A Randomized, Placebo-Controlled Trial of Ibuprofen Plus Metaxalone, Tizanidine, or Baclofen for Acute Low Back Pain

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Study objective: Patients with low back pain are often treated with nonsteroidal anti-inflammatory drugs and skeletal muscle relaxants. We compare functional outcomes and pain among patients with acute low back pain who were randomized to a 1-week course of ibuprofen plus placebo versus ibuprofen plus 1 of 3 skeletal muscle relaxants: baclofen, metaxalone, and tizanidine.

Methods: This was a randomized, double-blind, parallel-group, 4-arm study conducted in 2 urban emergency departments (EDs). Patients with nonradicular low back pain for less than or equal to 2 weeks were eligible if they had a score greater than 5 on the Roland-Morris Disability Questionnaire, a 24-item inventory of functional impairment caused by low back pain. All participants received 21 tablets of ibuprofen 600 mg, to be taken 3 times a day as needed. Additionally, they were randomized to baclofen 10 mg, metaxalone 400 mg, tizanidine 2 mg, or placebo. Participants were instructed to take 1 or 2 of these capsules 3 times a day as needed. All participants received a 10-minute educational session. The primary outcome was improvement on the Roland-Morris Disability Questionnaire between ED discharge and 1week later. Secondary outcomes included pain intensity 1 week after ED discharge (severe, moderate, mild, or none).

Results: Three hundred twenty patients were randomized. One week later, the mean Roland-Morris Disability Questionnaire score of patients randomized to placebo improved by 11.1 points (95% confidence interval [CI] 9.0 to 13.3), baclofen by 10.6 points (95% CI 8.6 to 12.7), metaxalone by 10.1 points (95% CI 8.0 to 12.3), and tizanidine by 11.2 points (95% CI 9.2 to 13.2). At 1-week follow-up, 30% of placebo patients (95% CI 21% to 41%) reported moderate to severe low back pain versus 33% of baclofen patients (95% CI 24% to 44%), 37% of metaxalone patients (95% CI 27% to 48%), and 33% of tizanidine patients (95% CI 23% to 44%).

Conclusion: Adding baclofen, metaxalone, or tizanidine to ibuprofen does not appear to improve functioning or pain any more than placebo plus ibuprofen by 1 week after an ED visit for acute low back pain. [Ann Emerg Med. 2019;74:512-520.]

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INTRODUCTION

Background

Low back pain is exceedingly common, with a global point prevalence of 18%.[1] Nonsteroidal anti-inflammatory drugs (NSAIDs) are considered first-line pharmacologic treatment.[2,3] NSAIDs alone often provide inadequate analgesia for patients with symptoms with severity sufficient to warrant an emergency department (ED) visit because one third of these patients who receive NSAIDs alone report moderate or severe low back pain 1 week later.[4]

Importance

Skeletal muscle relaxants are commonly used to treat low back pain both in the ED[5] and in ambulatory practice,[6] often in combination with NSAIDs. Evidence supporting efficacy of skeletal muscle relaxants in this role is generally of lower quality.[2,7] Previous clinical trials similarly indicate that use of naproxen in combination with cyclobenzaprine,[8] orphenadrine,[9] methocarbamol,[9] or diazepam[10] does not improve low back pain outcomes among ED patients any more than naproxen alone. In this study, we sought to determine whether there is any benefit from combining 3 other commonly used skeletal muscle relaxants—baclofen, metaxalone, and tizanidine—with an NSAID.

Goals of This Investigation

In this randomized, 4-arm, clinical trial conducted among a population of ED patients with acute, functionally impairing,

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, 4-arm, controlled trial of 320 adults, outcomes were similar at 7 days whether patients supplemented ibuprofen with placebo, baclofen, metaxalone, or tizanidine.

How this is relevant to clinical practice

Supplementing ibuprofen with baclofen, metaxalone, or tizanidine does not improve functional outcomes in patients with acute low back pain.

nonradicular low back pain, we wished to determine whether a daily regimen of ibuprofen plus baclofen, metaxalone, or tizanidine would provide greater relief of low back pain than ibuprofen plus placebo 1 week after an ED visit, as measured by improvement on the Roland-Morris Disability Questionnaire, a 24-item inventory of functional impairment caused by low back pain, which is commonly used in low back pain clinical research.[11]

MATERIALS AND METHODS

Study Design and Setting

This was a randomized, double-blind, parallel-group, comparative-effectiveness study, in which we enrolled patients during an ED visit for musculoskeletal low back pain and then followed up by telephone 2 and 7 days later. Every patient received standard-of-care therapy, consisting of ibuprofen and a low back pain education session. Patients were randomized to placebo, baclofen, metaxalone, or tizanidine. The Albert Einstein College of Medicine institutional review board reviewed and approved the protocol and provided continuing oversight. All participants provided written informed consent. This trial is reported in accordance with Consolidated Standards of Reporting Trials guidelines.

