain had not been reversed by this time. The pain responses were also increased, albeit to a lesser degree, after 1 week of a high-fat diet in the male rats. The 6-week high-fat diet was also associated with increased macrophage density in lumbar dorsal root ganglion, particularly in male rats, sensitised responses of peritoneal macrophages to lipopolysaccharide stimuli in vitro, increased levels of the nerve regeneration marker GAP43 (growth-associated protein–43) in the skin near the incision, and delayed wound healing. It will be interesting to see if there is a correlation between a high-fat diet and increased postoperative pain in humans in an observational study.

Reference: Pain 2018;159:1731–41

Abstract

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Perioperative lidocaine infusions for the prevention of chronic postsurgical pain

Authors: Bailey M et al.

Summary: This was a systematic review and meta-analysis of six trials reporting chronic postsurgical pain outcomes following perioperative lidocaine infusions versus placebo in adults who were pain free at baseline. The incidence of chronic postsurgical pain was found to be consistent with existing epidemiological data. Procedure-related pain at ≥3 months post-surgery (primary outcome) was reduced by perioperative lidocaine infusions (odds ratio 0.29 [95% CI 0.18–0.48]), but the difference in chronic postsurgical pain intensity as assessed by the short-form McGill Pain Questionnaire (four trials) did not reach statistical significance. The results were also affected by high publication bias and trial design limitations. Although each study reported no lignocaine-attributable adverse events, there was a lack of systematic safety surveillance strategies.

Comment: A Cochrane review in 2013 reported limited evidence that IV ketamine and regional anaesthesia reduced the incidence of chronic postsurgical pain at 6 months. Only one trial was reported on systemic lignocaine in the review. Lignocaine was shown to have anti-NMDA (N-methyl-D-aspartate) effects (ex vivo model), anti-inflammatory effects (in vivo model) and blocked voltage-gated sodium channels. This is a systematic review of six trials (n=420) suggesting that perioperative lignocaine infusions significantly reduce procedure-related pain at 3 months after surgery. Change in McGill Pain Questionnaire pain intensity did not reach significance. The optimal dosage and duration is difficult to ascertain due to the low number of trials. A previous study by Ferrante et al. showed plasma concentrations of 2–3 µg/mL are associated with analgesia in neuropathic pain. Further large multicentre trials are needed.

Reference: Pain 2018;159:1696–704
Abstract

Medical marijuana users are more likely to use prescription drugs medically and nonmedically

Authors: Caputi TL & Humphreys K

Summary: This research used simulations based on logistic regression analyses of US drug use and health data to examine if medical marijuana use is a risk or protective factor for prescription drug use, both medical and nonmedical. Compared with nonusers, users of medical marijuana were significantly more likely to report prescription drug use in the prior 12 months for both medical and nonmedical purposes [relative risk ratios 1.62 [95% CI 1.50–1.74] and 2.12 [1.67–2.62]], including pain relievers [1.95 [1.41–2.62]], stimulants [1.86 [1.09–3.02]] and tranquilisers [2.18 [1.45–3.16]].

Comment: Previous studies have shown that US states with medical marijuana access laws have lower rates of medical and nonmedical prescription drug use and related harm, such as opioid overdose. This is a large cross-sectional study based on a national survey in the US showing that medical marijuana users were at higher risk for medical and nonmedical prescription drug use. The relative risks for nonmedical stimulant and tranquiliser use were higher than for nonmedical pain reliever use. Further longitudinal study is warranted to determine whether patients substitute medical marijuana for prescription drugs, such as opioids.

Abstract

Peripherally restricted cannabinoid 1 receptor agonist as a novel analgesic in cancer-induced bone pain

Authors: Zhang H et al.

Summary: This murine-based research reported that acute and sustained administration of a peripherally selective CB1 cannabinoid-1 receptor agonist was able to effectively suppress cancer-induced bone pain. The analgesic effect of the agent (PrNMI) was able to be reversed when SR141716, a selective CB1 receptor antagonist, was administered systemically but not when administered via spinal injection. Furthermore, there was no exacerbation of cancer-induced bone pain on repeated PrNMI administration, and catalepsy and hypothermia (common side effects of cannabinoids) were detected only at supratherapeutic PrNMI doses. PrNMI administration was associated with mild sedation, but no detectable anxiety or decrease in limb movements.

