Yoga, physical therapy, or education for chronic low back pain

Authors: Saper RB et al.

Summary: Mostly low-income, racially diverse adults with nonspecific chronic LBP (n=320) were randomised to participate in weekly yoga classes for 12 weeks, attend 15 physical therapy sessions or receive an educational book and newsletters in this noninferiority trial. D during a maintenance phase, yoga drop-in classes and physical therapy booster sessions were compared with home practice. Compared with physical therapy, Roland Morris Disability Questionnaire and pain scores obtained from the yoga group met the criterion for noninferiority, but yoga was not superior to education for either outcome. Most of the secondary outcomes assessed (pain medication use, global improvement, satisfaction and health-related quality of life) were similar in the yoga and physical therapy groups, and participants from these respective groups were 21 and 22 percentage points less likely to use pain medication at 12 weeks than those in the education group. Improvements among yoga and physical therapy recipients persisted at 1 year with no between-group difference. Adverse events were mostly mild, self-limited joint and back pain and also did not differ significantly between the yoga and physical therapy groups.

Comment: Noninferiority studies are useful when a new therapy is statistically effective as accepted treatment and is reasonable to integrate into clinical practice. This is a 12-week, adequately powered, assessor blinded RCT showing noninferiority of yoga to physiotherapy in a community-based setting for pain and function. The outcome was maintained at 52 weeks. The study population was predominantly lower income patients with nonspecific chronic LBP, and average attendance was seven classes of yoga. Education was provided as a self-care book. The result is consistent with a previous study by Sherman and colleagues. Given that fees for physiotherapy may be prohibitory, especially for patients with lower socioeconomic status, yoga presents an alternative adjunct for multimodal pain management for LBP patients. It would be interesting to see a cost-effectiveness analysis of yoga versus physiotherapy.


Abstract

The pain course: a randomised controlled trial comparing a remote-delivered chronic pain management program when provided in online and workbook formats

Authors: Dr Tim Ho et al.

Summary: Individuals requiring pain management were randomised to an internet-based version of the ‘Pain Course’ pain management programme (n=84) or were mailed a workbook version (n=94); both versions of the programme consisted of an 8-week pain management programme showing significant improvement of pain and function at 3 months and is reasonable to integrate into clinical practice. This is a 12-week, adequately powered, assessor blinded RCT comparing a remote-delivered chronic pain management program when provided in online and workbook formats showing noninferiority of yoga to physiotherapy in a community-based setting for pain and function. The outcome was maintained at 52 weeks. The study population was predominantly lower income patients with nonspecific chronic LBP, and average attendance was seven classes of yoga. Education was provided as a self-care book. The result is consistent with a previous study by Sherman and colleagues. Given that fees for physiotherapy may be prohibitory, especially for patients with lower socioeconomic status, yoga presents an alternative adjunct for multimodal pain management for LBP patients. It would be interesting to see a cost-effectiveness analysis of yoga versus physiotherapy.

Comment: Previous study on internet-delivered pain management programmes has been encouraging in improving pain and function. However, there is a proportion of people who do not have reliable internet access. This is an RCT of an 8-week pain management programme showing significant improvement of pain and function at 3 months and is reasonable to integrate into clinical practice. The programme content was the same between the online and workbook formats, including psychoeducation, coping strategies and goal setting. The retention rate was high in the study. A low-tech remotely delivered pain management programme may be a useful alternative. However, it would be interesting to see the subgroup analysis of patients with severe pain and depression, as monitoring and face-to-face contact is likely to be needed.

Reference: Pain 2017;158(7):1289–301

Abstract
**Duloxetine 60mg for chronic low back pain**

**Authors:** Alej L et al.

**Summary:** This post hoc analysis of data pooled from four RCTs of duloxetine 60 mg/day (n=642) versus placebo (n=653) for 12–14 weeks in adults with chronic LBP sought to identify predictors of response to the active study drug. Compared with placebo, significantly greater proportions of duloxetine recipients achieved ≥30% and ≥50% reductions in Brief Pain Inventory scores (59.7% vs. 48.3% and 46.6% vs. 35.1%, respectively [p<0.001], particularly among those with early (versus later) improvement (relative risk 2.91 [95% CI 2.30–3.67] and 3.24 [2.44–4.31]) and women (versus men: 1.14 [1.00–1.30] and 1.17 [0.99–1.38]). Response rates did not differ significantly by age, chronic LBP duration or baseline average pain score. Compared with patients with isolated chronic LBP, those with multiple painful sites had greater responses to duloxetine for both ≥30% and ≥50% reductions in Brief Pain Inventory scores (relative respective risks 1.40 vs. 1.07 and 1.51 vs. 1.23).