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 both EDs 24 hours per day, 7 days per week during the study period.

Selection of Participants

We enrolled adults aged 18 to 64 years who presented to one of our EDs primarily for management of acute, nonradicular, nontraumatic, musculoskeletal low back pain, defined as pain originating between the lower border of the scapulae and the upper gluteal folds. Participants were required to have had low back pain for no longer than 2 weeks. If they had previous episodes of back pain, they could not have had them as frequently as once per month. Participation required functional impairment because of low back pain, which we defined as a baseline score of greater than 5 on the Roland-Morris Disability Questionnaire (http://www.rmdq.org).

Patients were excluded from participation if they were unavailable for follow-up; were pregnant or breastfeeding; were receiving medication for a chronic pain syndrome, which we defined as use of any analgesic medication daily or near daily; or had allergy to, intolerance of, or contraindication to any of the investigational medications.

Interventions

Patients were randomized in a 1:1:1:1 ratio to 1 of 4 medication regimens: the control arm received ibuprofen 600 mg plus placebo orally every 8 hours as needed; the baclofen arm received ibuprofen 600 mg plus baclofen 10 to 20 mg orally every 8 hours as needed; the metaxalone arm received ibuprofen 600 mg plus metaxalone 400 to 800 mg orally every 8 hours as needed; and the tizanidine arm received ibuprofen 600 mg plus tizanidine 2 to 4 mg orally every 8 hours as needed.

In an effort to maximize effectiveness while minimizing adverse effects, patients were instructed to take 1 ibuprofen plus 1 or 2 muscle relaxant capsules every 8 hours as needed. If one capsule of the muscle relaxant afforded sufficient relief, there was no need for the patient to take the second. However, if the participants did not experience sufficient relief within 60 minutes of taking one investigational medication capsule, they were instructed to take the second. All study participants were given a 7-day supply of ibuprofen and the muscle relaxant or placebo.

The pharmacist performed randomization in blocks of 8 based on a sequence generated at http://randomization.com. Ibuprofen was not masked. Metaxalone, tizanidine, baclofen, and placebo were masked by placing tablets into identical capsules, which were then packed with scant amounts of lactose and sealed. Research personnel presented participants with 2 bottles of medication

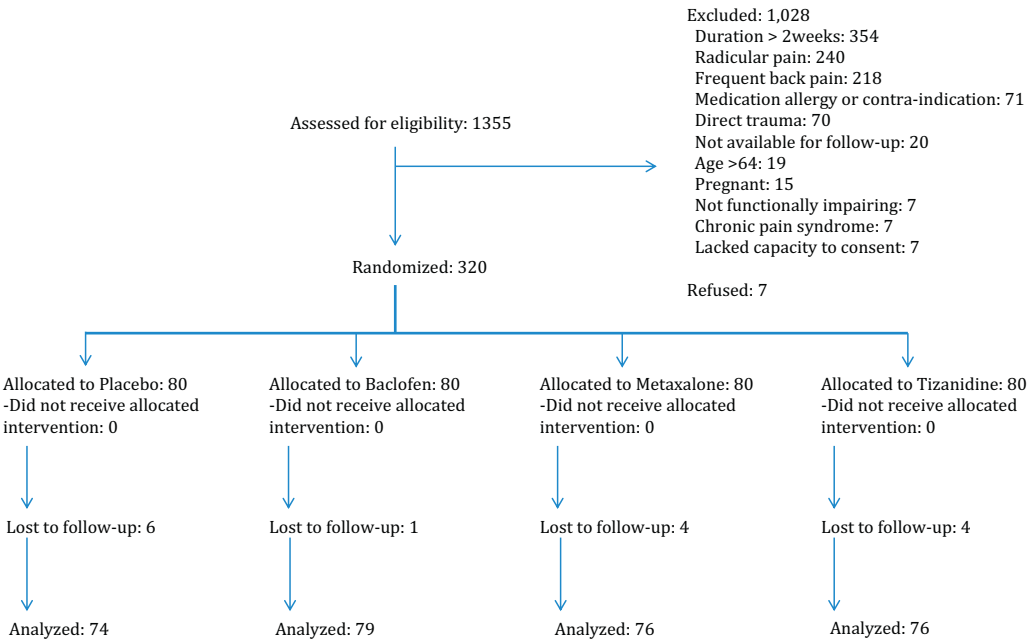

Figure 1. Consolidated Standards of Reporting Trials flow diagram.

