The Journal of Emergency Medicine, Vol. 31, No. 4, pp. 365–370, 2006

0736-4679/06 $–see front matter

ELSEVIER

doi:10.1016/j.jemermed.2005.09.023

Original Contributions

PARENTERAL CORTICOSTEROIDS FOR EMERGENCY DEPARTMENT PATIENTS WITH NON-RADICULAR LOW BACK PAIN

Benjamin W. Friedman, MD, MS,* Lynne Holden, MD,* David Esses, MD,* Polly E. Bijur, PHD,* Hong K. Choi, MD, MPH,* Clemecia Solorzano, RPH,† Joseph Paternoster, RN,‡ and E. John Gallagher, MD*

*Department of Emergency Medicine, Albert Einstein College of Medicine, Bronx, New York, †Department of Pharmacy and ‡Department of Emergency Medicine, Montefiore Medical Center, Bronx, New York

Reprint Address: Benjamin W. Friedman, MD, Department of Emergency Medicine, Albert Einstein College of Medicine, Montefiore Medical Center, 111 East 210th Street, Bronx, NY 10467

□ **Abstract—Although not recommended for low back pain, the efficacy of systemic corticosteroids has never been evaluated in a general low back pain population. To test the efficacy of systemic corticosteroids for Emergency Department (ED) patients with low back pain, a randomized, double-blind, placebo-controlled trial of long-acting methylprednisolone was conducted with follow-up assessment 1 month after ED discharge. Patients with non-traumatic low back pain were included if their straight leg raise test was negative. The primary outcome was a comparison of the change in a numerical rating scale (NRS) 1 month after discharge. Of 87 subjects randomized, 86 were successfully followed to the 1-month endpoint. The change in NRS between discharge and 1 month differed between the two groups by 0.6 (95% confidence interval −1.0 to 2.2), a clinically and statistically insignificant difference. Disability, medication use, and healthcare resources utilized were comparable in both groups. Corticosteroids do not seem to benefit patients with acute non-radicular low back pain. © 2006 Elsevier Inc.**

□ **Keywords—Low back pain; emergency department; methylprednisolone**

INTRODUCTION

Acute low back pain is common, frequently debilitating, and often causes morbidity weeks to months after an initial visit to a health care provider (1,2). Traditional medical management is only moderately effective—despite standard treatments, up to 50% of low back pain patients have poor functional outcomes 2 to 4 weeks after a medical visit and as many as 79% of low back pain patients report persistent pain or functional limitations three months after a visit to a general practitioner (3–7). Research in the field is complicated by the fact that a heterogeneous group of injuries cause low back pain and that a specific etiology for an individual's back pain is rarely found (1). Multiple well-designed studies help a physician choose acute treatment for low back pain patients, but few medical treatments have demonstrated long-term benefit (8).

Although non-steroidal agents have clear benefit in low back pain patients, the role of corticosteroids is insufficiently understood (9). A guideline statement from the Agency for Health Care Policy and Research did not endorse the use of corticosteroids for low back pain, but found inadequate evidence to comment on the topic definitively (10). The only systemic corticosteroid clinical trials performed to date do not pertain to the average patient seen in an Emergency Department (ED) or a general practitioner's office due to referral bias, selection bias, and because standard treatment has changed over the two to three decades since those studies were performed (11–13).

RECEIVED: 11 March 2005; FINAL SUBMISSION RECEIVED: 26 September 2005;
ACCEPTED: 9 May 2006

Due to the evidence gap with regard to this potentially important treatment, and due to the poor prognosis of many low back pain patients, we tested the hypothesis that one dose of a long-acting parenteral corticosteroid would improve low back pain in a homogenous group of patients with acute non-radicular low back pain 1 month after discharge from an ED.

METHODS

Study Design

This was a randomized, double-blind placebo-controlled clinical trial evaluating intramuscular methylprednisolone acetate as adjunctive therapy for low back pain. This trial randomized subjects after they had been evaluated and treated in the ED and were ready for discharge. All subjects were followed-up by telephone call 1 week and 1 month after ED discharge. In addition to the corticosteroid or placebo injection, all subjects were given a complimentary 1-week supply of naproxen 500 mg tablets, oxycodone 5 mg/acetaminophen 325 tablets and a detailed low back pain instruction sheet. This study was approved by the Montefiore Medical Center institutional review board.

