Diazepam Is No Better Than Placebo When Added to Naproxen for Acute Low Back Pain

Benjamin W. Friedman, MD, MS*; Eddie Irizarry, MD; Clemencia Solorzano, PharmD; Nauman Khankel, MD; Jennifer Zapata, DO; Eleftheria Zias, RPh; E. John Gallagher, MD

*Corresponding Author. E-mail: bwfriedmanmd@gmail.com, Twitter: @benjaminbwf.

Study objective: Low back pain causes more than 2.5 million visits to US emergency departments (EDs) annually. Low back pain patients are often treated with nonsteroidal anti-inflammatory drugs and benzodiazepines. The former is an evidence-based intervention, whereas the efficacy of the latter has not been established. We compare pain and functional outcomes 1 week and 3 months after ED discharge among patients randomized to a 1-week course of naproxen+diazepam versus naproxen+placebo.

Methods: This was a randomized, double-blind, comparative efficacy clinical trial conducted in an urban health care system. Patients presenting with acute, nontraumatic, nonradicular low back pain of no more than a duration of 2 weeks were eligible for enrollment immediately before discharge from an ED if they had a score greater than 5 on the Roland-Morris Disability Questionnaire, a validated 24-item inventory of functional impairment caused by low back pain. Higher scores on the questionnaire indicate greater functional disability. The primary outcome in the trial was improvement in the score between ED discharge and 1 week later. Secondary outcomes included pain intensity 1 week and 3 months after ED discharge, as measured on a 4-point descriptive scale (severe, moderate, mild, and none). All patients were given 20 tablets of naproxen 500 mg, to be taken twice a day as needed for low back pain. Additionally, patients were randomized to receive either 28 tablets of diazepam 5 mg or identical placebo, to be received as 1 or 2 tablets every 12 hours as needed for low back pain. All patients received a standardized 10-minute low back pain educational session before discharge. Using a between-group mean difference of 5 Roland-Morris Disability Questionnaire points, a previously validated threshold for clinical significance, we calculated the need for at least 100 patients with primary outcome data.

Results: Enrollment began in June 2015 and continued for 9 months. Five hundred forty-five patients were screened for eligibility. One hundred fourteen patients met selection criteria and were randomized. Baseline demographic characteristics were not substantially different between the 2 groups. One hundred twelve patients (98%) provided 1-week outcome data. The mean Roland-Morris Disability Questionnaire score of patients randomized to naproxen+diazepam improved by 11 (95% confidence interval [CI] 9 to 13), as did the mean score of patients randomized to naproxen+placebo (11; 95% CI 8 to 13). At 1-week follow-up, 18 of 57 diazepam patients (32%; 95% CI 21% to 45%) reported moderate or severe low back pain versus 12 of 55 placebo patients (22%; 95% CI 13% to 35%). At 3-month follow-up, 6 of 50 diazepam patients (12%; 95% CI 5% to 24%) reported moderate or severe low back pain versus 5 of 53 placebo patients (9%; 95% CI 4% to 21%). Adverse events were reported by 12 of 57 diazepam patients (21%; 95% CI 12% to 33%) and 8 of 55 placebo patients (15%; 95% CI 7% to 26%).

Conclusion: Among ED patients with acute, nontraumatic, nonradicular low back pain, naproxen+diazepam did not improve functional outcomes or pain compared with naproxen+placebo 1 week and 3 months after ED discharge. [Ann Emerg Med. 2017;70:169-176.]

Please see page 170 for the Editor's Capsule Summary of this article.

Readers: click on the link to go directly to a survey in which you can provide **feedback** to *Annals* on this particular article.
A **podcast** for this article is available at www.annemergmed.com.

0196-0644/$-see front matter

http://dx.doi.org/10.1016/j.annemergmed.2016.10.002

INTRODUCTION

Background

Low back pain is responsible for 2.4% of visits to US emergency departments (EDs), resulting in 2.7 million visits annually.[1] Pain outcomes for these patients are generally poor.[2] One week after an ED visit in an unselected low back pain population, 70% of patients report persistent back pain–related functional impairment and 69% report continued analgesic use.[2] Three months later, 48% reported functional impairment and 46% reported persistent analgesic use. Among the subset of ED patients who present with acute, new-onset low back pain, outcomes are generally better; most will recover, although more than 20% of this group will also report moderate or severe low back pain 3 months later and 30% will report low back pain–related functional impairment.[3]

Editor's Capsule Summary

What is already known on this topic

Benzodiazepines are often added to analgesic regimens for patients with acute lower back pain in the belief that sedation or relaxation will improve recovery.

What question this study addressed

Does oral diazepam improve outcomes when added to naproxen in emergency department patients with acute nontraumatic and nonradicular low back pain?