capsules. The bottle containing the ibuprofen was labeled in a typical manner. The second bottle, containing the muscle relaxant or placebo, was labeled as investigational medication. Thus, the investigators, clinicians, participants, and research associates (outcome assesors) were blinded to treatment received. Patients were instructed to receive the medications only as needed for low back pain.

Research personnel provided each participant with a 10-minute educational intervention. This was based on the National Institute of Arthritis and Musculoskeletal and Skin Diseases Handout on Health: Back Pain information Web page (available at https://www.niams.nih.gov/health-topics/back-pain). Research personnel reviewed each section of the information sheet with the study participant and elicited questions.

Methods of Measurement

We used the Roland-Morris Disability Questionnaire, a validated 24-item low back pain functional scale recommended for use in low back pain research, to measure low back pain functional impairment[12] (http://www.rmdq.org). To measure pain, we used an ordinal pain scale on which participants described their pain as severe, moderate, mild, or none. To determine how often participants experienced low back pain after enrollment in the study, we asked them to describe their pain frequency by using the words "always," "usually," "sometimes," "rarely," or "not at all." At baseline, we recorded participants' age, sex, work status, Roland-Morris Disability Questionnaire score, the duration of the current episode of low back pain, frequency of previous episodes of low back pain, and presence of depression, using a 2-item screening instrument from the Patient Health Questionnaire depression module.[13]

Outcome Measures

The primary outcome for this study was improvement in Roland-Morris Disability Questionnaire score between the baseline ED visit and the 1-week follow-up (Roland-Morris Disability Questionnaire$_{baseline}$–Roland-Morris Disability Questionnaire$_{1week}$). Secondary outcomes included severity and frequency of pain at 48 hours and 1 week, requirement of medication for low back pain at each of these points, and an assessment of how long it took patients to return to work or usual activities. We also assessed adverse effects by asking, "Did you have any adverse effects from the medications you were taking?" and recording their dichotomous responses. We also determined, by asking participants, how often they visited any health care provider during the week after ED discharge.

Primary Data Analysis

We report baseline characteristics, including age, sex, work status, baseline Roland-Morris Disability Questionnaire score, duration and history of low back

Table 1. Baseline characteristics.

Variable	Ibuprofen + Placebo (n = 80)	Ibuprofen + Baclofen (n = 80)	Ibuprofen + Metaxalone (n = 80)	Ibuprofen + Tizanidine (n = 80)
Mean age (SD), y	39 (11)	39 (12)	37 (10)	40 (11)
Sex				
Men	44 (55)	57 (71)	44 (55)	42 (53)
Women	36 (45)	23 (29)	36 (45)	38 (48)
Work status				
Unemployed	6 (8)	10 (13)	5 (6)	6 (8)
Student	1 (1)	2 (3)	2 (3)	0
<30 h/wk	8 (10)	5 (6)	13 (16)	6 (8)
≥30 h/wk	65 (81)	63 (79)	60 (75)	68 (85)
Median RMDQ at ED visit (IQR)	20 (15–23)	20 (16–23)	18 (15–22)	19 (15–22)
Actual RMDQ score at ED visit				
<10	5 (6)	5 (6)	5 (6)	1 (1)
10–19	35 (44)	30 (38)	43 (54)	45 (56)
20–24	40 (50)	45 (56)	32 (40)	34 (43)
Median duration of low back pain before presentation to ED (IQR), h	72 (24–96)	72 (24–114)	48 (24–83)	48 (24–72)
Previous episodes of low back pain				
Never	15 (19)	15 (19)	22 (28)	21 (26)
A few	52 (65)	52 (65)	47 (59)	45 (56)
At least once/y	13 (16)	13 (16)	11 (14)	14 (18)
Depression screen result positive*	3 (4)	2 (3)	4 (5)	3 (4)

