

## EPIDURAL CORTICOSTEROID INJECTIONS FOR SCIATICA DUE TO HERNIATED NUCLEUS PULPOSUS

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### ABSTRACT

**Background** Although epidural corticosteroid injections are commonly used for sciatica, their efficacy has not been established.

**Methods** In a randomized, double-blind trial, we administered up to three epidural injections of methylprednisolone acetate (80 mg in 8 ml of isotonic saline) or isotonic saline (1 ml) to 158 patients with sciatica due to a herniated nucleus pulposus. All patients had Oswestry disability scores higher than 20 (on a scale of 1 to 100, with scores of 20 or less indicating minimal disability, and higher scores greater disability).

**Results** At three weeks, the Oswestry score had improved by a mean of  $-8.0$  in the methylprednisolone group and  $-5.5$  in the placebo group (95 percent confidence interval for the difference,  $-7.1$  to  $2.2$ ). Differences in improvements between the groups were not significant, except for improvements in the finger-to-floor distance ( $P=0.006$ ) and sensory deficits ( $P=0.03$ ), which were greater in the methylprednisolone group. After six weeks, the only significant difference was the improvement in leg pain, which was greater in the methylprednisolone group ( $P=0.03$ ). After three months, there were no significant differences between the groups. The Oswestry score had improved by a mean of  $-17.3$  in the methylprednisolone group and  $-15.4$  in the placebo group (95 percent confidence interval for the difference,  $-9.3$  to  $5.4$ ). At 12 months, the cumulative probability of back surgery was 25.8 percent in the methylprednisolone group and 24.8 percent in the placebo group ( $P=0.90$ ).

**Conclusions** Although epidural injections of methylprednisolone may afford short-term improvement in leg pain and sensory deficits in patients with sciatica due to a herniated nucleus pulposus, this treatment offers no significant functional benefit, nor does it reduce the need for surgery. (N Engl J Med 1997; 336:1634-40.)

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**S**CIATICA due to a herniated nucleus pulposus is an important medical and socioeconomic problem.<sup>1</sup> Although the majority of patients recover with conservative management, 10 to 15 percent need surgery.<sup>2</sup> Epidural corticosteroid injections were first used to treat sciatica in the early 1950s, as reported by Lièvre et al.<sup>3,4</sup> Of 12 controlled trials that have subsequently been reported, half found that the injections were more effective

than the reference treatment,<sup>5-10</sup> and the other half found them to be no better or worse.<sup>11-16</sup> A critical analysis of these studies showed that most had methodologic deficiencies.<sup>17</sup> Reviews of the literature<sup>18-20</sup> and reports on series of thousands of patients<sup>21,22</sup> attest to the relative safety of epidural corticosteroid injections.

We conducted a double-blind, placebo-controlled trial to evaluate the efficacy of up to three epidural corticosteroid injections as compared with epidural saline injections in patients with sciatica due to a herniated nucleus pulposus.

### METHODS

#### Study Group

The study was conducted at the Centre Hospitalier de l'Université Laval, in Quebec City, Canada, and Notre-Dame Hospital, in Montreal. The protocol was approved by the ethics committees at both institutions.

Information about the trial was sent to over 300 primary care physicians and specialists, who were encouraged to refer patients who met the criteria for enrollment in the study. Patients were eligible if they were 18 years old or older and had a first or recurrent episode of sciatica that had lasted for a minimum of four weeks but less than one year. Sciatica was defined as the presence of constant or intermittent pain in one or both legs, radiating below the knee. Signs of nerve-root irritation (a positive straight-leg test, defined as reproduction of radicular pain by elevation of the leg) or nerve-root compression (motor, sensory, or reflex deficits), or both, had to be present, with computed tomographic (CT) evidence of a herniated nucleus pulposus at a level corresponding to the symptoms and clinical findings. In addition, patients had to have a score higher than 20 on the Oswestry Low Back Pain Disability Questionnaire.<sup>23</sup>

Patients were excluded if they had symptoms and clinical findings compatible with the cauda equina syndrome, if the CT scan showed evidence of nerve-root compression from causes other than a herniated nucleus pulposus, if they had received epidural corticosteroid injections for the current episode in the preceding year, or if they had undergone low back surgery. Patients who were pregnant or who had a known blood-coagulation disorder or an allergy to local anesthetics were also excluded.