What this study adds to our knowledge

In a single-site, placebo-controlled, randomized trial with 114 subjects, diazepam did not improve 7-day or 3-month relief and did not alter adverse effects or subjective functioning.

How this is relevant to clinical practice

Diazepam should not be routinely added to nonsteroidal analgesics for these patients.

Importance

Nonsteroidal anti-inflammatory drugs are recommended as first-line therapy for patients with acute low back pain.[4] However, it is not clear whether the addition of other classes of therapeutic agents to nonsteroidal anti-inflammatory drugs can further improve low back pain outcomes. Benzodiazepines are often mentioned as useful for these patients and are used in 300,000 US ED visits for low back pain annually, although scant evidence exists to determine the appropriateness of this approach.[5,6] Efficacy of benzodiazepines, if any, may be related to direct or centrally mediated action on skeletal muscle or may work entirely or in part by mitigating patient anxiety about the condition.[7]

Goals of This Investigation

Because of the poor pain and functional outcomes that persist beyond an ED visit for musculoskeletal low back pain, we conducted a double-blind, randomized, clinical trial to evaluate whether combining a benzodiazepine with a nonsteroidal anti-inflammatory drug is more efficacious than nonsteroidal anti-inflammatory drug monotherapy for the treatment of acute, nontraumatic, nonradicular low back pain. Specifically, we wished to evaluate the following hypothesis: A daily regimen of naproxen+diazepam would provide greater relief of functional impairment caused by low back pain than naproxen+placebo, as measured by improvement in the Roland Morris Disability Questionnaire score 1 week after an ED visit.

MATERIALS AND METHODS

Study Design and Setting

This was a randomized, double-blind, ED-based, comparative efficacy study conducted in 2 EDs of an urban health care system. We enrolled patients during an ED visit for acute musculoskeletal low back pain and followed them by telephone 7 days and 3 months later. Every patient received standard-of-care therapy, consisting of naproxen and a low back pain education session, in addition to either diazepam or placebo. The Albert Einstein College of Medicine Institutional Review Board reviewed and approved this study. We obtained written consent from all participants. Enrollment commenced in June 2015 and continued for 9 months.

We conducted this study in 2 EDs of Montefiore Medical Center, an urban teaching medical center, with 178,000 adult visits annually. Salaried, trained, fluently bilingual (English and Spanish) research associates staffed the EDs 24 hours per day, 7 days per week during the accrual period.

Selection of Participants

Our goal was to include a broad representation of patients with musculoskeletal back pain who were likely to respond to the investigational medications. We included adults aged 21 to 69 years who presented to the ED primarily for management of acute low back pain, defined as pain originating between the lower border of the scapulae and the upper gluteal folds. The primary clinical diagnosis at the conclusion of the ED visit was required to be one consistent with nontraumatic, nonradicular, musculoskeletal low back pain. We included only patients who were to be discharged home and those who had functionally impairing back pain, defined as a score of greater than 5 on the Roland-Morris Disability Questionnaire. The questionnaire is a validated 24-item tool commonly used to measure low back pain and related functional impairment, on which 0 represents no impairment and 24 represents maximum impairment (Appendix E1, available online at http://www.annemergmed.com).

We excluded patients from participation for radicular pain, defined as pain radiating below the gluteal folds in a dermatomal distribution, pain duration greater than 2 weeks (336 hours), or a baseline low back pain frequency of once per month or more frequently. We required the absence of nonmusculoskeletal cause of low back pain, such

as urinary tract infection or influenzalike illness. Patients with direct trauma to the back within the previous month were excluded, as were those who were unavailable for follow-up; those who were pregnant or breast-feeding; those with a chronic pain syndrome, defined as use of any analgesic medication daily or almost daily; and those who were allergic to or intolerant of the investigational medications. We did not exclude patients for use of a nonsteroidal anti-inflammatory drug before ED presentation. Finally, patients could be enrolled only once.

Interventions

The pharmacist performed randomization in blocks of 4 according to a random-number sequence generated at http://randomization.com. Patients were randomized in a 1:1 manner to one of 2 interventions: the benzodiazepine arm (naproxen 500-mg tablets received twice per day plus diazepam 5 mg taken as 1 or 2 tablets every 12 hours) or the control arm (naproxen 500-mg tablets taken twice per day plus placebo received as 1 or 2 tablets every 12 hours).

In an effort to maximize effectiveness while minimizing adverse effects, we instructed patients to take 1 or 2 pills of the investigational medication every 12 hours. If one tablet of the investigational medication afforded sufficient relief, then there was no need for the patient to take the second tablet. However, if the patient had not experienced sufficient relief within 30 minutes of taking 1 investigational medication tablet, they were instructed to take the second tablet. We gave all study patients 20 naproxen tablets, a 10-day supply, and 28 tablets of the investigational medication, enough to last 7 days if the patient took the maximum dose of 2 tablets every 12 hours.