RMDQ, Roland-Morris Disability Questionnaire (a 24-item instrument measuring low back pain–related functional impairment; on this instrument, 0 represents no impairment and 24 represents maximum impairment).
Data are presented as No. (%) unless otherwise stated.
*Patients were asked 2 screening questions from the Patient Health Questionnaire: "Before your back pain began, how often were you bothered by little pleasure or interest in doing things?" and "Before your back pain began, how often were you bothered by feeling down, depressed, or hopeless?" Patients who responded to either question "more than half the days" or "nearly every day" were considered to screen positive for depression.

pain, and results of depression screen, as mean (SD), median (interquartile range), or percent, as appropriate. For the primary outcome, improvement in Roland-Morris Disability Questionnaire score between baseline and 1 week, we performed an intention-to-treat analysis among all patients for whom primary outcome data were available. We report these results as means with 95% confidence intervals (CIs). We considered between-group differences statistically significant if the 95% CI of the difference did not cross zero. Secondary outcomes are reported as rates.

We based the sample size calculation on a minimum clinically important difference of 5 units on the Roland-Morris Disability Questionnaire, a within-group SD of 8.9 estimated from an earlier study,[8] a standard α of .05, and a β of .20. Using these criteria, we determined the need for 50 subjects in each arm. To account for protocol violations, patients lost to follow-up, and nonadherence to the investigational medication regimen,[8,9] we enrolled 80 patients in each arm.

RESULTS

Enrollment commenced in May 2017 and concluded in July 2018. During these 15 months, 1,355 patients were screened for participation and 320 were enrolled (Figure 1). Baseline characteristics are reported in Table 1. In general, patients reported a substantial amount of baseline functional impairment; the median Roland-Morris Disability Questionnaire score among all participants at enrollment was 19 (interquartile range 15 to 23).

Overall, 1 week after ED discharge, participants reported a mean improvement in Roland-Morris Disability Questionnaire score of 10.8 (95% CI 9.8 to 11.8). There were no clinically important or statistically significant differences among the study

Table 2. One-week outcomes.

Outcome Variable	Ibuprofen + Placebo (n = 80)	Ibuprofen + Baclofen (n = 80)	Ibuprofen + Metaxalone (n = 80)	Ibuprofen + Tizanidine (n = 80)
Mean improvement in RMDQ score* between baseline and 1 wk (95% CI)	11.1 (9.0–13.3)	10.6 (8.6–12.7)†	10.1 (8.0–12.3)‡	11.2 (9.2–13.2)§
Missing	6	1	4	4
Median absolute RMDQ score (IQR)	3 (0–15)	6 (0–16)	5 (0–16)	3 (0–15)
Missing	6	1	4	4
Worst low back pain during previous 24 h, No. (%)				
Mild/none	51 (70)	53 (67)	48 (63)	51 (67)
Moderate/severe	22 (30)	26 (33)	28 (37)	25 (33)
Missing	7	1	4	4
Frequency of low back pain during previous 24 h, No. (%)				
Never/rarely	39 (53)	38 (48)	33 (43)	45 (59)
Sometimes	22 (30)	20 (25)	19 (25)	13 (17)
Frequently/always	12 (16)	21 (27)	24 (32)	18 (24)
Missing	7	1	4	4
Use of medication for low back pain during the 24 h before 1-wk follow-up, No. (%)				
No medications	27 (37)	30 (38)	27 (36)	28 (37)
Used medications	46 (63)	49 (62)	49 (64)	48 (63)
Missing	7	1	4	4
Median days until usual activities (IQR)	2 (2–7)	4 (2–>7)‖	3 (2–7)	3 (2–7)
Missing	7	1	4	4

*The RMDQ is a 24-item instrument measuring low back pain–related functional impairment. On this instrument, 0 represents no impairment and 24 represents maximum impairment.
†The 95% CI for the 0.5 difference between the ibuprofen+placebo arm and the ibuprofen+baclofen arm was −2.4 to 3.4.
‡The 95% CI for the 1.0 difference between the ibuprofen+placebo arm and the ibuprofen+metaxalone arm was −2.0 to 4.0.
§The 95% CI for the 0.1 difference between the ibuprofen+placebo arm and the ibuprofen+tizanidine arm was −2.8 to 3.0.
‖Greater than 25% of patients had not yet returned to usual activities before the 7-day follow-up.