#### Treatment

Randomization took place after we had obtained written informed consent from the study participants and gathered base-line information. The assignment scheme was generated from a table of

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random numbers. Random assignments to the treatment groups were stratified according to study center and balanced after every four to six assignments. The opaque prenumbered envelopes containing the assignments were kept by the hospital pharmacist.

The patients received injections of either 80 mg (2 ml) of methylprednisolone acetate (Depo-Medrol, Upjohn) mixed with 8 ml of isotonic saline or 1 ml of isotonic saline in the epidural space, according to the technique described by Barry and Kendall.<sup>24</sup> The injections were administered with the patient lying in the lateral decubitus position. The skin was first anesthetized with 2 percent lidocaine. The syringes were prepared by the hospital pharmacist and given to the anesthesiologist by a nurse only after the epidural space had been reached. The injections were repeated after three and six weeks in the patients who did not report an overall marked or very marked improvement of their condition and who continued to have scores higher than 20 on the Oswestry questionnaire. A letter was sent to each referring physician explaining the nature of the trial and the importance of withholding concurrent interventions. In addition to the study treatment, patients were given a supply of acetaminophen tablets (325 mg) and a form on which to record each tablet taken.

### Follow-up and Assessment of Outcome

The patients were reevaluated three weeks, six weeks, and three months after randomization. At each visit, the distance from the fingers to the floor on maximal forward flexion was measured, and a standard neurologic examination was performed. Information on the use of acetaminophen and other treatments was recorded. Each patient was examined by the same physician throughout the trial. The physicians and nurses involved in these assessments were unaware of the treatment received, and none of the anesthesiologists who administered the injections performed the follow-up evaluations.

The patients rated the perceived degree of overall improvement or deterioration on a descriptive seven-item scale that ranged from very marked improvement to very marked deterioration. The intensity of leg pain in the week preceding the visit was assessed on a visual-analogue scale ranging from 0 (no pain) to 100 (worst pain possible). The patients completed two components of the McGill Pain Questionnaire.<sup>25</sup> The first component measures the present intensity of pain on the basis of the response to one question, recorded as a number from 0 (no pain) to 5 (excruciating pain). The second component is a pain-rating index involving 77 pain descriptors (e.g., lancinating, cramping, and burning) grouped into 20 categories. The descriptors in each category are ranked numerically according to the severity of pain. Patients can choose no more than one descriptor per category. The score on the pain-rating index, which corresponds to the sum of the numerical values of the descriptors chosen by the patient, ranges from 0 (no pain) to 77 (the most severe pain in every category).

Functional disability was assessed with the Oswestry Low Back Pain Disability Questionnaire<sup>23</sup> and the Sickness Impact Profile,<sup>26</sup> both slightly modified by adding "and/or leg" to all statements that contained the word "back." The Oswestry Low Back Pain Disability Questionnaire has 10 sections (e.g., on walking, sleeping, and social activities). The overall score ranges from 0 to 100, with a score of 20 or less indicating minimal disability for which no treatment is usually indicated and higher scores indicating greater disability.<sup>23</sup> The Sickness Impact Profile measures perceived health status and changes in functional status due to sickness.<sup>26</sup> It consists of 136 questions grouped into 12 categories (e.g., physical dimensions and psychosocial dimensions). Both instruments have been shown to be reliable and sensitive to changes in patients with low back pain.<sup>23-27</sup> The patients also reported the number of days in the previous two weeks when they had limited their activities because of back or leg pain.

### Statistical Analysis

We selected the Oswestry score at three months as the primary outcome. We estimated that with 80 patients in each group, we

would be able to detect a 10-point difference in the mean Oswestry score between the two groups (statistical power, 80 percent, with a two-sided alpha level of 0.05 and a standard deviation of 22, as estimated in a preliminary study of 100 patients with sciatica), allowing for an expected withdrawal rate of 15 percent.