Setting

This study took place in the Bronx, New York at Montefiore Medical Center, the primary teaching hospital of the Albert Einstein College of Medicine. This ED sees 80,000 adult patients annually. Enrollment took place continuously between July 2003 and October 2004.

Selection of Participants

The attending emergency physician referred all adult patients (at least 21 years old) who presented with a chief complaint of non-traumatic low back pain during all ED operating hours. The department's research assistants (five trained, full-time employees) were responsible for enrolling the subjects under the supervision of the investigators. The research assistants determined eligibility using an explicit checklist containing detailed inclusion and exclusion criteria. When interviewing a subject, the research assistants employed this checklist in a predetermined, standardized fashion. Eligibility was confirmed by the principal investigator before unblinding. The research assistants included in this study any patient who had low back pain for less than 1 week and was 50 years of age or younger. Low back pain was described as pain originating below the tips of the scapulae and above the buttocks. Due to the desire to maintain a homogeneous group of subjects who would represent the average low back pain patient, patients were included only if their straight leg raise test, as described below, was negative. Patients were included if their back pain was caused by a twisting or lifting mechanism but excluded if they had been in a motor vehicle collision, had experienced direct blunt trauma to the back, or if they had a fall from greater than 4 feet. Patients were also excluded if the emergency physician felt there was a high likelihood the patient had a secondary cause of low back pain, e.g., metastatic bone disease or infection. Patients were also excluded for temperature greater than 37.9°C (100.3°F), pregnancy, lactation, allergy to or intolerance of a study medication. Patients could only enroll once. Patients could not have had another episode of back pain within 4 weeks before the current back pain attack. Patients were excluded for systemic steroid use within 4 weeks, a history of back surgery, a neoplasia known to metastasize, a chronic pain syndrome, an inflammatory arthritis, and suspected vascular, urologic or gynecologic pathology.

Rationale for the Straight Leg Raise Test

Although the precise test characteristics of the straight leg raise test are unknown, a positive ipsilateral straight leg raise is a sensitive marker for a herniated intervertebral disc (14). Therefore, if this test is negative, it can help rule-out the disease. To maintain a homogeneous cohort, subjects were stratified based on results of the straight leg raise test. Many definitions of the straight leg raise test exist. To identify distinct populations, the research assistants were given a strictly defined, conservative definition of this test: namely, the test was considered positive if a subject had ipsilateral pain shooting below the knee when either leg was raised between 30 and 70 degrees, as measured with a protractor. Contralateral pain below the knee, considered more specific for a herniated disc, was also classified as a positive straight leg raising test and rendered patients ineligible for study entry (14).

Randomization and Blinding

Randomization was done by the pharmacist in blocks of six using computer-generated random number tables available online. In an order determined by these random number tables, the pharmacist inserted study medication or placebo into vials and placed these vials into sequentially numbered research bags. The research bags were then used in order by the research assistants. Assignment was known only by the

pharmacist. The active arm contained 160 mg of methylprednisolone acetate in a 2-cc solution. A comparable amount of identical-appearing placebo was placed into identical vials. A sealed opaque manila envelope containing the assignment accompanied each study packet. These envelopes were not opened during the course of the study.

Protocol

All patients with low back pain were treated at the discretion of the attending physician. When the patient's pain had been controlled to a level sufficient for the patient to be discharged, the research assistant would approach the patient, explain the study, and ask for the patient's consent to participate as a research subject. After consent was obtained, the research assistant would ask demographic questions, perform a straight leg raise test, and baseline pain. Subjects would then get an intramuscular injection of methylprednisolone acetate or placebo. All subjects were discharged with a "back pack" containing 14 tablets of naproxen 500 mg, 12 tablets of oxycodone 5 mg/acetaminophen 325 tablets, and a standardized discharge instruction sheet.

Subjects were followed-up by telephone at 1 week and 1 month after discharge. At each of these telephone interviews, the research assistants would read standardized questions about pain and activity limitations from the data collection instrument.