The pharmacists masked diazepam and placebo by placing tablets into identical capsules, which were packed with scant amounts of lactose and sealed. They performed the masking within the pharmacies, secure locations inaccessible to ED personnel. We then presented patients with 2 containers of medication. The container with the naproxen, labeled in a typical manner, was not masked. The second container, holding diazepam or placebo, was labeled as investigational medication.

Before discharge, research personnel delivered verbally to each participant a 10-minute educational intervention, based on the National Institute of Arthritis and Musculoskeletal and Skin Diseases's 5-page "What is back pain?" information sheet from the National Library of Medicine's Fun Facts: An Easy-to-Read Series of Publications for the Public (available at http://www.niams.nih.gov/Health_Info/Back_Pain/back_pain_ff.asp). We informed each participant that carefully chosen exercises and stretches may help pain and prevent future occurrences and that hot or cold packs, physical therapy, massage therapy, and acupuncture may help some patients.

Outcome Measures

The primary outcome for this study was improvement on the Roland Morris Disability Questionnaire between ED discharge and the 7-day telephone follow-up. A 5-point improvement on this scale is generally considered a clinically significant one.[8] Secondary outcomes 1 week and 3 months after ED discharge were as follows: 1 week after ED discharge, we determined (1) participants' worst pain during the previous 24 hours, using a 4-item ordinal scale (severe, moderate, mild, or none, dichotomized as severe/moderate versus mild/none for analysis); (2) the frequency of low back pain during the previous 24 hours, using a 5-item scale (not at all, rarely, sometimes, usually, and always, trichotomized as not at all/rarely versus sometimes versus usually/always for analysis); (3) the frequency of any analgesic or low back pain medication use during the previous 24 hours (dichotomized as use versus no use); (4) satisfaction with treatment, as measured by response to the question, "The next time you have back pain, do you want to take the same medications you've been taking this past week?"; (5) the number of days it took after ED discharge for the participant to return to usual activities; and (6) the frequency of visits to any clinician during the follow-up period. We determined how frequently participants used naproxen and the investigational medication by asking them to categorize their use of each as more than once per day, once per day, sometimes, only once, or never. Three months after ED discharge, we determined participants' absolute Roland-Morris Disability Questionnaire score; their worst low back pain during the previous 72 hours, using the same ordinal scale as above; the frequency of low back pain during the previous 72 hours, using the same scale as above; and the frequency of use of any low back pain medication during the previous 72 hours, again dichotomized as use versus no use. Adverse events were ascertained by asking patients to report any symptoms from the medications. We specifically asked participants to describe whether the medications made them tired or dizzy or irritated their stomachs. For these latter 3 symptoms, participants were asked to use the descriptions "a lot," "a little," or "none." These measures have been used previously.[3] Research associates, who were blinded to study assignment, performed the follow-up telephone calls.

Primary Data Analysis

The primary analysis was intention to treat. All eligible participants with available outcome data were analyzed according to group assignment. The primary outcome was a comparison of the change in Roland-Morris Disability Questionnaire score between baseline and 1 week. These results are reported as means with 95% confidence interval (CI) and difference between the means of the 2 comparison groups with 95% CI. Dichotomous secondary outcomes are reported as proportions and difference between proportions with 95% CI.

We based our assumptions for the sample size calculation on a recently completed randomized controlled trial of low back pain treatment.[3] The mean improvement in Roland-Morris Disability Questionnaire score among patients who received naproxen alone was 10.2 (SD 8.9). A widely accepted minimum clinically important improvement of 5 points on the Roland-Morris Disability