The primary analysis was based on an intention-to-treat principle. All patients were included in the analysis, even those who withdrew from the study. In the case of withdrawals, the data at the time of withdrawal or from the most recent assessment were imputed to all subsequent evaluations. For continuous variables, the mean change from the base-line value was estimated for each group, and the mean changes in the two groups were compared with the use of unpaired *t*-tests.<sup>28</sup> The treatment effect was defined as the difference between the mean changes. The precision and statistical significance of this difference are indicated by the 95 percent confidence interval. A similar approach was followed for categorical variables. All tests were two-sided. Secondary analyses were carried out with actual data on all randomized patients, without any imputation of data in the case of patients who withdrew from the study. Comparisons of median values and proportions of patients were based on Wilcoxon tests<sup>29</sup> and chi-square tests,<sup>28</sup> respectively. Kaplan-Meier survival analysis<sup>30</sup> was used to estimate the cumulative probability of undergoing back surgery in the 12 months after randomization. Survival curves were compared with the results of the log-rank test.<sup>30</sup> An analysis of covariance<sup>31</sup> was conducted to adjust for the two base-line variables not evenly distributed between the two groups (male sex and living with a partner). Since the adjusted values for all outcomes were very similar to the unadjusted values, only unadjusted results are presented.

## RESULTS

### Study Group

Between October 1992 and January 1996, 158 patients were enrolled in the study, with 78 patients in the methylprednisolone group and 80 in the placebo group. The base-line characteristics were similar in the two groups (Table 1), except that more of the patients were men, more were living with a partner, and the finger-to-floor distance was greater in the methylprednisolone group than in the placebo group.

### Withdrawals

A total of 156 patients completed the three follow-up visits. One patient in the methylprednisolone group did not return after receiving the first injection, and one patient in the placebo group did not return for the last two visits (Table 2). Twelve patients in the methylprednisolone group and 20 in the placebo group discontinued treatment because of lack of efficacy (chi-square = 1.70, *P* = 0.19). Nine of the 12 patients in the methylprednisolone group and 8 of the 20 in the placebo group subsequently underwent back surgery. Of these 17 patients, 14 reported marked or very marked improvement at the three-month evaluation, and 6 had an Oswestry score of 20 or less; the mean leg-pain score had decreased from 72.7 at base line to 21.2.

### Compliance and Concurrent Interventions

In the methylprednisolone group, 17 patients (22 percent) received one injection according to the protocol, 38 (49 percent) received two injections, and 23 (29 percent) received three injections, as

**TABLE 1.** BASE-LINE CHARACTERISTICS OF 158 PATIENTS WITH SCIATICA RANDOMLY ASSIGNED TO RECEIVE EPIDURAL METHYLPREDNISOLONE OR PLACEBO.\*

CHARACTERISTIC	METHYLPREDNISOLONE (N = 78)	PLACEBO (N = 80)
Age (yr)	39.0±9.3	40.6±11.3
Male sex (% of patients)	71.8	58.8
Education (yr)	13.0±3.6	12.3±3.2
Living with partner (% of patients)	79.5	66.3
Employment (% of patients)		
Unemployed	24.4	27.5
Not working because of back pain	55.1	51.3
Employed	20.5	21.3
Receiving disability compensation (% of patients)	24.4	21.3
Median duration of current episode of leg pain (wk)	12.9	13.0
First episode of sciatica (% of patients)	75.6	76.2
Median interval from CT scan to randomization (days)	13.0	13.0
Level affected on CT scan (% of patients)		
L3–L4	6.4	1.3
L4–L5	48.7	51.3
L5–S1	44.9	47.5
Oswestry score†	49.6±15.7	50.0±15.5
Visual-analogue pain score for previous week‡	65.6±21.6	61.5±21.4
McGill score§		
Present intensity of pain	2.6±1.1	2.8±1.0
Pain-rating index	27.8±12.0	26.2±10.7
Sickness Impact Profile¶		
Overall	21.7±10.5	21.4±9.7
Physical dimensions	18.6±11.6	17.8±10.8
Psychosocial dimensions	16.2±11.8	17.6±12.1
Restricted activity in previous two weeks (no. of days)	9.9±6.1	9.7±6.1
Physical examination		
Finger-to-floor distance (cm)	37.4±14.9	32.8±15.7
Positive straight-leg test (% of patients)	91.0	92.5
Motor deficit (% of patients)	29.5	28.8
Sensory deficits (% of patients)	62.8	53.8
Reflex changes (% of patients)	35.9	41.3

\*Plus-minus values are means ±SD. There were no differences between the two groups in the type of treatment previously received for the current episode of sciatica, the number of days of bed rest in the previous two weeks, or the duration of the current episode of back pain (data not shown).

†The score on the Oswestry Low Back Pain Disability Questionnaire ranges from 0 to 100, with higher scores indicating worse functional status.