Outcome Measurements

An 11-point numerical rating scale for pain was used as the primary measurement tool for this trial. This instrument has been shown to be valid and reliable for acute pain patients in an ED setting—specifically, it is comparable in direction and magnitude to a visual analog scale, while being easier to administer and complete (15). As secondary measures, this trial utilized a 4-point descriptive scale on which subjects were asked to characterize their low back pain as "none, mild, moderate, or severe" and a validated low back pain disability scale, the Roland-Morris-18 (16).

The primary endpoint was the 1-month pain score, as determined by a follow-up telephone call. The primary outcome was change in numerical rating scale (NRS) score at 1 month ($NRS_{baseline} - NRS_{1\ month}$). Potential scores included negative numbers if the pain at follow-up was worse than the pain at ED discharge. The 1-month NRS score reflected the numerical value of the subject's worst back pain over the previous 24 h. Secondary endpoints included the 1-week change in NRS score ($NRS_{baseline} - NRS_{1\ week}$), the RM-18 score at 1 week and 1 month, the need for pain medication over the previous 24 h at 1 week and 1 month, the proportion of patients in each group who were "pain free" at 1 week and 1 month, and the ability to return to usual daily activities at 1 week and 1 month.

Due to our fear that ED subjects would be difficult to follow-up at 1 month, the primary endpoint was initially established as the 1-week pain score. However, during the course of this trial, it became apparent that the 1-month follow-up was feasible. Because 1 month is the more clinically important endpoint, the primary endpoint was switched to 1 month before the randomization allocation was unblinded.

Data Collection and Processing

The entire data collection process was performed by the research assistants. Data were double-entered into Epi Info V.3.2 (Centers for Disease Control, Atlanta, GA) initially by the research assistants and a research secretary, and then checked for accuracy before unblinding by two of the investigators.

Sample Size Calculation

A review of recent pain trials that reported both the mean change on an eleven point pain scale and its standard deviation revealed a typical standard deviation of approximately 3.0 (17–20). Although smaller changes might have clinical significance, a change of 2.0 was chosen as the cut-off for this trial because it has robust clinical significance (21). For this sample size calculation, a normal distribution was assumed. With a two-sided $\alpha = .05$ and a power of 0.8, a difference of 2.0 in ($NRS_{baseline} - NRS_{1\ month}$) could be detected with a sample size of 37 subjects in each group.

Analysis

Students *t*-tests were used to compare between-group mean differences in the change in pain scores over 1 month. Chi-square analysis was used to compare rates. Multivariate linear regression models were used to analyze the influence of heterogeneous baseline characteristics. Between-group differences were expressed as means or proportions, bounded by 95% confidence intervals (95% CI).

RESULTS

There were 241 patients screened by the research assistants, of whom 107 were eligible for the trial. The most

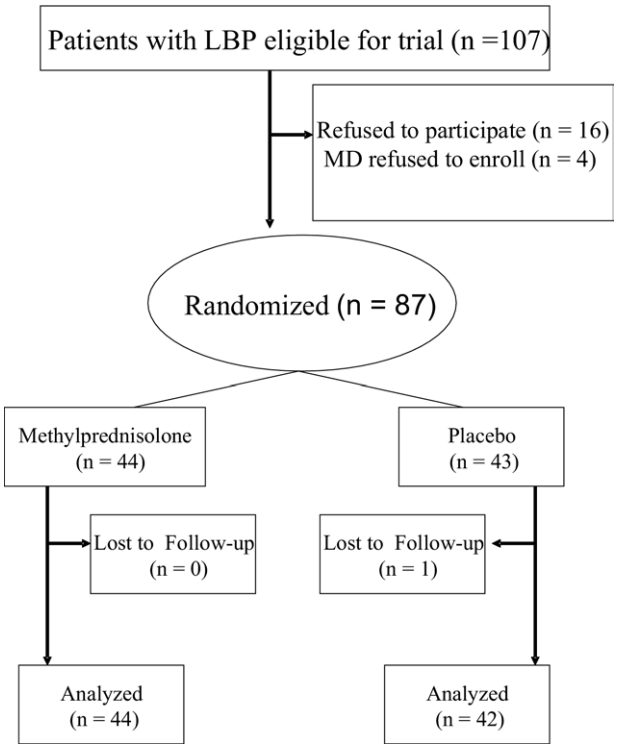

Figure 1. CONSORT outline.

frequent reasons for ineligibility were age greater than 50 years (n = 36), straight leg raise positive (n = 30), recent trauma as defined previously (n = 27), and non-acute pain (n = 25). Twenty patients were excluded for refusal to participate, or because the attending physician did not wish to enroll the patient (see CONSORT diagram, Figure 1). Subjects were enrolled continuously until the predetermined number of patients completed the primary endpoint.