arms (Table 2 and Figure 2). Any functional impairment (Roland-Morris Disability Questionnaire score >0) was reported by 189 of 305 participants (62%; 95% CI 56% to 67%), whereas 141 of 305 (46%; 95% CI 41% to 52%) reported substantial functional impairment (Roland-Morris Disability Questionnaire score >5). Secondary outcomes 1 week (Table 2) and 48 hours (Table 3) after ED discharge did not reveal clinically important differences among the study arms. Overall, 166 of 312 participants (53%; 95% CI 48% to 59%) reported moderate or severe pain at 48 hours and 101 of 304 (33%; 95% CI 28% to 39%) reported moderate or severe pain at 1 week. Use of medication for low back pain was reported by 285 of 312 participants (91%; 95% CI 88% to 94%) at 48 hours and 192 of 304 (63%; 95% CI 58% to 68%) at 1 week.

Use of additional health care resources during the week after ED discharge was uncommon and comparable among the study arms (Table 4). Overall, 33 of 304 participants (11%; 95% CI 8% to 15%) visited any health care provider, of whom the majority were primary care providers.

Adverse effects were reported by 24 of 283 participants (8%; 95% CI 6% to 12%) (Table 5). These did not differ among the study arms. None were serious.

We conducted a sensitivity analysis to determine the effect of missing data on the primary outcome. In this analysis, we assumed no improvement in the Roland-Morris Disability Questionnaire score in the placebo arm and a median improvement (11 Roland-Morris Disability Questionnaire points) in each of the active arms. This had no meaningful influence on the primary outcome; the between-group difference

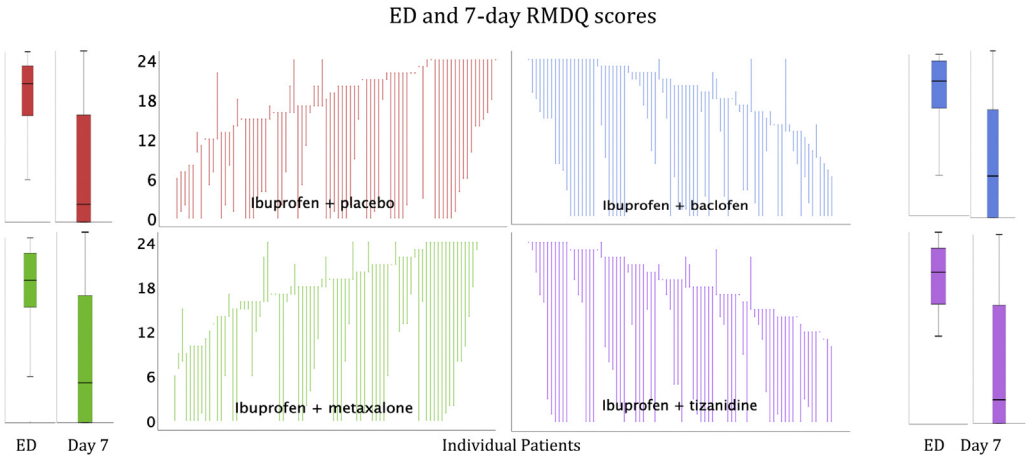

Figure 2. Baseline and 7-day Roland-Morris Disability Questionnaire scores. The *y* axis indicates the RMDQ scores of 0 to 24; higher scores indicate worse functional outcomes. Median and interquartile range of ED (baseline) and 7-day (follow-up) RMDQ data are depicted in the box and whisker plots. In these graphs, the median is represented by a horizontal line, the IQR by the box, and the complete range of data by the whiskers. The high-low graphs depict the baseline and 7-day RMDQ score for every individual. These data are sorted by baseline RMDQ score, so upward spikes represent patients who worsened.

in improvement in Roland-Morris Disability Questionnaire score was less than 1.0 among all groups.

Data on frequency of use of the study medications are presented in Tables E1 and E2, available online at http://www.annemergmed.com.

Table 3. Forty-eight–hour outcomes.