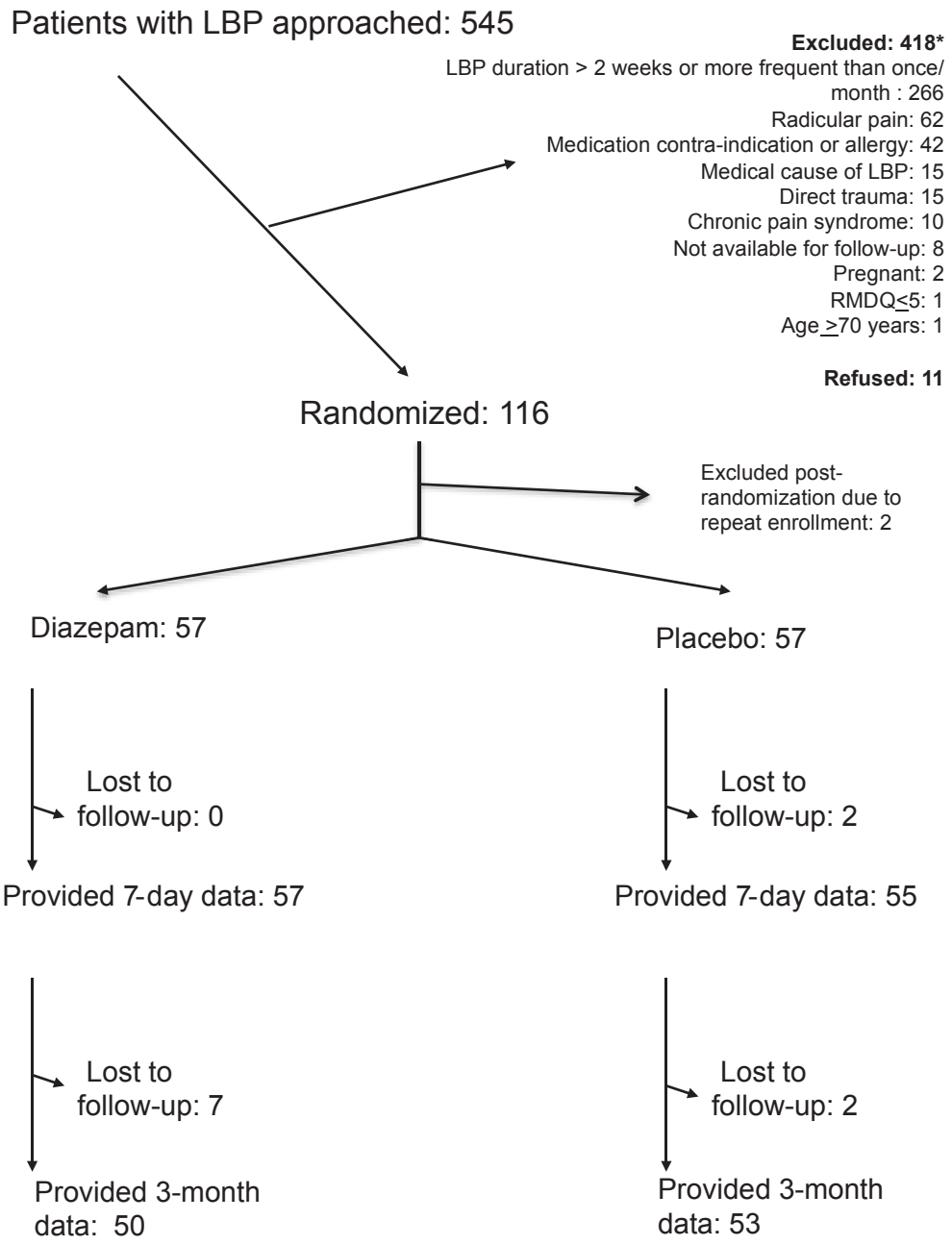

Figure. Consolidated Standards of Reporting Trials (CONSORT) flow diagram. *LBP*, Low back pain; *RMDQ*, Roland-Morris Disability Questionnaire (a 24-item instrument measuring LBP-related functional impairment). *Four patients were excluded for more than one reason.

Questionnaire[8] therefore would have required patients randomized to diazepam to demonstrate a mean improvement of 15.2 on the Roland Morris scale. We believed that if one group had a decrease in the Roland-Morris Disability Questionnaire score that was 5 points (or more) greater than that of the other group, this would be a clinically significant difference between the groups. Using a standard 2-tailed α of .05 and a β of .20, we determined the need for 50 subjects in each arm. To account for protocol violations and patients lost to follow-up, we planned to enroll 115% of our calculated sample size, or 16 additional patients.

RESULTS

Characteristics of Study Subjects

During the study period, we approached 545 patients with low back pain for participation and randomized 114 eligible patients (Figure). Baseline characteristics were comparable between the groups (Table 1 and Appendix E2 [available online at http://www.annemergmed.com]). The median initial Roland-Morris Disability Questionnaire score of 18 demonstrated substantial baseline functional impairment on presentation. Most patients had pain for no more than 2 or 3 days before presenting to the ED.

Table 1. Baseline characteristics.

Variable	Naproxen+ Diazepam, n=57	Naproxen+ Placebo, n=57
Age, mean (SD), y	34 (12)	38 (12)
Sex		
Men	30 (53)	33 (58)
Women	27 (47)	24 (42)
Work status		
Unemployed	11 (19)	3 (5)
Student	1 (2)	6 (11)
<30 h/wk	6 (11)	4 (7)
>30 h/wk	39 (68)	44 (77)
Median RMDQ at ED visit (IQR)	18 (16, 21)	18 (15, 20)
Median duration of LBP before presentation to ED (IQR), h	72 (24, 108)	48 (12, 96)
Previous episodes of LBP		
Never before	28 (50)	22 (39)
Few times before	25 (45)	29 (52)
At least once/year	3 (5)	5 (9)
Missing	1	1
Depression screen positive*	3/57 (5)	2/57 (4)

0 represents no LBP-related functional impairment and 24 represents maximum functional impairment).
Data are presented as No. (%) unless otherwise stated.
*Patients were asked 2 screening questions from the Patient Health Questionnaire: (1) Before your back pain began, how often were you bothered by little pleasure or interest in doing things? (2) 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. We discuss the presence or absence of spasm at baseline and discordance in work status in Appendix E2 (available online at http://www.annemergmed.com).