Forty-four subjects were randomized to the methylprednisolone arm. None of these subjects was lost to follow-up at 1 month. Of these, 5 could not be contacted at 1 week. Forty-three subjects were randomized to the placebo arm. Only 1 subject was lost to follow-up at 1 month. Of these, 5 could not be contacted at 1 week.

As shown in Table 1, age and gender were comparable in the two arms. There were slight imbalances in ethnicity, body mass index, and low back pain duration. The effects of these random imbalances are discussed below.

Numerical rating scale pain scores were as noted in Table 2. The primary outcome, a comparison of the change in NRS scores between ED discharge and 1 month, demonstrated a clinically and statistically non-significant difference of 0.6 (95% CI −1.0–2.2). Similarly, a comparison of the change in NRS scores between ED discharge and 1 week, demonstrated a clinically and statistically non-significant difference of 0.6 (95% CI −0.9–2.2). The 1-week analysis excluded the five pain scores that were missing from each arm. A sensitivity analysis was performed to determine the impact of these missing values. The analysis biased findings in favor of the steroid arm by assigning an NRS pain score of 10 to the missing patients in the placebo arm at 1 week and an NRS pain score of 0 to the missing patients in the steroid arm at 1 week. In this analysis, the 1-week outcomes did not change—the analysis demonstrated a clinically and statistically non-significant difference of 0.5 (95% CI −1.0–2.1).

Table 1. Baseline Characteristics

	Methylprednisolone	Placebo
Age mean (SD)	36 (7)	36 (7)
Female	64%	54%
Latino	63%	42%
Black	23%	44%
White	12%	7%
Body mass index Mean (SD)	30.6 (7.1)	28.7 (8.8)
Duration of back pain Mean h (SD)	44 (45)	63 (52)
NRS at ED presentation Mean (SD)	8.6 (1.7)	9.1 (1.4)
Prior episodes of back pain that prevented ADLs Mean (SD)	1.8 (3.4)	2.2 (3.5)
Transported by EMS	11%	19%

Secondary outcomes at 1 month and 1 week, including rates of "back pain-free," use of pain medication, return to usual daily activities, visits to health care providers, and scores on the RM-18 disability scale, were comparable between the two groups, as listed in Tables 3 and 4.

Within the 1-month study period, there were no reports of hyperglycemia requiring medical attention, infection, or gastrointestinal bleeding. At 1 week, 55% of subjects in the placebo group reported no adverse medication effects. Seventy-nine percent of subjects in the methylprednisolone group reported no adverse medication effects (difference = 24% [95% CI 16–35%]). The most common adverse effects in both groups were complaints related to the upper gastrointestinal tract, drows-

Table 2. Numerical Rating Scale Pain Scores—Means (SD)

	Methylprednisolone	Placebo
ED discharge (baseline)	7.6 (2.4)	8.1 (1.8)
1 week	3.5 (3.3)	3.3 (3.2)
1 month	2.4 (3.3)	2.3 (3.4)