Outcome Variable	Ibuprofen+Placebo (n=80)	Ibuprofen+Baclofen (n=80)	Ibuprofen+Metaxalone (n=80)	Ibuprofen+Tizanidine (n=80)
Worst low back pain during previous 24 h, No. (%)				
Mild/none	29 (38)	41 (52)*	35 (45)†	41 (53)‡
Moderate/severe	48 (62)	38 (48)	43 (55)	37 (47)
Missing	3	1	2	2
Frequency of low back pain during previous 24 h, No. (%)				
Never/rarely	16 (21)	22 (28)	19 (24)	19 (24)
Sometimes	32 (42)	27 (34)	31 (40)	35 (45)
Frequently/always	29 (38)	30 (38)	28 (36)	24 (31)
Missing	3	1	2	2
Use of medication for low back pain during the 24 h before 48-h follow-up, No. (%)				
No medications	5 (6)	7 (9)	7 (9)	8 (10)
Used medications	72 (94)	72 (91)	71 (91)	70 (90)
Missing	3	1	2	2
Resumed work or usual activities, No. (%)				
Yes	36 (47)	40 (51)	32 (41)	36 (46)
No	41 (53)	39 (49)	46 (59)	42 (54)
Missing	3	1	2	2

*The 95% CI for the 14% difference between the ibuprofen+placebo arm and the ibuprofen+baclofen arm was −1% to 30%.
†The 95% CI for the 7% difference between the ibuprofen+placebo arm and the ibuprofen+metaxalone arm was −8% to 23%.
‡The 95% CI for the 15% difference between the ibuprofen+placebo arm and the ibuprofen+tizanidine arm was −1% to 30%.

Table 4. Use of additional health care resources.

Outcome Variable	Ibuprofen + Placebo (n = 80)	Ibuprofen + Baclofen (n = 80)	Ibuprofen + Metaxalone (n = 80)	Ibuprofen + Tizanidine (n = 80)
Visited any health care provider after ED visit, No. (%)	12 (16)	7 (9)*	5 (7)†	9 (12)‡
Subsequent ED visit	2	2	1	3
Primary care	8	1	3	4
MD specialist§	1	2	1	2
Physical therapy	0	1	0	0
Complementary therapy‖	1	0	0	0
Missing	7	1	4	4

*The 95% CI for the 8% rounded difference between the ibuprofen+placebo arm and the ibuprofen+baclofen arm was −3% to 18%.
†The 95% CI for the 10% rounded difference between the ibuprofen+placebo arm and the ibuprofen+metaxalone arm was 0% to 20%.
‡The 95% CI for the 5% rounded difference between the ibuprofen+placebo arm and the ibuprofen+tizanidine arm was −7% to 16%.
§Spine surgeon, pain management.
‖Massage.

LIMITATIONS

Our study had several limitations. First, the doses of medication we used in this study were not based on previous dose-finding studies, which we could not find in the published literature. We hoped to overcome this limitation by using a patient-centered self-titration mechanism, in which patients who required more medication could receive a second pill. Still, it is possible that we underdosed some or all of the investigational medications. Second, this study was conducted in 2 urban EDs. It is unclear whether these results can be generalized to other clinical arenas. It is possible that low back pain outcomes are associated with access to care.

DISCUSSION

In this ED-based, randomized, double-blind, comparative-effectiveness study, combining each of 3 commonly used muscle relaxants with ibuprofen did not improve 1-week functional outcomes more than ibuprofen plus placebo among ED patients with acute, functionally impairing low back pain. Although most of these patients with nonradicular low back pain enjoyed good pain and functional outcomes by 1 week after the ED visit, approximately one third reported moderate or severe pain, one quarter reported frequent low back pain, and nearly half reported substantial functional impairment. Among this ED cohort, only 11% accessed the health care system during the week after the ED visit.

When considered as a class, monotherapy with skeletal muscle relaxants has generally outperformed placebo in regard to short-term pain relief among patients with acute low back pain.[14] However, although baclofen, metaxalone, and tizanidine are frequently used for back pain, there is not a robust literature supporting efficacy for these patients. We identified only one such study of baclofen: in a randomized, placebo-controlled study of baclofen for acute low back pain, 200 patients were randomized to monotherapy with baclofen 80 mg/day or to placebo.[15] Although outcomes at 4 and 10 days favored baclofen, these were of marginal clinical importance. We identified 2 identically designed, randomized, placebo-controlled

Table 5. Adverse effects.