Main Results

One week after the ED visit, patients randomized to diazepam improved by a mean of 11 (95% CI 9 to 13) Roland-Morris Disability Questionnaire points, whereas placebo patients improved by 11 (95% CI 8 to 13) (95% CI for mean difference of 0.3: –2.8 to 3.5). The between-group difference achieved neither clinical nor statistical significance. Secondary outcomes were also comparable between the groups (Table 2 and Appendix E3 [available online at http://www.annemergmed.com]).

A majority of patients took naproxen at least once per day (Table 3). Use of the investigational medication

Table 2. One-week outcomes among study participants who completed 1-week follow-up.

Outcome Variable	Naproxen+ Diazepam, n=57	Naproxen+ Placebo, n=55	Difference Between Diazepam and Placebo to % (95% CI)
Worst LBP during previous 24 h			
Mild/none	39 (68)	43 (78)	–10 (–26 to 7)
Moderate/severe	18 (32)	12 (22)	
Frequency of LBP during previous 24 h			
Never/rarely	28 (49)	30 (56)	–6 (–25 to 12)*
Sometimes	16 (28)	11 (20)	
Frequently/always	13 (23)	13 (24)	
Missing		1	
Use of medication for LBP during the 24 h before 1-wk follow-up			
None	31 (54)	30 (55)	0 (–19 to 18)
Medication taken	26 (46)	25 (46)	
Desires same medications during subsequent episode of LBP†			
Yes	44 (77)	37 (70)	7 (–9 to 24)‡
No	9 (16)	12 (23)	
Not sure	4 (7)	4 (8)	
Missing		2	
Median number of days until able to return to usual activities (IQR)§	4 (2, >7)	5 (2, >7)	–0.4 (–0.6, 1.4)‖

Data are presented as No. (%) unless otherwise stated. Data in the fourth column have been rounded to the nearest integer. We detail use of off-protocol medication in Appendix E3 (available online at http://www.annemergmed.com).
*Never/rarely versus sometimes/frequently/always.
†Participants were asked, "The next time you have back pain, do you want to take the same medications you've been taking this past week?"
‡Yes versus no/not sure.
§Patients who had not yet recovered at the 1-week telephone call were categorized as greater than 7 days.
‖Difference in mean number of days.

Table 3. Use of investigational medication and health care resources within 1 week of ED discharge.

Outcome	Naproxen+ Diazepam, No. (%), N=57	Naproxen+ Placebo, No. (%), N=55
Frequency of naproxen use		
More than once/day	45 (79)	34 (63)
Once/day	6 (11)	13 (24)
Sometimes	1 (2)	2 (4)
Only once	5 (9)	3 (6)
Never	0	2 (4)
Missing	0	1
Frequency of placebo/diazepam use		
More than once/day	21 (38)	21 (38)
Once/day	18 (32)	16 (29)
Sometimes	9 (16)	5 (9)
Only once	6 (11)	5 (9)
Never	2 (4)	8 (15)
Missing	1	0
Health care resources used		
No visit to any clinician	49 (88)	40 (77)
Subsequent ED visit	3 (5)	2 (4)
Primary care	1 (2)	6 (12)
MD specialist*	1 (2)	1 (2)
Complementary therapy†	2 (4)	3 (6)
Missing	1	3

*Orthopedics.
†Physical therapy, chiropractor.

(diazepam or placebo) among the study cohort was less common. Most of our patients did not visit another health care provider within 1 week of ED discharge (Table 3).

Adverse events were relatively infrequent and comparable between the groups (Table 4). Other than the symptoms reported in Table 4, no more than 1 participant reported any other adverse event. There were no serious or unexpected adverse events.

By 3 months after the ED visit, most patients had recovered completely (Table 5). Similar to the findings at 1-week follow-up, differences in 3-month pain or functional outcomes between groups were neither clinically nor statistically significant.

Table 4. Adverse medication effects.

Adverse Event	Naproxen+ Diazepam, n/N (%)	Naproxen+ Placebo, n/N (%)	Difference Between Diazepam and Placebo, % (95% CI)
Any adverse event	12/57 (21)	8/52 (15)	6 (−9 to 20)
Tired (a lot)*	4/56 (7)	1/52 (2)	5 (−2 to 13)
Dizzy (a lot)*	1/56 (2)	0/51	2 (−2 to 5)
Stomach irritation (a lot)*	1/57 (2)	1/52 (2)	0 (−5 to 5)

*At the 7-day follow-up, we asked study participants specifically whether they experienced dizziness, feeling tired, and stomach irritation. They were asked to choose among the following options: "no," "a little," and "a lot."