**Comment:** Previous phase 3 RCTs have shown efficacy of duloxetine in the treatment of chronic LBP. This is a post hoc analysis of four RCTs of duloxetine 60mg for the treatment of chronic LBP looking at predictive factors for responders. Significant predictors identified were greater level of improvement within the first 2 weeks and greater number of painful body sites. This is consistent with previous studies of duloxetine for other pain conditions and consistent with the descending inhibitory pathway theory. I wonder whether withdrawal symptoms at cessation of duloxetine would be less severe with a time-contingent trial of duloxetine 60mg for 2 weeks (as compared with a longer duration, higher dose trial).


**Abstract**

**The effect of a lay-led, group-based self-management program for patients with chronic pain**

**Authors:** Mihlesem M et al.

**Summary:** Adults from Denmark with pain of any aetiology and great variation in pain history were randomised to a lay-led version of the CPSMP (Chronic Pain Self-Management Programme) comprising of six 2.5-hour weekly workshops on managing pain in daily life (n=216) or treatment as usual (n=208). CPSMP did not significantly impact on the primary outcome of pain-related disability or on health expenditure during the intervention or 3-month follow-up, although emotional distress and illness worry were positively affected by a small degree at 3 months.

**Comment:** A previous feasibility study of a Danish lay-led version of the CPSMP showed modest improvements in pain outcomes and a high rate of patient satisfaction at 3 months. The programme focused on self-efficacy to implement behaviour change. This is a large, adequately powered RCT of the Danish lay-led CPSMP; however, it showed no effect on pain-related disability, pain, catastrophisation or self-efficacy at 3 months after the course. This is consistent with a Cochrane review of lay-led patient education programmes for chronic conditions.

**Reference:** Pain 2017;158(8):1437–45

**Preserved analgesia with reduction in opioids through the use of an acute pain protocol in enhanced recovery after surgery for open hepatectomy**

**Authors:** Grant MC et al.

**Summary:** These researchers prospectively collected and analysed data for 60 consecutive patients who underwent open hepatectomy before implementation of an ERAS (enhanced recovery after surgery) pathway and another 120 patients in whom such surgery was performed after the ERAS pathway was introduced. Compared with patients who were operated on pre-ERAS, those who were managed using the ERAS pathway had significantly lower median morphine equivalent requirements at 24, 48 and 72 hours (10.0 vs. 116.0mg, 10.1 vs. 65.4mg and 2.5 vs. 60.0mg, respectively [p<0.001 for all]) and a lower average numerical pain scale score at 24 hours (4.1 vs. 5.1) and other timepoints. Participants treated in the ERAS pathway who received (n=67) versus did not receive (n=33) epidurals also had significantly lower median morphine equivalent requirements at 24 and 48 hours (2.8 vs. 65.0mg and 8.0 vs. 50.0mg, respectively [p<0.001 for both]), but not at 72 hours (1.3 vs. 4.5mg [p=0.58]), and lower average visual analogue scale pain scores at 24 and 48 hours (3.8 vs. 5.0 and 3.4 vs. 4.7, respectively [p=0.001]). Provision of fluids, clinically significant hypotension rates and lengths of hospital stay did not differ significantly between the epidural and nonepidural groups.

**Comment:** A previous ERAS study demonstrated evidence of epidurals in reducing pulmonary complications, attenuating cardiac arrhythmia and improving analgesia, however, recent studies have linked the use of epidurals with increased length of stay, increased fluid requirement and a marginal improvement in analgesia. This observational cohort study showed significant less postoperative opioid use (with similar analgesia and less nausea and vomiting), less fluid and a trend toward earlier return of bowel function, and not linked to increased length of stay or fluid use, with the ERAS protocol. In this study, there was a shift of the ERAS paradigm to goal-oriented fluid administration, leading to a significant reduction in overall fluid administration, which allows lower central venous pressure in liver resection patients. The ERAS-epidural protocol was associated with a significantly reduced morphine requirement with less pain in the first 48 hours. A previous rat model has shown that immunomodulatory effects of neuroaxial anaesthesia and reduction of perioperative opioids may reduce subsequent tumour burden by 70%. Further study looking at disease recurrence, readmission rates and hospital costs would be interesting.


**Abstract**
**Product Information**


**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.

**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, trembling, confusion, altered mood, anxiety, nervousness, euphoric state, sleep disorders, 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 50 kg 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.

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**Triple action pain relief**

**Well tolerated**

* Paracetamol reduces prostaglandin synthesis via inhibition of COX-1 and COX-2 enzymes providing central and peripheral analgesic effects.† Tramadol acts centrally by activating μ-opioid receptors as well as inhibiting noradrenaline-serotonin reuptake reducing both the perception and transmission of pain. Republicated from [www.researchreview.com.au](http://www.researchreview.com.au).
Association between persistent pain and memory decline in a longitudinal cohort of elders

Authors: Whitlock EL et al.