Table 3. Secondary Outcomes, 1 Week

	Methylprednisolone	Placebo
No back pain in previous 24 h	33% (95% CI 20–49%)	40% (95% CI 26–56%)
Back pain in previous 24 h no worse than mild	74% (95% CI 59–85%)	68% (95% CI 52–81%)
Required medication for back pain in last 24 h	53% (95% CI 38–68%)	36% (95% CI 22–52%)
Returned to usual activities	87% (95% CI 71–95%)	79% (95% CI 63–89%)
RM-18 = 0 (no disability)	71% (95% CI 55–83%)	74% (95% CI 58–85%)
RM-18 mean (95% CI)	2.6 (95% CI 0.7–4.5)	3.4 (95% CI 1.3–5.5)
RM-18 median (IQR)	0 (1.3)	0 (5.3)

iness, and weakness, possibly related to the naproxen pills and oxycodone/acetaminophen pills that all subjects received. Upper gastrointestinal complaints were reported in 21% of subjects in the placebo arm and 8% of subjects in the active arm (difference = 13% [95% CI 7–22%]). At 1 month, 90% (95% CI 77–96%) of subjects in the placebo group reported no adverse medication effects. Ninety-one percent (95% CI 79–96%) of subjects in the methylprednisolone group reported no adverse medication effects. Upper gastrointestinal complaints, drowsiness, and weakness were the most common adverse medication reactions and were comparable between the two groups.

Imbalances existed between the two groups with regard to ethnicity, body mass index, and duration of back pain (Table 1). The importance of these imbalances was examined by testing the association between each of these covariates and the 1 month/1 week pain scores as well as testing the influence of each of these covariates on the association between study medication and primary and secondary outcomes. The purpose of these analyses was to determine if the relationships between study medication and the outcomes were confounded by the unbalanced baseline characteristics. A correlation matrix built between these covariates and the outcomes revealed no quantitatively important or statistically significant associations. A univariate linear regression model was built using study medication as the independent variable. The beta coefficient remained unchanged when the imbalanced covariates were added to the model.

DISCUSSION

We did not identify any previously published randomized clinical trials of corticosteroids for low back pain in a general population using a PubMed search and an exhaustive search of references in guideline statements, topic reviews and meta-analyses. In our clinical trial, we could find no convincing clinical or statistical benefit that corticosteroids conferred upon these patients. Although guideline statements have recommended against the use of corticosteroids in a general low back pain population, there had been insufficient evidence to support this conclusion (10). The results of this study support the guideline statements and should be incorporated into practice by emergency physicians and general practitioners when choosing interventions for their back pain patients.

LIMITATIONS

Although only 1 subject was lost to follow-up, 5 subjects in each arm could not be contacted in time to record 1-week outcomes. However, the 1-week conclusions do not change even if extreme assumptions are made about the potential benefit of corticosteroids.

Secondly, the study population is primarily composed of under-represented urban minorities. Whether the results can be generalized to other populations is unclear.

Finally, we chose to use long-acting parenteral methylprednisolone rather than a 7-day course of tapering corticosteroids because we wished to be certain that any

Table 4. Secondary Outcomes, 1 Month

	Methylprednisolone	Placebo
No back pain in previous 24 h	55% (95% CI 40–69%)	57% (95% CI 42–71%)
Back pain in previous 24 h no worse than mild	77% (95% CI 63–87%)	74% (95% CI 59–85%)
Required medication for back pain in last 24 h	25% (95% CI 15–39%)	19% (95% CI 10–33%)
Returned to usual activities	85% (95% CI 71–93%)	80% (95% CI 65–90%)
RM-18 = 0 (no disability)	77% (95% CI 63–87%)	74% (95% CI 59–85%)
RM-18 mean (95% CI)	2.6 (95% CI 0.8–4.3)	3.1 (95% CI 1.3–5.0)
RM-18 median (IQR)	0 (0)	0 (3.5)
Provider visit for back pain	17% (95% CI 8–33%)	22% (95% CI 12–38%)

treatment effect would not be attenuated by patient nonadherence to a medical regimen.

CONCLUSIONS

We were unable to demonstrate a benefit of intramuscular corticosteroids in non-radicular low back pain patients who were discharged from the ED. Despite treatment with naproxen and oxycodone/acetaminophen, only 37% of these subjects were back pain free 1 week after discharge. Twenty-five percent of these subjects continued to experience functional limitations due to their back pain 1 month after discharge. Emergency physicians should ensure that their patients have appropriate expectations and follow-up care at the time of discharge from the ED.

