NSAIDs reduce osteoarthritic knee pain in the short term; long term effects are unknown

Synopsis


Question What is the analgesic effect of NSAIDs, including coxibs, in patients with knee osteoarthritis? Data Sources MEDLINE, EMBASE, and The Cochrane Controlled Trials Register (CENTRAL) from 1966 to April 2004. Reference lists from relevant articles were scanned. Relevant studies were also traced by contacting experts. Study selection Randomised controlled trials of patients whose knee osteoarthritis had been verified by clinical examination according to the American College of Rheumatology criteria and by X-ray, where the intervention groups had to have received matched placebo drug or adequate NSAID dose and the outcome measure was pain. Data extraction Methodological quality was assessed according to predefined criteria (Jadad scale). It is not reported if selection and assessment of trials were done by one or more reviewers.

Results Twenty-three trials of moderate or good methodological quality were included. The included patients (n = 10 845) had a median age of 62.5 years, 67.9% were women, and the median duration of symptoms was 8.2 years. Thirteen trials used an additional inclusion criterion by requiring a predefined minimum flare of symptoms when NSAID treatment was discontinued in the pretreatment washout period. Only one trial reported long term effects on pain but found no significant difference between NSAID and placebo at one, two, three, and four years after start of treatment. For short term effects (2–13 weeks) the pooled effect size in change in pain between the treatment and the placebo groups was 0.32 (95% CI 0.24 to 0.39), comparable to 10.1 mm on visual analogue scale (VAS) (7.4 to 12.8) or 15.6% better than placebo. For the subgroup of 10 trials (n = 4565) that did not require patients to have a minimum flare of symptoms after treatment with NSAIDs was stopped before the trial, the pooled effect size for pain was 0.23 (0.16 to 0.31) or 5.9 mm on VAS (3.8 to 7.9). Conclusion NSAIDs can reduce short term pain in osteoarthritics of the knee slightly better than placebo. Evidence of long term effects from oral NSAIDs is still lacking.

Commentary

Osteoarthritis (OA) is the most common cause of musculoskeletal disability and pain, and the prevalence is increasing with the increasing age of population. Painful joints often lead to a downward spiral of inactivity, muscle dysfunction and weight gain, increased disability and reduced participation in life activities. According to the EULAR recommendations (Jordan et al 2003), current treatment for knee OA includes non-pharmacological treatments (for example exercise and education), and pharmacological treatments (paracetamol, NSAIDs, and topical treatments). How is the current evidence to support these treatment alternatives?

The present high quality review showed that NSAIDs may have a small to moderate short-term effect on pain whereas long-term use of NSAIDs is not supported. For short-term effects (2–13 weeks) the pooled effect size in change in pain between the treatment and the placebo groups was moderate (0.32). For the subgroup of 10 trials that did not require patients to have a minimum flare of symptoms after treatment with NSAIDs was stopped before the trial, the pooled effect size for pain was small (0.23).

Recent high quality trials, systematic reviews and reports have concluded that therapeutic exercises are beneficial for patients with knee OA (Jordan et al 2003, Roddy et al 2005, Fransen et al 2002, Nasjonalt kunnskapssenter for helsetjenesten 2004). The Roddy et al (2005) review concluded that strengthening and aerobic exercise had moderate effects on pain (effect size range 0.44 to 0.70) and function (effect size range 0.37 to 0.76).

According to current evidence, therapeutic exercises are of benefit for patients with knee OA, and NSAIDs may give short-term pain reduction. The combination of these two interventions might be beneficial, administered as long-term, guided exercise programs, supplemented with short term use of NSAIDs to allow patients to start training or overcome painful periods.