LIMITATIONS

The first limitation is that in the interest of maintaining homogeneity for this study, we screened but did not include many patients because they did not meet our strict entry criteria. Thus, the study participants represent only a subset of patients who present to the ED with acute nontraumatic, nonradicular low back pain. These results therefore cannot be generalized to patients with other types of back pain, nor do they extend to those with chronic low back pain.

A second limitation is that we conducted this study in 1 urban health care system serving a socioeconomically depressed population. Because back pain outcomes may be associated with socioeconomic variables, our results can be generalized most appropriately to EDs that serve similar disadvantaged patient populations.

A third limitation is that we tested the combination of diazepam with naproxen, not diazepam alone. Thus, we do not know how diazepam would have fared by itself.

A fourth limitation is that we did not insist that patients receive these medications on a standing schedule but instead allowed them to receive the medications as needed. Therefore, it is possible that the true efficacy of diazepam was missed because of insufficient dosing. However, our study more closely mirrors the clinical reality of emergency practice.

Finally, we did not use presence or absence of muscle spasm on clinical examination as an entry criterion because the clinical significance of this finding is uncertain.[9] Furthermore, it cannot be assessed pragmatically in a reliable and accurate manner. It is plausible that patients with true muscular spasm would have fared better with the active medication.

DISCUSSION

Diazepam is currently used in approximately 300,000 visits for low back pain to US EDs annually.[1] Given its frequent usage, there is a surprising paucity of evidence in regard to its efficacy. We identified 4 studies in which diazepam was compared with placebo for low back pain and 1 in which it was compared with aspirin. Brotz et al[10] prescribed physiotherapy and diclofenac to 60 patients hospitalized with lumbar disc prolapse and then randomized the patients into placebo and diazepam study arms. When compared with the diazepam group, the placebo group was found to have a shorter hospital stay and a higher probability of greater than 50% reduction in pain by day 7. However, there were no differences

Table 5. Three-month outcomes.

Outcome Variable	Naproxen+ Diazepam (%), n=50	Naproxen+ Placebo (%), n=53	Difference Between Diazepam and Placebo, % (95% CI)
Median RMDQ (IQR)	0 (0, 1)	0 (0, 6)	−2.0 (−4.2 to 0.3)*
Worst LBP during previous 72 h			
Mild/none	44 (88)	48 (91)	−3 (−15 to 9)
Moderate/severe	6 (12)	5 (9)	
Frequency of LBP during previous 72 h			
Never/rarely	42 (84)	42 (79)	5 (−10 to 20)†
Sometimes	7 (14)	5 (9)	
Frequently/always	1 (2)	6 (11)	
Use of medication for LBP within 72 h			
None	42 (84)	47 (89)	−5 (−18 to 9)
Medication taken	8 (16)	6 (11)	

The RMDQ is a 24-item instrument measuring LBP-related functional impairment. On this instrument, zero represents no LBP-related functional impairment and 24 represents maximum functional impairment.
*Difference between mean 3-month RMDQ scores.
†Never/rarely versus sometime/frequently/always.

in functional outcome. Hingorani[5] randomized 50 hospitalized patients with various causes of acute low back pain to diazepam or placebo and found no difference in subjective or objective outcomes. Brown and Womble[11] randomized 49 patients with chronic back or neck pain to diazepam, cyclobenzaprine, or placebo groups and used a global outcome measure that encompassed change in level of pain, spasm, mobility, tenderness to palpation, and restriction in activities. The cyclobenzaprine patients had better outcomes than the diazepam patients, who had better outcomes than patients randomized to placebo. Basmajian[12] randomized 105 patients with neck or back pain to diazepam, cyclobenzaprine, and placebo and found no statistically significant differences among the groups.

Our data contribute to an increasing body of literature suggesting that, in general, most medications do not improve acute low back pain. We demonstrated previously that adding cyclobenzaprine or oxycodone/acetaminophen to naproxen is unlikely to benefit patients with new-onset nonradicular low back pain.[3] Similarly, patients with nonradicular low back pain appear to receive no benefit from either corticosteroids[13] or acetaminophen.[14] Complementary therapies, including acupuncture,[15] yoga,[16] and massage[17] may be offered but have been inadequately studied to assess efficacy in an acute low back pain population. Spinal manipulation is unlikely to benefit ED patients with acute low back pain who are well managed medically.[18] Physical therapy may be useful for some patients.[19] Emergency physicians should counsel their patients that passage of time will bring improvement and eventual relief to most of them.