Comment: Cannabinoids have been shown to modulate osteoblasts and osteoclasts, and the activation of peripheral cannabinoid receptors has been shown to inhibit chronic pain, including bone cancer pain. This is a mouse study showing that PrNMI, a peripherally restricted CB1 receptor agonist, significantly reduced spontaneous pain behaviours in a mouse model of cancer-induced bone pain, and reversed by SR141716, a selective CB1 receptor antagonist, peripherally but not with spinal application. There was no exacerbation of bone loss, and no catalepsy or hypothermia at supratherapeutic doses. CB1 receptors are upregulated in primary perineural terminals in pathological conditions. Peripheral CB1 receptor agonists may reduce spontaneous activity and nociceptor sensitisation. I look forward to the next instalment of the study.

Abstract

Neuropsychological functioning and treatment outcomes in acceptance and commitment therapy for chronic pain

Authors: Herbert MS et al.

Summary: This secondary analysis of data from 117 veterans with chronic pain who underwent 8 weeks of ACT (acceptance and commitment therapy) reported improvements in pain interference, pain severity, quality of life, activity levels, depression and pain-related anxiety. Relationships were seen between neuropsychological performance and changes in depression and pain-related anxiety during treatment; specifically, associations were seen between: i) relative reductions in both executive functioning and processing speed and greater decreases in depressive symptoms; and ii) relatively lower processing speed and greater decreases in pain-related anxiety. Patients with relatively lower neuropsychological functioning attained greater benefit from psychosocial treatment, even though most study outcomes did not differ as a function of neuropsychological performance.

Comment: The effect sizes for treatment outcomes of chronic pain with cognitive behavioural therapy/ACT are generally small to medium, and a subgroup do not benefit from treatment. As psychosocial therapy involves cognitive domains, differences in neuropsychiatric functioning may explain variability in treatment outcomes. This is a secondary analysis of neuropsychological performance in veterans with chronic pain (n=117) undergoing 8 weeks of ACT, showing that lower neuropsychiatric functioning at baseline was related to greater decreases in pain-related depression and anxiety; most of the pain outcomes otherwise were not related to neuropsychiatric functioning. The clinical implication is that neuropsychiatric functioning is not necessarily a determinant of suitability for ACT in chronic pain treatment.

Abstract
Minimum Product Information: ZALDIAR® (tramadol hydrochloride 37.5 mg and paracetamol 325 mg). Indications: For the treatment of moderate pain.

Contraindications:
- Hypersensitivity to any ingredient; acute alcohol intoxication, hypnotic drugs, centrally-acting analgesics, opioids or psychotropic drugs; patients receiving monoamine oxidase inhibitors (MAOIs) or use within two weeks of their withdrawal; severe hepatocellular insufficiency, hepatic failure or decompensated active liver disease; epilepsy not controlled by treatment.

Precautions:
- Recommended dose must not be exceeded; advise patients not to use other paracetamol or tramadol products concurrently. Hepatic or renal impairment. Patients at risk of respiratory depression. Opioid-dependent patients or concomitant use of opioid agonists-antagonists. Increased intracranial pressure, head trauma, shock or reduced levels of consciousness. Potential for misuse or abuse. Withdrawal symptoms. Risk of seizures. Anaesthesia. Children; elderly; pregnancy (category C); lactation. May affect ability to drive and use machines. (See full PI).

Interactions:
- Use with MAOIs is contraindicated. Carbamazepine and other enzyme inducers; inhibitors of CYP2D6 or CYP3A4 isozymes; opioid agonists-antagonists; opioid derivatives; CNS depressants; alcohol; SSRIs; SNRIs; tricyclic antidepressants; warfarin; drugs that reduce seizure threshold. (See full PI).

Adverse effects:
- Dizziness, somnolence, nausea, vomiting, constipation, diarrhoea, dry mouth, abdominal pain, dyspepsia, flatulence, headache, tremor, confusional state, altered mood, anxiety, nervousness, euphoric state, sleep disorders, hyperhidrosis, pruritus. (See full PI).

Dosage and administration:
- Patients 12 years and older: two tablets every 6 hours as needed. Maximum 8 tablets in 24 hours. Do not administer for longer than necessary. Adjust dose according to patient response. (See PI for dose in patients weighing 50kg or less). Monitor patients requiring repeated or longer-term treatment. (Based on full PI last amended 6 September 2013).