Hanne Dagfinrud
National Resource Center for Rehabilitation in Rheumatology, Norway

References

Acupuncture does not produce a significant clinical effect in chronic neck pain

Synopsis


**Question** Is acupuncture effective for the treatment of chronic mechanical pain compared with placebo? **Design** Randomised controlled trial. **Setting** The outpatient departments of two major hospitals in the UK. **Patients** 135 patients suffering from chronic mechanical neck pain were randomised into an acupuncture (n = 70) and a placebo group (n = 65). **Interventions** Patients received over a period of 4 weeks 8 treatments with acupuncture or with mock transcutaneous electrical stimulation of acupuncture points using a decommissioned electroacupuncture stimulation unit. **Outcomes** The primary outcome was pain (as measured on a visual analogue, VAS, scale) at 1 week after treatment. Secondary outcomes were pain assessed at other time points (until 12 months follow-up), disease-specific quality of life measured with the Neck Disability Index and more generic quality of life as measured with the Short-Form 36. **Main results** Acupuncture and placebo had similar credibility. For the primary outcome (weeks 1 to 5), a statistically significant difference in VAS score in favour of acupuncture of 6.3 mm (95% CI, 1.4 to 11.3) was observed between the 2 study groups, after adjustment for baseline pain and other covariates. This difference was, however, not clinically significant because it demonstrated only a 12% (95% CI, 3% to 21%) difference between acupuncture and placebo. Secondary outcomes showed a similar pattern. **Conclusion** Acupuncture reduced neck pain and produced a statistically, but not clinically, significant effect compared with placebo.

Commentary

Acupuncture is defined as puncturing specific points in the skin (‘acupuncture points’), which have been shown to have electrical and radioactive characteristics which make them actually different from the rest of the skin. It is already known that needling anywhere in the skin leads to an effect that is slightly more powerful than inert placebos, such as sham TENS, sugar pills or non-needling acupuncture (Ernst 1998, Ezzo et al 2000). This may be due to needling having a potential nonspecific biological effect, to it triggering a particularly intense placebo effect, or to a potential unknown confounder. Further studies comparing needling acupuncture with placebos other than puncturing non-acupuncture points are likely to be irrelevant, since their results are likely, as in White’s study, to reflect just the demonstrated different sizes of placebo effect associated with different procedures.

To date, there is no consistent evidence that acupuncture provides anything more than a placebo effect in the treatment of neck and low back pain (Ernst 1998, Ezzo et al 2000, van Tulder et al 2004). In the treatment of those conditions, acupuncture provides results that are comparable (as effective as, slightly better or slightly worse) to those of other techniques that have not consistently shown effectiveness vs a sham procedure (Ernst 1998, Ezzo et al 2000, van Tulder et al 2004). Therefore, it is not possible to rule out the notion that those studies are just comparing the size of the placebo effect triggered by different procedures.

For acupuncturists to satisfactorily to explore the efficacy of their technique for the treatment of neck or low back pain, high quality trials comparing needling of acupuncture vs non-acupuncture points should be undertaken. Since it is difficult to ensure therapist blindness in studies on acupuncture, at least randomisation, outcome assessment, and statistical analysis should be masked, as has been done for assessing acupuncture in the treatment of other conditions. Similarly, to show the effectiveness of the procedure, high quality randomised controlled trials should be undertaken vs other procedures that have shown on their own to be superior to placebo.

In this respect, the main pragmatic contribution of White’s trial is to further support that there is no evidence to recommend the use of acupuncture for the treatment of neck or low back pain.