REFERENCES

1. Deyo RA, Weinstein JN. Low back pain. N Engl J Med 2001;344: 363–70.
2. Frymoyer JW. Back pain and sciatica. N Engl J Med 1988;318: 291–300.
3. Cherkin DC, Deyo RA, Street JH, Barlow W. Predicting poor outcomes for back pain seen in primary care using patients' own criteria. Spine 1996;21:2900–7.
4. Coste J, Delecoeuillerie G, Cohen de Lara A, Le Parc JM, Paolaggi JB. Clinical course and prognostic factors in acute low back pain: an inception cohort study in primary care practice. BMJ 1994;308: 577–80.
5. Carey TS, Garrett J, Jackman A, McLaughlin C, Fryer J, Smucker DR. The outcomes and costs of care for acute low back pain among patients seen by primary care practitioners, chiropractors, and orthopedic surgeons. The North Carolina Back Pain Project. N Engl J Med 1995;333:913–7.
6. Croft PR, Macfarlane GJ, Papageorgiou AC, Thomas E, Silman AJ. Outcome of low back pain in general practice: a prospective study. BMJ 1998;316:1356–9.
7. Von Korff M, Saunders K. The course of back pain in primary care. Spine 1996;21:2833–7; discussion 2838–9.
8. van Tulder MW, Koes BW, Bouter LM. Conservative treatment of acute and chronic nonspecific low back pain. A systematic review of randomized controlled trials of the most common interventions. Spine 1997;22:2128–56.
9. van Tulder MW, Scholten RJ, Koes BW, Deyo RA. Nonsteroidal anti-inflammatory drugs for low back pain: a systematic review within the framework of the Cochrane Collaboration Back Review Group. Spine 2000;25:2501–13.
10. Bigos S, Bowyer O, Braen G, et al. Acute Low Back Problems in Adults (Clinical Practice Guideline No. 14. AHCPR Publication No. 95-0642). Rockville, MD: Agency for Health Care Policy and Research, Public Health Service, U.S. Department of Health and Human Services; 1994.
11. Hedeboe J, Buhl M, Ramsing P. Effects of using dexamethasone and placebo in the treatment of prolapsed lumbar disc. Acta Neurol Scand 1982;65:6–10.
12. Haimovic IC, Beresford HR. Dexamethasone is not superior to placebo for treating lumbosacral radicular pain. Neurology 1986; 36:1593–4.
13. Porsman O, Friis H. Prolapsed lumbar disc treated with intramuscularly administered dexamethasonephosphate. A prospectively planned, double-blind, controlled clinical trial in 52 patients. Scand J Rheumatol 1979;8:142–4.
14. Deville WL, van der Windt DA, Dzaferagic A, Bezemer PD, Bouter LM. The test of Lasegue: systematic review of the accuracy in diagnosing herniated discs. Spine 2000;25:1140–7.
15. Bijur PE, Latimer CT, Gallagher EJ. Validation of a verbally administered numerical rating scale of acute pain for use in the emergency department. Acad Emerg Med 2003;10:390–2.
16. Stratford PW, Binkley JM. Measurement properties of the RM-18. A modified version of the Roland-Morris Disability Scale. Spine 1997;22:2416–21.
17. Dougados M, Behier JM, Jolchine I, et al. Efficacy of celecoxib, a cyclooxygenase 2-specific inhibitor, in the treatment of ankylosing spondylitis: a six-week controlled study with comparison against placebo and against a conventional nonsteroidal antiinflammatory drug. Arthritis Rheum 2001;44:180–5.
18. Corbo J, Esses D, Bijur PE, Iannaccone R, Gallagher EJ. Randomized clinical trial of intravenous magnesium sulfate as an adjunctive medication for emergency department treatment of migraine headache. Ann Emerg Med 2001;38:621–7.
19. Cameron JD, Lane PL, Speechley M. Intravenous chlorpromazine vs intravenous metoclopramide in acute migraine headache. Acad Emerg Med 1995;2:597–602.
20. Lines CR, Vandormael K, Malbecq W. A comparison of visual analog scale and categorical ratings of headache pain in a randomized controlled clinical trial with migraine patients. Pain 2001;93: 185–90.
21. Kelly AM. Does the clinically significant difference in visual analog scale pain scores vary with gender, age, or cause of pain? Acad Emerg Med 1998;5:1086–90.