Overall, 1-week and 3-month outcomes in this study were generally better than in other ED-based work.[2,3,13,20] This is partly explained by our selection criteria, which excluded patients with chronic or frequent episodic low back pain, who have been shown to have worse outcomes.[21] However, in all ED-based studies, 25% to 40% of patients with acute, new-onset low back pain report moderate or severe low back pain 1 week after ED discharge, and 10% to 25% of these patients report moderate or severe pain 3 months later. Ideally, patients at higher risk of poor outcome should be targeted for close follow-up, with the goal of preventing the transition from acute to chronic pain. Unfortunately, it is difficult to predict which patients with acute low back pain are at risk of poor outcomes.

Enrollment in this study did not commence until an individual was ready for discharge from the ED. Therefore, we do not know whether diazepam has a role in the acute management of acute low back pain, ie, whether it can increase the likelihood of discharge among patients who arrive in the ED with marked functional impairment because of low back pain of sufficient severity that hospitalization may be necessary. Also, we excluded from participation patients with chronic or frequent episodic low back pain. A systematic review suggests that these patients are at increased risk of poor outcomes if they are prescribed benzodiazepines.[4]

In conclusion, diazepam does not appear to confer any benefit beyond that of placebo when added to naproxen for the treatment of nonradicular, nontraumatic, acute low back pain.

Supervising editor: Donald M. Yealy, MD

Author affiliations: From the Department of Emergency Medicine, Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, NY (Friedman, Irizarry, Khankel, Zapata, Gallagher); and the Department of Pharmacy, Montefiore Medical Center, Bronx, NY (Solorzano, Zias).

Author contributions: BWF, CS, and EJG conceived the study and designed the trial. BWF, EI, CS, and EZ supervised the conduct of the trial and data collection. BWF, EI, and JZ managed the data, including quality control. BWF analyzed the data. BWF and NK drafted the article, 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.

Funding and support: By *Annals* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist. This publication was supported in part by the Harold and Muriel Block Institute for Clinical and Translational Research at Einstein and Montefiore (grant UL1TR001073).

Publication dates: Received for publication August 21, 2016. Revisions received September 27, 2016, and September 29, 2016. Accepted for publication October 3, 2016. Available online February 7, 2017.

Trial registration number: NCT02646124

REFERENCES

1. 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.
2. Friedman BW, O'Mahony S, Mulvey L, et al. One-week and 3-month outcomes after an emergency department visit for undifferentiated musculoskeletal low back pain. *Ann Emerg Med*. 2012;59:128-133.e3.
3. 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.
4. Chou R, Qaseem A, Snow V, et al. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med*. 2007;147:478-491.
5. Hingorani K. Diazepam in backache. A double-blind controlled trial. *Ann Phys Med*. 1966;8:303-306.
6. 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.
7. Chou R, Peterson K. Oregon Health & Science University; Drug Effectiveness Review Project (DERP). Available at: http://www.ohsu.edu/xd/research/centers-institutes/evidence-based-policy-center/evidence/derp/index.cfm. Accessed November 14, 2016.
8. Roland M, Fairbank J. The Roland-Morris Disability Questionnaire and the Oswestry Disability Questionnaire. *Spine*. 2000;25:3115-3124.
9. Simons DG, Mense S. Understanding and measurement of muscle tone as related to clinical muscle pain. *Pain*. 1998;75:1-17.
10. Brotz D, Maschke E, Burkard S, et al. Is there a role for benzodiazepines in the management of lumbar disc prolapse with acute sciatica? *Pain*. 2010;149:470-475.
11. Brown BR Jr, Womble J. Cyclobenzaprine in intractable pain syndromes with muscle spasm. *JAMA*. 1978;240:1151-1152.
12. Basmajian JV. Cyclobenzaprine hydrochloride effect on skeletal muscle spasm in the lumbar region and neck: two double-blind controlled clinical and laboratory studies. *Arch Phys Med Rehabil*. 1978;59:58-63.
13. Friedman BW, Holden L, Esses D, et al. Parenteral corticosteroids for emergency department patients with non-radicular low back pain. *J Emerg Med*. 2006;31:365-370.
14. Williams CM, Maher CG, Latimer J, et al. Efficacy of paracetamol for acute low-back pain: a double-blind, randomised controlled trial. *Lancet*. 2014;384:1586-1596.
15. Furlan AD, van Tulder M, Cherkin D, et al. Acupuncture and dry-needling for low back pain: an updated systematic review within the framework of the cochrane collaboration. *Spine*. 2005;30:944-963.
16. Cramer H, Lauche R, Haller H, et al. A systematic review and meta-analysis of yoga for low back pain. *Clin J Pain*. 2013;29:450-460.
17. Furlan AD, Imamura M, Dryden T, et al. Massage for low back pain: an updated systematic review within the framework of the Cochrane Back Review Group. *Spine (Phila Pa 1976)*. 2009;34:1669-1684.
18. Juni P, Battaglia M, Nuesch E, et al. A randomised controlled trial of spinal manipulative therapy in acute low back pain. *Ann Rheum Dis*. 2009;68:1420-1427.
19. Hill JC, Whitehurst DG, Lewis M, et al. Comparison of stratified primary care management for low back pain with current best practice (STarT Back): a randomised controlled trial. *Lancet*. 2011;378:1560-1571.
20. Friedman BW, Esses D, Solorzano C, et al. A randomized placebo-controlled trial of single-dose IM corticosteroid for radicular low back pain. *Spine*. 2008;33:E624-E629.
21. Friedman BW, Mulvey L, Davitt M, et al. Predicting 7-day and 3-month functional outcomes after an ED visit for acute nontraumatic low back pain. *Am J Emerg Med*. 2012;30:1852-1859.