**Francisco Kovacs**
Spanish Back Pain Research Network

References

Critically Appraised Paper

‘Usual’ physiotherapy is more effective than brief physiotherapy for neck pain

Synopsis


Questions For patients with neck pain, is a brief physiotherapy intervention as effective as ‘usual’ physiotherapy? Do patient preferences for treatment influence outcome? Design Non-inferiority randomised controlled trial with concealed allocation and blinded assessors. Setting Eight community services in Yorkshire and Lincolnshire, UK, involving 28 participating physiotherapists (12 trained to provide brief intervention). Patients 268 patients (average age 48 years) with subacute/chronic neck pain, GP referred, randomly assigned to brief intervention (139) or ‘usual’ physiotherapy (129). Patient preference measured independently at baseline. Similar loss to follow-up at 12 months (17% and 18% respectively). Interventions Brief intervention of up to 3 treatments encouraging self-management and early return to normal daily activities. ‘Usual’ care (variably electrotherapy, manual therapy, education, advice) determined by individual professional judgment. Outcomes Main outcome measure was Northwick Park neck pain questionnaire (NPQ), secondary outcome measures were SF-36 instrument, Tampa Kinesophobia Scale, Distress scale scored 0–10. All measures administered pre-intervention, 3 and 12 months follow-up. Results The results generally favoured ‘usual’ physiotherapy. NPQ showed significant difference at 12 months (1.99 (0.45 to 3.52)). Significant changes at 3 months in SF-36 domains of mental health (-4.68 (-8.37 to -0.98) and energy and fatigue (-4.55 (-8.80 to -0.29), and at 12 months in SF-36 domains of Role Physical (-6.70 (-12.96 to -0.44)), Role Emotional (-11.72 (-17.57 to -5.86)), Energy and Fatigue (-9.24 (-14.66 to -3.82)), Pain (-6.74 (-13.18 to -0.38)) and General Health (-8.15 (-12.35 to -3.95)). Significant changes in Tampa scale at 3 months (-2.23 (-3.73 to -0.74)) favoured the brief intervention. Patients who preferred the brief intervention and received it had similar outcomes to patients receiving ‘usual’ physiotherapy. Conclusion ‘Usual’ physiotherapy was generally more effective than brief physiotherapy intervention at 3 and 12 months follow-up. The effect of patient preference on outcome is unclear.

Commentary

The clinical implication of this methodologically strong study is that ‘usual’ physiotherapy was marginally more effective than ‘brief’ physiotherapy at 3 and 12 months follow-up. Moreover, patients who preferred, and were allocated to, the brief intervention may have an outcome as successful as that of patients given ‘usual’ care. These findings are consistent with earlier findings that patient expectations were among the key factors that influenced outcome of physiotherapy (Klaber Moffett and Richardson 1997). Research by May (2001) and Potter et al (2003) suggested that patient expectations of physiotherapy care include key components of education, self-management strategies which are underpinned by effective communication, and patient-centred approaches. These findings have been validated by this author’s doctoral research at the University of South Australia, where 74 physiotherapy patients’ expectations of quality care included empowerment (education, self management strategies) and patient centred care (Kumar 2005).

The findings of this investigation, coupled with those from earlier research support the need to better understand partnership approaches between patient and physiotherapist, reflecting education, self management and early return to normal duties. These seem particularly relevant in the management of chronic musculoskeletal conditions such as neck pain.

Saravana Kumar
University of South Australia

References

Clinical rule predicts patients likely to benefit from spinal manipulation

Synopsis


Question Is it possible to identify the low back pain patients who will respond to spinal manipulation?

Design Randomised controlled trial with pre-planned subgroup analysis.

Setting Eight physical therapy clinics in USA.

Patients Patients aged 18–60, with a primary complaint of low back pain and an Oswestry Disability score of at least 30%. Exclusions were serious spinal pathology, nerve root compromise, pregnancy, and previous surgery. 543 patients were screened; 131 were eligible and were randomised using sealed envelopes to a manipulation group (70 patients) or an exercise group (61 patients).

Interventions Patients in both groups attended physiotherapy for 5 sessions over 3 weeks. The manipulation group received a high velocity thrust spinal manipulation during the first two sessions and then low stress aerobic and lumbar strengthening exercises. The exercise group received exercise alone. Two participants in the manipulation group and 9 in the exercise group discontinued treatment. An independent examiner assessed the patients and classified them as positive on the clinical prediction rule if they met 4 of the 5 following criteria: symptom duration < 16 days, no symptoms distal to knee, < 19 on Fear Avoidance Beliefs Questionnaire, at least one hypomobile segment and at least one hip with > 35 degrees of internal rotation.

Outcomes The primary outcome was disability measured using the 0–100% Oswestry disability index, measured at baseline, 1 week, 4 weeks, and 6 months. Treatment success was defined as 50% reduction in disability. All participants completed the baseline assessment and 1 week follow-up, 130/131 the 4 week follow-up, and 92/131 the 6 month follow-up. Analysis was by intention to treat with pre-planned subgroup analysis.