Summary: The relationship between persistent pain, which may reflect chronic pain, and subsequent cognitive decline was explored in a cohort of 10,065 community-dwelling older adults aged ≥62 years in 2000 and who had responded to pain and cognition questionnaires in both 1998 and 2000. Biennial interviews were conducted, and the data analysis took place in 2016. Persistent pain was present at baseline in 10.9% of the participants, and was associated with worse depressive symptoms and more limitations in activities of daily living. Compared with participants without persistent pain, memory decline in those with persistent pain occurred 9.2% more rapidly, which after 10 years implied 15.9% and 11.8% increased relative risks of inability to independently manage medications and finances, respectively. There was a 7.7% quicker increase in the adjusted probability of dementia, which translated to an absolute 2.2% increase in dementia probability at 10 years among participants with persistent pain.

Comment: Previous study has shown that elderly adults with more severe pain perform poorer on memory tests and executive function. This is a large longitudinal population observational cohort study showing that persistent reports of moderate-to-severe pain is associated with accelerated cognitive decline and increased dementia probability; specifically a 9.2% more rapid decline in memory score and a 12–16% increased risk of inability to manage medications/finances at 10 years. Notably, data on potential confounders such as medication, physical activity and social participation were not available. Giving that a causal relationship is difficult to determine from this study, a mediation analysis may be interesting.


Pain catastrophizing moderates relationships between pain intensity and opioid prescription: nonlinear sex differences revealed using a learning health system

Authors: Sharifzadeh Y et al.

Summary: In this retrospective observational study, data from 1794 adults presenting at a large tertiary-care pain treatment centre were analysed to evaluate relationships between opioid prescription, pain intensity and pain catastrophizing. Prescriptions for ≥1 opioid medication were recorded for 57% of the patients. The authors identified a significant interaction and main effects of pain intensity and pain catastrophising on opioid prescription (p<0.04). Sex differences in the relationships between pain catastrophizing, pain intensity and opioid prescription were evident, with opioid prescriptions more common at lower pain catastrophising levels among women compared with men.

Comment: Pain catastrophisation accounts for about 20% of pain intensity. This is a large retrospective study of chronic pain patients showing a significant relationship between pain intensity and opioid prescription; a mediation analysis suggested that pain catastrophising and female sex serve as significant moderating variables, strengthening the relationship between pain intensity and opioid prescription. A prospective, longitudinal study at the time of prescription is needed to establish a causal relationship. However, I wonder if we need to look at treating pain catastrophisation at a lower threshold (e.g. above 20 instead of above 30) in women clinically. It will be also interesting to look at relationships between pain intensity, pain catastrophisation and benzodiazepine use.


IKK/NF-κB-dependent satellite glia activation induces spinal cord microglia activation and neuropathic pain after nerve injury

Authors: Lim H et al.

Summary: Ikkκ conditional knockout mice (Cnp-Cre+/–/Ikkκ±/–, cIkkκ–/–), in which IKK/NF-κB-dependent proinflammatory satellite glial cell activation was abrogated, were used to assay the roles of microglia and satellite glial cells in the development of neuropathic pain after peripheral nerve injury. Compared with control mice, these experimental mice exhibited significant attenuation of nerve injury-induced spinal cord microglia activation and pain hypersensitivity, and their expression of nerve injury-induced proinflammatory genes and macrophage infiltration into the dorsal root ganglion were severely compromised. However, there was a minimal effect of macrophages recruited into the dorsal root ganglion on spinal cord microglia activation, indicating a possible causal effect for satellite glial cell activation on spinal cord microglia activation. To determine the molecular mechanisms, Csf1 expression was measured in the dorsal root ganglion. There was amelioration of nerve injury-induced Csf1 upregulation in the cIkkκ–/– mice, suggesting that Csf1 expression was induced in sensory neurones by IKK/NF-κB-dependent satellite glial cell activation.

Comment: Satellite glial cells respond rapidly to peripheral nerve injury and express inflammatory mediators such as TNF-α; in turn, inhibition of TNF-α has an anti-allodynic effect in animal neuropathic pain models. TNF-α was thought to induce the NF-κB/IKKκ transcription pathway to activate microglial cells. This is an animal pain study using an NF-κB knockout mice neuropathic pain model, showing nerve injury-induced satellite glial activation, leading to cytokine colony stimulating-factor 1, which triggers activation of spinal cord microglia. Blockade of satellite glial cell activation in knockout mice attenuated neuropathic pain (mechanical and thermal hyperalgesia) without affecting acute pain sensation. Further research targeting satellite glial cell activation for neuropathic pain is warranted.

Reference: Pain 2017;158(9):1666–77

Independent commentary by Dr Tim Ho, who is a rehabilitation and pain specialist at Inner West Pain Centre. Tim also works in work capacity centre and addiction medicine. His interests are chronic musculoskeletal pain, neuropathic pain, visceral pain and headache. His research interests are management of comorbid chronic pain and addiction, return-to-work programmes, osseointegration and nursing home resident pain management.

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