A Randomized, Double-Blind, Placebo-Controlled Trial of Naproxen With or Without Orphenadrine or Methocarbamol for Acute Low Back Pain

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Study objective: In US emergency departments (EDs), patients with low back pain are often treated with nonsteroidal anti-inflammatory drugs and muscle relaxants. We compare functional outcomes among patients randomized to a 1-week course of naproxen+placebo versus naproxen+orphenadrine or naproxen+methocarbamol.

Methods: This was a randomized, double-blind, comparative effectiveness trial conducted in 2 urban EDs. Patients presenting with acute, nontraumatic, nonradicular low back pain were enrolled. The primary outcome was improvement on the Roland-Morris Disability Questionnaire (RMDQ) between ED discharge and 1 week later. All patients were given 14 tablets of naproxen 500 mg, to be used twice a day, as needed for low back pain. Additionally, patients were randomized to receive a 1-week supply of orphenadrine 100 mg, to be used twice a day as needed, methocarbamol 750 mg, to be used as 1 or 2 tablets 3 times per day as needed, or placebo. All patients received a standardized 10-minute low back pain educational session before discharge.

Results: Two hundred forty patients were randomized. Baseline demographic characteristics were comparable. The mean RMDQ score of patients randomized to naproxen+placebo improved by 10.9 points (95% confidence interval [CI] 8.9 to 12.9). The mean RMDQ score of patients randomized to naproxen+orphenadrine improved by 9.4 points (95% CI 7.4 to 11.5). The mean RMDQ score of patients randomized to naproxen+methocarbamol improved by 8.1 points (95% CI 6.1 to 10.1). None of the between-group differences surpassed our threshold for clinical significance. Adverse events were reported by 17% (95% CI 10% to 28%) of placebo patients, 9% (95% CI 4% to 19%) of orphenadrine patients, and 19% (95% CI 11% to 29%) of methocarbamol patients.

Conclusion: Among ED patients with acute, nontraumatic, nonradicular low back pain, combining naproxen with either orphenadrine or methocarbamol did not improve functional outcomes compared with naproxen+placebo. [Ann Emerg Med. 2018;71:348-356.]

Please see page 349 for the Editor's Capsule Summary of this article.

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INTRODUCTION

Background

Low back pain causes 2.4% of visits to US emergency departments (EDs), resulting in 2.6 million visits annually.[1] In general, outcomes for these patients are unfavorable. One week after ED discharge, 70% of patients report persistent back-pain-related functional impairment and 69% report analgesic use within the previous 24 hours.[2] Among the subset of ED patients who present with acute, new-onset low back pain, outcomes are generally better; most will recover, although 10% to 20% of this group reports moderate or severe low back pain 3 months later and 30% report persistent low back pain–related functional impairment.[3,4]

Importance

It is not clear which medications should be prescribed for acute low back pain. Nonsteroidal anti-inflammatory drugs are more efficacious than placebo in regard to low back pain relief, global improvement, and requirement of analgesic medication[5] but are insufficient treatment for as many as half of all ED patients with low back pain, who continue to experience discomfort after ED discharge despite use of nonsteroidal anti-inflammatory drugs.

Editor's Capsule Summary

What is already known on this topic

Muscle relaxants are sometimes prescribed for acute low back pain.

What question this study addressed

When added to nonsteroidal anti-inflammatory drugs, do muscle relaxants improve functional outcomes for acute low back pain?

What this study adds to our knowledge

In this well-powered, 3-arm, controlled trial of 240 adults, outcomes were similar at 7 days regardless of whether patients received a nonsteroidal anti-inflammatory drug with placebo, orphenadrine, or methocarbamol.

How this is relevant to clinical practice

On average, supplementing nonsteroidal anti-inflammatory drugs with orphenadrine or methocarbamol does not improve functional outcomes in patients with acute low back pain.

Treatment of low back pain with multiple concurrent medications is common in the ED; emergency physicians often prescribe skeletal muscle relaxants or opioids in combination with nonsteroidal anti-inflammatory drugs.[1] However, combining oxycodone and acetaminophen, diazepam, or cyclobenzaprine (a skeletal muscle relaxant) with a nonsteroidal anti-inflammatory drug does not improve outcomes.[3] It remains uncertain whether adding other skeletal muscle relaxants to nonsteroidal anti-inflammatory drugs improves low back pain outcomes.

Two specific skeletal muscle relaxants, orphenadrine and methocarbamol, are used in more than 250,000 US ED visits for low back pain annually, although scant evidence exists to determine the appropriateness of this approach.[6] Orphenadrine is a centrally acting medication with prominent anticholinergic and antihistaminic properties. The mechanism of action is not understood. Efficacy in low back pain may be related to nonspecific analgesic properties. The mechanism of action of methocarbamol has also not been established. Its efficacy is thought to be related to central nervous system effects rather than direct effects on skeletal muscles.

Goals of This Investigation

Given the poor pain and functional outcomes that persist beyond an ED visit for acute low back pain, we conducted a clinical trial to determine whether combining either orphenadrine or methocarbamol with a nonsteroidal anti-inflammatory drug is more effective than nonsteroidal anti-inflammatory drug monotherapy for the treatment of acute, nontraumatic, nonradicular low back pain. We specifically evaluated the following 2 hypotheses: that the combination of naproxen+orphenadrine provides greater relief of low back pain than naproxen+placebo 1 week and 3 months after an ED visit, as measured by the Roland-Morris Disability Questionnaire (RMDQ); and that the combination of naproxen+methocarbamol provides greater relief of low back pain than naproxen+placebo 1 week and 3 months after an ED visit, as measured by the RMDQ.

MATERIALS AND METHODS

Study Design and Setting

This was a randomized, double-blind, comparative effectiveness study, in which we enrolled ED patients with musculoskeletal low back pain at discharge and followed them by telephone 7 days and 3 months later. Every patient received standard-of-care therapy, consisting of naproxen and a brief low back pain educational session. Patients were then randomized to orphenadrine, methocarbamol, or placebo. The Albert Einstein College of Medicine Institutional Review Board reviewed and approved this study. Written consent to participate was obtained for all study participants. Enrollment commenced in March 2016 and continued for 11 months. We report this trial in accordance with Consolidated Standards of Reporting Trials standards.

This study was performed in the 2 academic EDs of Montefiore Medical Center (Bronx, NY), with a combined annual census of 180,000 adult visits. Salaried, full-time, bilingual (English and Spanish), technician-level research associates staffed the EDs 18 to 24 hours per day, 7 days per week during the study period.

Selection of Participants

Our goal was to include a broad representation of patients with musculoskeletal back pain who would potentially respond to the investigational medications. The presence or absence of palpable spasm of the paraspinal muscles was not used as an entry criterion because the clinical significance and reliability of this finding are uncertain.[7] Patients were included if they were aged 18 years and no older than 69 years and presented to one of the participating EDs primarily for management of low back pain, defined as pain originating between the lower border of the scapulae and the upper gluteal folds. At the conclusion of the ED visit, the patient was required to have received a diagnosis consistent with nontraumatic, nonradicular, musculoskeletal low back pain