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Research Paper Review

Efficacy of paracetamol for acute low-back pain: a double-blind, randomized controlled trial

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Reviewed by Dr. Jeff Muir DC (Research Review Service)

ABSTRACT

Background

Regular paracetamol is the recommended first-line analgesic for acute low-back pain; however, no high-quality evidence supports this recommendation. We aimed to assess the efficacy of paracetamol taken regularly or as-needed to improve time to recovery from pain, compared with placebo, in patients with low-back pain.

Methods

We did a multicentre, double-dummy, randomised, placebo controlled trial across 235 primary care centres in Sydney, Australia, from Nov 11, 2009, to March 5, 2013. We randomly allocated patients with acute low-back pain in a 1:1:1 ratio to receive up to 4 weeks of regular doses of paracetamol (three times per day; equivalent to 3990 mg paracetamol per day), as-needed doses of paracetamol (taken when needed for pain relief; maximum 4000 mg paracetamol per day), or placebo. Randomisation was done according to a centralised randomisation schedule prepared by a researcher who was not involved in patient recruitment or data collection. Patients and staff at all sites were masked to treatment allocation. All participants received best-evidence advice and were followed up for 3 months. The primary outcome was time until recovery from low-back pain, with recovery defined as a pain score of 0 or 1 (on a 0-10 pain scale) sustained for 7 consecutive days. All data were analysed by intention to treat. This study is registered with the Australian and New Zealand Clinical Trial Registry, number ACTN 12609000966291.

Findings

550 participants were assigned to the regular group (550 analysed), 549 were assigned to the as-needed group (546 analysed), and 553 were assigned to the placebo group (547 analysed). Median time to recovery was 17 days (95% CI 14-19) in the regular group, 17 days (15-20) in the as-needed group, and 16 days (14-20) in the placebo group (regular vs placebo hazard ratio 0·99, 95% CI 0·87-1·14; as-needed vs placebo 1·05, 0·92-1·19; regular vs as-needed 1·05, 0·92-1·20). We recorded no difference between treatment groups for

time to recovery (adjusted p=0·79). Adherence to regular tablets (median tablets consumed per participant per day of maximum 6; 4·0 [IQR 1·6-5·7] in the regular group, 3·9 [1·5-5·6] in the as-needed group, and 4·0 [1·5-5·7] in the placebo group), and number of participants reporting adverse events (99 [18·5%] in the regular group, 99 [18·7%] in the as-needed group, and 98 [18·5%] in the placebo group) were similar between groups.

Interpretation

Our findings suggest that regular or as-needed dosing with paracetamol does not affect recovery time compared with placebo in low-back pain, and question the universal endorsement of paracetamol in this patient group.

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ANALYSIS

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Background Information

Paracetamol (acetaminophen) is universally recommended as a first-line analgesic for low back pain (LBP), appearing in most clinical practice guidelines worldwide (1, 2). However, there is little to no direct evidence in support of this recommendation. In fact, a recent systematic review (3) found no evidence to support the use of paracetamol for LBP, as the trials eligible for this review were all methodologically flawed and only one trial included more than 25 participants per group. No trials have compared regular paracetamol with a placebo, or on an as-needed basis! To address these gaps in the literature, and in view of the uncertainties surrounding the use of paracetamol for LBP, the authors undertook the Paracetamol for Low-Back Pain (PACE) Study to investigate the efficacy of paracetamol taken regularly or as-needed to improve time to recovery from pain, compared with placebo for patients with acute LBP. PACE also sought to establish whether regular or as-needed paracetamol improved short-term pain (1–12 weeks), disability, function, global rating of symptom change, sleep, or quality of life compared with placebo.

PERTINENT RESULTS

Participants

Between November 2009 and December 2012, 4606 patients were screened for inclusion and 1652 were randomly assigned to one of the three treatment groups. Their average age was 45 years (standard deviation = 16) and 53% of participants were male. 550 patients were allocated to the regular paracetamol group, 546 to the as-needed group and 547 to the placebo group. The primary outcome could be determined for 97% of patients in each group.

Results:

- Treatment adherence was similar across all groups. All groups reported increased adherence in the first 2 weeks of the intervention. The "regular" group reported dosing equivalent to 3500 mg/day in week 1 and 2800 mg/day in week 2. The "as-needed" group reported a median of 1.9 tablets daily in week 1 (1000 mg/day) and 1.0 tablets daily overall (500 mg/day).
- By 12 weeks, 466 (85%) participants in the regular group, 452 (83%) in the as-needed group, and 461 (84%) in the placebo group had achieved sustained recovery, which was defined as the first day of 0 or 1 pain intensity, measured on a 0–10 pain scale, maintained for 7 consecutive days.
- Most patients (1042 of 1408; 74%) were satisfied with treatment. The use of rescue medications such as naproxen was low and similar in each study group. The use of other drugs or GP visits during the study period was likewise low and similar across study groups.
- Time to recovery did not significantly differ between groups (p = 0.55).