What Review Topics do you want to read in *Annals*? We are seeking your favorite topics for clinical review articles (and suggestions for expert authors). Please email *Annals*' managing editor, Tracy Napper (tnapper@acep.org), with your ideas for suggested topics and authors.

APPENDIX E1

Roland-Morris Disability Questionnaire for low back pain

1.	During the last 24 h, I have stayed home most of the time because of my back pain:	No Yes
2.	During the last 24 h, I changed position frequently to try to get my back comfortable:	No Yes
3.	During the last 24 h, I walked more slowly than usual because of my back:	No Yes
4.	During the last 24 h, I have not been doing any jobs that I usually do around the house because of my back pain:	No Yes
5.	During the last 24 h, I used a handrail to get upstairs because of my back pain:	No Yes
6.	During the last 24 h, I lay down to rest more often because of my back pain:	No Yes
7.	During the last 24 h, I have had to hold on to something to get out of an easy chair because of my back pain:	No Yes
8.	During the last 24 h, I have tried to get other people to do things for me because of my back pain:	No Yes
9.	During the last 24 h, I got dressed more slowly than usual because of my back pain:	No Yes
10.	During the last 24 h, I stood up for only short periods because of my back pain:	No Yes
11.	During the last 24 h, I tried not to bend or kneel because of my back pain:	No Yes
12.	During the last 24 h, I found it difficult to get out of a chair because of my back pain:	No Yes
13.	During the last 24 h, my back was painful almost all of the time:	No Yes
14.	During the last 24 h, I found it difficult to turn over in bed because of my back pain:	No Yes
15.	During the last 24 h, my appetite was not very good because of my back pain:	No Yes
16.	During the last 24 h, I have had trouble putting on my socks (or stockings) because of the pain in my back or leg:	No Yes
17.	During the last 24 h, I could walk only short distances because of my back pain:	No Yes
18.	During the last 24 h, I slept less well because of my back:	No Yes
19.	During the last 24 h, I got dressed with the help of someone else because of my back pain:	No Yes
20.	During the last 24 h, I sat down for most of the day because of my back:	No Yes
21.	During the last 24 h, I avoided heavy jobs around the house because of my back pain:	No Yes
22.	During the last 24 h, I was more irritable and bad tempered with people than usual because of my back pain:	No Yes
23.	During the last 24 h, I went upstairs more slowly than usual because of my back pain:	No Yes
24.	During the last 24 h, I stayed in bed most of the time because of my back pain:	No Yes

APPENDIX E2

Baseline characteristics

Spasm

For every participant, we asked the attending physician, "Did muscle spasm contribute to this patient's pain?"

Spasm	Diazepam (%)	Placebo (%)
No	2 (4)	5 (9)
Yes	55 (96)	49 (89)
Not sure	0	1 (2)

We then performed a linear regression model, in which spasm (yes versus no) was included as an independent variable and improvement in RMDQ was the dependent variable.

The B coefficient was 3.5 (95% CI –2.9 to 9.9).

Because so many patients were thought to have spasm, we were unable to control for investigational medication in this model.

Work Status

Primary outcome (mean improvement in RMDQ, 95% CI) by work status

Unemployed: 12.4, 95% CI 7.0 to 17.7

Student: 12.9, 95% CI 7.3 to 18.4

Work <30 h/wk: 10.6, 95% CI 3.7 to 17.5

Work >30 h/wk: 10.6, 95% CI 8.8 to 12.4

APPENDIX E3

Follow-up data

Use of off-protocol medications

At the 7-day follow-up telephone call, we asked participants what medications they had used for LBP within the previous 24 h.

Medication	Diazepam	Placebo
Acetaminophen	0	1
Skeletal muscle relaxant	0	2
Opioid	0	0