Adverse Event	Ibuprofen + Placebo (n = 80)	Ibuprofen + Baclofen (n = 80)	Ibuprofen + Metaxalone (n = 80)	Ibuprofen + Tizanidine (n = 80)
Any, No. (%)				
No	62 (93)	66 (90)	64 (91)	67 (92)
Yes	5 (7)	7 (10)	6 (9)	6 (8)
Missing	13	7	10	7

Adverse effects reported by patients in the ibuprofen+placebo group were drowsiness (2), headache, nausea, diarrhea, and urinary complaint. Adverse effects reported by patients in the ibuprofen+baclofen group were dizziness (2), drowsiness (4), nausea (3), headache, diplopia, and muscle spasm (2). Adverse effects reported by patients in the ibuprofen+metaxalone group were constipation, drowsiness (2), dry mouth, abdominal pain, dizziness, and vaginal bleeding. Adverse effects reported by patients in the ibuprofen+tizanidine group were anxiety, dry mouth, dizziness (2), and drowsiness (3).

studies of metaxalone 3,200 mg/day among patients with acute or acute exacerbations of chronic low back pain. These demonstrated substantial benefit, with effects sizes of nearly 50% in regard to symptomatic improvement.[16] Each of these studies enrolled 100 patients. Randomized studies of tizanidine versus placebo or combinations of tizanidine plus NSAIDs versus NSAIDs alone did not consistently demonstrate that use of tizanidine resulted in tangible benefits for patients with acute low back pain (Table E3, available online at http://www.annemergmed.com).[17-21]

The results of this study are similar to those of other studies of ED patients with acute, nonradicular low back pain: adding skeletal muscle relaxants,[8,9] diazepam,[10] or opioids[8] to NSAIDs does not improve short- or long-term functional or pain outcomes. Despite standard-of-care treatment, a large subset of these patients continue to experience moderate or severe pain and functional impairment by 1 week after the ED visit.[4] It is becoming increasingly apparent that currently available medication is an inadequate remedy for patients with acute, functionally impairing low back pain. It is still uncertain whether nonmedical therapies such as spinal manipulation, physical therapy, massage, or stretching help patients with acute low back pain treated concurrently with NSAIDs.[22,23]

In conclusion, compared with ibuprofen plus placebo, adding baclofen, metaxalone, or tizanidine to ibuprofen does not improve functioning or pain by 1 week after an ED visit for acute low back pain.

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Author contributions: BWF and EJG conceived the study. BWF, CS, EZ, and EJG designed the trial. BWF, EI, SP, AW, MPJ, and PDS collected data and supervised conduct of the trial. BWF analyzed the data. BWF and EI drafted the manuscript and all authors contributed substantially to its revision. BWF takes responsibility for the paper as a whole.

All authors attest to meeting the four ICMJE.org authorship criteria: (1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND (2) Drafting the work or revising it critically for important intellectual content; AND (3) Final approval of the version to be published; AND (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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REFERENCES

1. Hoy D, Bain C, Williams G, et al. A systematic review of the global prevalence of low back pain. *Arthritis Rheum*. 2012;64:2028-2037.
2. Chou R, Deyo R, Friedly J, et al. Systemic pharmacologic therapies for low back pain: a systematic review for an American College of Physicians clinical practice guideline. *Ann Intern Med*. 2017;166:480-492.
3. Qaseem A, Wilt TJ, McLean RM, et al; Clinical Guidelines Committee of the American College of Physicians. Noninvasive treatments for acute, subacute, and chronic low back pain: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2017;166:514-530.
4. Friedman BW, Conway J, Campbell C, et al. Pain one week after an emergency department visit for acute low back pain is associated with poor three-month outcomes. *Acad Emerg Med*. 2018;25:1138-1145.
5. Friedman BW, Chilstrom M, Bijur PE, et al. Diagnostic testing and treatment of low back pain in United States emergency departments: a national perspective. *Spine*. 2010;35:E1406-E1411.
6. Luo X, Pietrobon R, Curtis LH, et al. Prescription of nonsteroidal anti-inflammatory drugs and muscle relaxants for back pain in the United States. *Spine (Phila Pa 1976)*. 2004;29:E531-E537.
7. Roelofs PD, Deyo RA, Koes BW, et al. Nonsteroidal anti-inflammatory drugs for low back pain: an updated Cochrane review. *Spine (Phila Pa 1976)*. 2008;33:1766-1774.
8. Friedman BW, Dym AA, Davitt M, et al. Naproxen with cyclobenzaprine, oxycodone/acetaminophen, or placebo for treating acute low back pain: a randomized clinical trial. *JAMA*. 2015;314:1572-1580.
9. Friedman BW, Cisewski D, Irizarry E, et al. A randomized, double-blind, placebo-controlled trial of naproxen with or without orphenadrine or methocarbamol for acute low back pain. *Ann Emerg Med*. 2018;71:348-356.e5.
10. Friedman BW, Irizarry E, Solorzano C, et al. Diazepam is no better than placebo when added to naproxen for acute low back pain. *Ann Emerg Med*. 2017;70:169-176.
11. Roland M, Fairbank J. The Roland-Morris Disability Questionnaire and the Oswestry Disability Questionnaire. *Spine*. 2000;25:3115-3124.
12. Deyo RA, Battie M, Beurskens AJ, et al. Outcome measures for low back pain research. A proposal for standardized use. *Spine*. 1998;23:2003-2013.
13. Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire–2: validity of a two-item depression screener. *Med Care*. 2003;41:1284-1292.
14. van Tulder MW, Touray T, Furlan AD, et al. Cochrane Back Review Group. Muscle relaxants for nonspecific low back pain: a systematic review within the framework of the Cochrane Collaboration. *Spine (Phila Pa 1976)*. 2003;28:1978-1992.