CLINICAL APPLICATION & CONCLUSIONS

Neither regular nor as-needed paracetamol (acetaminophen) improved recovery from acute low back pain as compared with placebo. Paracetamol also had no effect on pain, disability, function, global symptom change, sleep, or quality of life. Adverse events between treatment groups did not differ.

The results of this trial support those from similar trials that have shown no effect of paracetamol on low back pain, as well as a recent Cochrane review (4) that concluded that the effect of NSAIDs were equal to paracetamol (3 trials, n = 309) and only marginally better than that of placebo (4 trials, n = 745). Based on this evidence, clinicians should reconsider the general recommendation of utilizing paracetamol for low back pain.

The results of this trial are valuable for clinicians as they highlight that, while paracetamol does contribute to pain relief when used on a regular or as-needed basis, it does so as a temporary measure and does not contribute to long-term recovery. Practitioners should use this information to help educate patients regarding the value of using paracetamol for pain management only, while focusing on the rehabilitative treatments that have been shown to contribute to long-term LBP resolution.

EDITOR'S NOTE: I agree with Dr. Muir's closing statements – they represent the main take home messages from this paper. As you may know, this study received a lot of popular press and social media attention, with many claiming that paracetamol should now be considered 'useless' as an intervention for acute LBP. I would argue that paracetamol's role has never been to 'cure' acute LBP in an overt sense. Rather, it was proposed as a reasonable option for patients in clinical guidelines, along with other treatments including SMT, exercise, etc. Its role has, and could continue to be, providing temporary pain relief so acute LBP patients can 'get on with it' (so to speak), including getting back to regular exercise, into your office for manual therapy, and so on. NSAIDs and other over-the-counter pain medications can also fit this role – most patients have their preference!

STUDY METHODS

Study Design

PACE was a multicentre, double-dummy, randomized, placebo controlled trial. The study protocol (5) and analysis plan (6) were previously published. 235 primary care clinicians across Sydney, Australia

screened consecutive patients who sought care/advice for acute low back pain.

Participants

Inclusion Criteria:

- New episode of acute low-back pain (defined as pain between the 12th rib and buttock crease that was shorter than 6 weeks' duration and preceded by 1 month of no pain) with or without leg pain, and
- At least moderate-intensity pain (measured by an adaptation of item 7 of the Short Form-36 Health Survey).

Exclusion Criteria:

- Suspected serious spinal pathology (eg, spinal cancer, infection, fracture),
- Current use of full, regular recommended doses of an analgesic,
- Spinal surgery in the preceding 6 months,
- Contraindication to paracetamol,
- Use of psychotropic drugs for a disorder judged to prevent reliable recording of study information, or
- Pregnant or planning pregnancy.

Randomization and Masking

Concealed random allocation to one of the three treatment groups (regular paracetamol, as-needed paracetamol, or placebo) was done in a 1:1:1 ratio. Participants were provided with advice to remain active and avoid bed rest and were provided a sealed box of study medicines, unidentifiable as to study group.

Procedures

Each participant, regardless of group, received identical-looking study medicine boxes, each containing two separate "types" of medications. All participants were instructed to take two types of tablets for up to 4 weeks: two tablets from the "regular" box every 6–8 h (six tablets per day), and one or two tablets from the "as-needed" box when needed for pain relief (4–6 h apart, to a maximum of eight tablets per day). Participants in the "regular" group were given 665 mg modified-release paracetamol tablets in the "regular" box and placebo in the "as-needed" box. Participants in the "as-needed" group received placebo in the "regular" box and 500 mg paracetamol immediate-release tablets in the "as-needed" box. Participants in the placebo group received entirely placebo medication. Participants were asked to continue the study medicine until they recovered or for 4 weeks, whichever occurred first.

Outcome Measures & Follow-Up

Primary outcome was time until recovery from pain (in days). Secondary outcomes included: pain intensity, disability, function, global rating of symptom change, sleep quality, and quality of life. Measurements included: adherence to drug; concomitant treatment use and work absenteeism; treatment satisfaction and patient masking.

Statistical Analysis

All data were analysed by intention to treat. Effects of treatment on the primary outcome were estimated by a Cox proportional-hazard model, with adjustment made for baseline pain intensity because it is an important prognostic factor. Hazard ratios (HRs) and median survival times with 95% CIs were calculated for each group.

STUDY STRENGTHS / WEAKNESSES

Limitations

- Despite being instructed to do so, participants typically did not take the full recommended dose of paracetamol, and
- Some participants used other treatments during the intervention period, as opposed to the recommended rescue medication, despite advice to not take additional treatments.

Strengths

- The study methodology regarding blinding, randomization and control were sound, and
- The risk of bias was limited by several study features, including central randomization, allocation concealment, masking, very low attrition and previous publication of the statistical analysis plan.

Additional References

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