Results 47/131 participants were positive to the rule. ANOVA revealed that the outcome depended upon the both the participant’s treatment group and status on the rule. Pairwise disability mean (95%CI) differences at one week were: manipulation vs exercise 9.2 (4.4 to 14.1), manipulation (+ve on rule) vs manipulation (-ve on rule) 15.0 (8.5 to 21.5), manipulation (+ve on rule) vs exercise (+ve on rule) 20.4 (13.0 to 28.8) and exercise (+ve on rule) vs exercise (-ve on rule) 1.9 (8.6 to 4.9). (+ve values signify greater improvement with the first named group in a pair). At 1 week 44% of the manipulation group had a successful outcome, however the success rate was 92% in the manipulation subgroup positive to the rule and only 7% in the subgroup who met less than 3 of the criteria.

Conclusion Patients were more likely to benefit from spinal manipulation if they met the clinical prediction rule.

Commentary 1

The evidence supporting the validity of schemes that guide treatment in non-specific low back pain is sparse and contradictory. Such schemes are useful only if they improve prognostic accuracy, or result in more effective treatment decisions.

The approach that Childs and co-workers (2004) have taken is novel to non-specific low back pain research. The clinical prediction rule is derived empirically, and pragmatically side-steps the minefield of pathoanatomical labelling. The prediction rule was derived in a clinical population (patients within the armed services presenting with short-term non-specific low back pain and at least moderate activity limitation) to identify responders to a particular manipulation and range-of-motion exercise regimen. Importantly, it has been validated in this multi-centre study. Without the prediction rule clinicians could expect that about one in two patients will respond to this treatment regimen (pre-test probability 44%); by using the prediction rule clinicians can expect greater confidence in knowing which patients will and will not respond to this regimen. A patient who is positive on the prediction rule has a 91% probability (95%CI 73% to 98%) of a favourable response, while a patient who is negative on the prediction rule has only a 7% probability (95%CI 2% to 25%) of responding to this treatment regime. Approximately one in three patients were positive on the prediction rule. This is very useful information for referrers, treaters, and researchers.

However, there are reasons for caution and these may impact the capacity of this prediction rule to influence clinician behaviour. The prediction rule was derived and validated using a particular patient population, and requires replication in more diverse patient populations (non-military, low activity limitation, and other cultures) for it to have unreserved generalisability. It was also derived for a treatment regime consisting of a specific manipulative technique and range-of-motion exercise. Its generalisability to other manipulative techniques is unknown, although there is some evidence that technique choice may not make much difference (Chiradejnant et al 2003).

Peter Kent
La Trobe University

Reference

This high quality study provides information about three important issues.

First it tells us about *prognosis* for people aged 18–60 presenting to physiotherapy clinics with moderate or severe low back pain (Oswestry scores ≥ 30%). The data are reliable because they were obtained from a near-consecutive sample with a high rate of follow-up, and they are relevant because the patients were those presenting to physiotherapy clinics. In this heterogeneous group, including patients with acute and chronic pain, there were moderate to large reductions in disability over time. In subjects who received exercise and subjects with negative prediction rules who received manipulation the average reduction in disability was of the order of 20% at 1 week, and 40%–50% at 4 weeks and 6 months. Subjects with positive prediction rules who received manipulation experienced greater average reductions in disability: about a 70% reduction at 1 week and 80% at 4 weeks and 6 months. These reductions in disability are due to a range of factors, including the natural course of back pain and the effects of intervention.

This study also tells us about *effects of manipulation* compared to exercise. Again, the findings are credible because the trial used rigorous methods, including concealed random allocation, analysis by intention to treat, and excellent follow-up. When manipulation is applied to this heterogeneous group it produces, on average, a reduction of just less than 10 percentage points on the Oswestry disability scale.

Last, and most important, this study has shown that a simple decision rule can be used to *identify subgroups of patients in whom manipulation is and is not effective*. This study is one of very few to examine treatment effect modifiers nominated a priori in the context of a randomised trial, so it provides rare evidence of a treatment effect modifier. The study shows that the average effect of manipulation (compared to exercise) is about 20 points in patients who are positive to the prediction rule, but only about 4 points in patients who are negative to the prediction rule (calculated from data). (It would be interesting to know how much more likely a positive outcome is in people who test positive and are manipulated compared to people who test positive and receive exercise, but these data were not provided.) Until more refined prediction rules become available, physiotherapists should consider manipulation for patients with low back pain who are positive to the prediction rule, and they should consider not manipulating people who are negative to the prediction rule.

Rob Herbert
University of Sydney