References:

PBS Information: This product is not listed on the PBS.
Intravenous remifentanil patient-controlled analgesia versus intramuscular pethidine for pain relief in labour (RESPITE)

Authors: Wilson MJA et al., on behalf of the RESPITE Trial Collaborative Group

Summary: Pregnant females aged ≤16 years who were beyond 37 weeks' gestation and in labour with a singleton cephalic presentation, and who had requested opioid pain relief, were randomised to open-label IV remifentanil PCA (evaluable n=201) or IM pethidine (evaluable n=199). Compared with pethidine, remifentanil PCA was associated with a significantly lower proportion of participants converting to epidural analgesia (primary outcome; 19% vs. 41%; risk ratio 0.48 [95% CI 0.34–0.66]). No serious adverse events or drug reactions directly attributable to study analgesia were reported.

Comment: Epidural analgesia is effective in labour pain, but is associated with increased instrumental delivery; even with the modern low-dose epidural technique, the risk is not completely mitigated. A previous systematic review showed a reduced epidural conversion rate with remifentanil compared with pethidine based on four poor-quality studies. This is a multicentre open-label RCT (n=401) showing a 19% conversion rate to epidural analgesia in the remifentanil PCA group, compared with 41% in the pethidine group. Remifentanil PCA was given as a 40µg bolus with a 2-minute lockout. As-required IM pethidine was given at 100mg every 4 hours, up to 400mg in 24 hours. This is consistent with a previous study that showed one-third of women with labour pain having pethidine converted to epidural analgesia. Given the higher epidural analgesia conversion rate and thus the risk of instrumental vaginal delivery, this study suggests pethidine use in labour should not be routinely used.

Reference: Lancet 2018;392:662–72

Abstract

Postoperative continuous adductor canal block for total knee arthroplasty improves pain and functional recovery

Authors: Leung P et al.

Summary: Patients undergoing unilateral TKA for end-stage degenerative joint disease were randomised to continuous adductor canal block (n=82) or a sham catheter (n=83) for postoperative epidural analgesia, with 38 and 32 participants from the respective arms completing the study. Compared with the sham catheters, continuous adductor canal block was associated with 22.5mg less opioid use over the first 20 hours (p=0.03), a 7.8mm decrease in visual analogue scale area under the curve value (p=0.04), and better physical function score at 3 weeks (p=0.04), but no significant difference for the secondary outcomes (visual analogue scale score, knee range of motion, ambulation distance and physical function) on postoperative day 2. Paired outcomes showed that by 6 weeks, continuous adductor canal block had significantly improved knee range of motion from baseline (mean difference 11.77° [p=0.01]).

Comment: Adductor canal block spares the majority of the motor contribution to the lower limb, and it has been shown to provide effective analgesia after TKA. This double-blind RCT of 165 elective unilateral TKAs showed that postoperative continuous adductor canal block for 1 day was associated with reduced total opioid consumption and pain scores compared with sham catheters at 20 hours, as well as earlier functional recovery function (improved WOMAC [Western Ontario and McMaster Universities Osteoarthritis] index at 3 weeks, and increased range of motion at 6 weeks). This study further validates the value of adductor canal block in post-TKA multimodal analgesia.

Reference: J Clin Anesth 2018;49:46–52

Abstract

A systematic review and meta-analysis of the effectiveness of psychological interventions delivered by physiotherapists on pain, disability and psychological outcomes in musculoskeletal pain conditions

Authors: Silva Guerrero AV et al.

Summary: This is a systematic review and meta-analysis of 30 RCTs comparing physiotherapist-delivered combined physiotherapy-psychological interventions versus physiotherapy alone or usual care. Low- to high-quality evidence was seen for significantly decreased pain with the combined psychological-physiotherapy interventions in both the short and long term, along with significantly decreased disability in the short term; however, the effect sizes were small. There was also low- to high-quality evidence for small-to-medium effects of some psychological outcomes in the short and long term.

Comment: Evidence suggests that adding the psychological component of physical therapy significantly improves health outcomes. Given the low availability of group pain programmes and pain clinic services, delivering the psychological component by physiotherapists may improve accessibility and reduce health costs. This is a meta-analysis of 30 RCTs showing low- to high-quality evidence that physiotherapist-delivered psychological interventions and physiotherapy decrease pain and disability (with improved confidence in managing pain and reduce pain-related fear and negative affect), with small effect sizes. The result is similar to a recent meta-analysis of multidisciplinary biopsychosocial rehabilitation for chronic lower back pain. Further study to integrate psychological therapy into physiotherapy is warranted.


Abstract