15. Dapas F, Hartman SF, Martinez L, et al. Baclofen for the treatment of acute low-back syndrome. A double-blind comparison with placebo. *Spine (Phila Pa 1976)*. 1985;10:345-349.
16. Fathie K. A second look at a skeletal muscle relaxant: a double-blind study of metaxalone. *Curr Ther Res Clin Exp*. 1964;6:677-683.
17. Ketenci A, Ozcan E, Karamursel S. Assessment of efficacy and psychomotor performances of thiocolchicoside and tizanidine in patients with acute low back pain. *Int J Clin Pract*. 2005;59:764-770.
18. Berry H, Hutchinson DR. A multicentre placebo-controlled study in general practice to evaluate the efficacy and safety of tizanidine in acute low-back pain. *J Int Med Res*. 1988;16:75-82.
19. Berry H, Hutchinson DR. Tizanidine and ibuprofen in acute low-back pain: results of a double-blind multicentre study in general practice. *J Int Med Res*. 1988;16:83-91.
20. Pareek A, Chandurkar N, Chandanwale AS, et al. Aceclofenac-tizanidine in the treatment of acute low back pain: a double-blind, double-dummy, randomized, multicentric, comparative study against aceclofenac alone. *Eur Spine J*. 2009;18:1836-1842.
21. Lepisto P. A comparative trial of DS 103-282 and placebo in the treatment of acute skeletal muscle spasms due to disorders of the back. *Curr Ther Res*. 1979;26:454-459.
22. Chou R, Deyo R, Friedly J, et al. Nonpharmacologic therapies for low back pain: a systematic review for an American College of Physicians clinical practice guideline. *Ann Intern Med*. 2017;166:493-505.
23. Rothberg S, Friedman BW. Complementary therapies in addition to medication for patients with nonchronic, nonradicular low back pain: a systematic review. *Am J Emerg Med*. 2017;35:55-61.

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DIAGNOSIS:

Rectovesical fistula. The most common causes of rectovesical fistula are malignancy and inflammatory conditions such as diverticulitis and Crohn's disease. Fistulas may also be caused by trauma, surgery, bladder stones, or pelvic radiation.[1] Gouverneur's syndrome, the constellation of tenesmus, urinary frequency, dysuria, and suprapubic pain, should suggest the diagnosis.[2] Most patients present with recurrent urinary tract infections and pneumaturia or fecaluria.[3] Passage of urine per rectum occurs in 15% of cases.[3] Detection of charcoal or poppy seeds in the urine after an oral challenge can confirm the diagnosis.[3]

The imaging modality of choice is CT scan of the abdomen and pelvis with intravenous contrast, with sensitivity of 60% to 100%.[3] Cystoscopy and colonoscopy are less sensitive but may demonstrate the cause of the fistula.[3] Most patients require surgical repair, although a trial of conservative management with Foley decompression of the bladder may be attempted.[3]

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REFERENCES

1. Golabek T, Szymanska A, Szopinski T, et al. Enterovesical fistulae: aetiology, imaging, and management. *Gastroenterol Res Pract*. 2013;2013:617967.
2. Chebli JMF, Figueriredo AA, Gaburri PD. Gouverneur's syndrome in a patient with abdominal pain: mind Crohn's disease! *Rev Assoc Med Bras*. 2014;60:196-197.
3. Scozzari G, Arezzo A, Morino M. Enterovesical fistulas: diagnosis and management. *Tech Coloproctol*. 2010;14:293-300.