Mulling muscle relaxants

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A patient presenting with acute low back pain poses a treatment dilemma

CLINICAL SCENARIO

HARRY, a 55-year-old hospital cleaner, saw me with acute low back pain after lifting a heavy bag of linen. I recalled reading that skeletal muscle relaxants might be helpful in acute low back pain. Another of my patients had been prescribed orphenadrine citrate in the emergency department for the same indication. It's one of the few non-benzodiazepine muscle relaxants available in Australia. I wondered if this would be a good option for Harry. What is the evidence?

CLINICAL QUESTION

What is the effect of oral orphenadrine citrate on acute low back pain recovery?

What does the research evidence say?

Step 1: The Cochrane Library

A rather old Cochrane systematic review published in 2003 exists for the question of muscle relaxants for low back pain.[1] Although this review suggested that non-benzodiazepines may be effective, most of the included trials used other agents, and the few that used orphenadrine were decades old and problematic.

Step 2: TripDatabase

I conducted a search using the TripDatabase PICO search tool (Participant: "low back pain", Intervention: "orphenadrine", Comparator: "placebo", Outcomes: blank). The search identified a new key randomised trial from 2017 as the first hit.[2] This trial compared orphenadrine and another muscle relaxant (methocarbamol, which is not available in Australia). The study assessed the effect of the muscle relaxants given with an NSAID, compared with NSAID therapy alone. I did a quick search through PubMed, and this appeared to be the most appropriate piece of evidence to review.

Let's look at Friedman et al. (2017), published in the Annals of Emergency Medicine, in more detail.

CRITICAL APPRAISAL

I will use the randomised controlled trial appraisal sheet from the Centre for Evidence-Based Medicine.[3]

PICO

Participants: who was studied?

The study included 240 adults (aged between 18 and 69), recruited from two academic EDs in New York, US, presenting with acute low back pain. The patient was required to have received a diagnosis consistent with non-traumatic, non-radicular, musculoskeletal low back pain, and was to be discharged home.

Important exclusions: radicular pain below the gluteal folds, pain duration longer than two weeks, a baseline back pain frequency of at least once a month, direct trauma to the back within the previous month, pregnancy, breastfeeding, and use of any analgesic medication daily or near-daily.

The mean age of participants was 39, 55% were male, and the median duration of low back pain was two to three days.

Intervention: what was the exposure?

Orphenadrine group: naproxen 500mg/bd + orphenadrine 100mg/bd × 7 days.

Stat Facts

MINIMAL CLINICALLY IMPORTANT DIFFERENCE

THE minimal clinically important difference is a patient-centred concept that defines the "smallest amount an outcome must change to be meaningful to patients".[7]

When looking at study results, it is not enough that a difference between groups exist (statistically significant, or otherwise), but whether it is of sufficient magnitude to be important.

Methocarbamol group: naproxen 500mg/bd + methocarbamol 750mg 1-2 tabs/tds PRN × 7 days.

Comparator: what was the control/ alternative?
Placebo group 1: naproxen 500mg/bd + placebo 1 cap/bd.
Placebo group 2: naproxen 500mg/bd + placebo 1-2 cap/tds PRN.

Outcomes: what was measured?
Primary outcome: improvement in low back pain at one week, and three months after an ED visit, as measured by the Roland-Morris Disability Questionnaire (RMDQ). Note: this is a validated 24-item low back pain functional scale (0 = no low back pain-related functional impairment, and 24 = maximum impairment).

What were the results?
Primary outcome: the difference in low back pain-related impairment between the placebo group and orphenadrine group at one week was:

- 1.5 RMDQ points (95% confidence interval – 1.4 to 4.3) (result favouring placebo).
- Note: the "minimal clinically important difference" (see Stat Facts) for the RMDQ is estimated to be 4 or 5 points.[4]

DISCUSSION AND CONCLUSION

This was a well-conducted effectiveness trial undertaken in the American ED setting. It is likely informative, and probably externally valid in Australian general practice.

Although the aforementioned Cochrane systematic review identified that non-benzodiazepine skeletal muscle relaxants (and potentially oral orphenadrine) may have a beneficial effect for acute low back pain when used alone compared to placebo therapy, it was not at all certain how these agents compared to other known effective pharmacotherapy for acute low back pain.[1]

This study demonstrated no meaningful benefits to adding orphenadrine to naproxen. The point estimate is close to zero, and the extent of the 95% confidence interval most favouring benefit is still well within the minimal clinically significant difference for RMDQ scores. There was similarly no benefit from the other agent, methocarbamol.

Currently, acute low back pain guidelines recommend against the routine use of pharmacotherapy and, notably, the median time to recovery with no medicines is approximately 2.5 weeks.[5] When pharmacotherapy is used, NSAIDs might be reasonable, though side-effects need to be considered.[6]

For Harry, I provided reassurance that he will recover and recommended he try to maintain usual activities, to use heat packs, and to avoid bed rest. I did not recommend orphenadrine.

References on request

Internal Validity
Are the results valid?

Randomised patient assignment?
Yes. A research pharmacist performed the randomisation.
Groups similar at the start?
Yes. The groups were similar.[2]
Groups treated equally apart from assigned treatment?
Yes, but both clinician and patient would have been able to guess whether they were in the placebo vs orphenadrine, or placebo vs methocarbamol groups. It is reasonable to assume that this did not have an important effect on the outcome.
All patients accounted for?
Yes. Relatively few participants dropped out and the analysis was conducted on an intention-to-treat basis.
Measures objective? Or patients and clinicians kept blinded?
Yes. The authors undertook an assessment of blinding, and thus it seems that participants were successfully kept blinded.[2]