‡The visual-analogue scale ranges from 0 (no pain) to 100 (worst pain possible).

§The ratings for the present intensity of pain are 0 (absent), 1 (mild), 2 (discomforting), 3 (distressing), 4 (horrible), and 5 (excruciating). The pain-rating index (see the Methods section) ranges from 0 to 77 and is the sum of the numerical values corresponding to the pain descriptors chosen by the patient. Higher scores indicate more severe pain.

¶The overall score, physical-dimensions score, and psychosocial-dimensions score range from 0 to 100, with higher scores indicating worse functional status.

compared with 19 patients (24 percent), 37 (46 percent), and 24 (30 percent) in the placebo group. The mean number of injections per patient was the same in the two groups (2.1 injections).

At each visit, the patients in the placebo group reported greater use of acetaminophen than the patients in the methylprednisolone group. In the first three weeks after randomization, patients in the placebo group took a median of 76 pills, and those in the methylprednisolone group took a median of 60 pills ( $P=0.12$ ); from three to six weeks, the median numbers of pills taken were 50 and 17, respectively ( $P=0.01$ ). The number of patients receiving other types of treatment did not differ significantly between the groups. In the course of the three-month follow-up, nine patients in the methylprednisolone group and four in the placebo group received nonpharmacologic treatment (physiotherapy or chiropractic treatment) ( $P=0.24$ ). Twenty-seven patients in the methylprednisolone group and 32 in the placebo group received various drugs other than acetaminophen (narcotic agents, nonsteroidal antiinflammatory drugs, anxiolytic agents, or muscle relaxants) ( $P=0.55$ ).

#### Complications

In one patient in each group, the dura was accidentally punctured: both patients were given an epidural injection of 10 ml of blood drawn from the antecubital vein (blood patch). Twenty-one patients in the methylprednisolone group (27 percent) and 16 in the placebo group (20 percent) reported a transient headache within 24 hours after at least one of the epidural injections ( $P=0.30$ ).

#### Response to Treatment

Three weeks after the first injection, the groups did not differ significantly with respect to the primary outcome (Table 3). As compared with the base-line values, the Oswestry scores improved by a mean ( $\pm$ SD) value of  $-8.0\pm 15.3$  in the methylprednisolone group and  $-5.5\pm 14.3$  in the placebo group (95 percent confidence interval for the difference,  $-7.1$  to  $2.2$ ;  $P=0.30$ ). Thirty-three percent of the patients in the methylprednisolone group and 29 percent of those in the placebo group reported marked or very marked improvement ( $P=0.65$ ). In both groups, the visual-analogue scores for leg pain, the scores on the McGill Pain Questionnaire, the Sickness Impact Profile scores, the number of days of limited activity, and the physical-examination measures improved as compared with base-line values. Differences in improvements between the groups were not significant, except that the methylprednisolone group had greater improvement in the finger-to-floor distance ( $P=0.006$ ) and a smaller proportion of patients in this group had sensory deficits ( $P=0.03$ ).

The results at six weeks (data not shown) were very similar to those at three weeks. The mean change

**TABLE 2.** WITHDRAWALS FROM THE STUDY, ACCORDING TO TREATMENT GROUP.

REASON FOR WITHDRAWAL	METHYL- PREDNISOLONE (N = 78)	PLACEBO (N = 80)
	no. of patients (no. undergoing back surgery)	
Before the three-week visit		
Lack of efficacy	0	2 (1)
Lost to follow-up	1	0
Between the three-week and six-week visits		
Error in epidural administration	0	1
Lack of efficacy	4 (2)	9 (4)
Lost to follow-up	0	1
Between the six-week and three-month visits		
Lack of efficacy	8 (7)	9 (3)
Total	13 (9)	22 (8)

in the Oswestry score was greater in the methylprednisolone group than in the placebo group (difference in mean change,  $-3.2$ ; 95 percent confidence interval,  $-9.4$  to  $2.2$ ;  $P=0.30$ ). Other outcome variables continued to improve in both groups; the only significant difference was in the degree of improvement in leg pain, as assessed by the visual-analogue pain scale, which was greater in the methylprednisolone group (difference in mean change,  $-11.0$ ; 95 percent confidence interval,  $-21.1$  to  $-0.9$ ;  $P=0.03$ ).

Three months after enrollment, the two groups did not differ statistically in any of the outcome measures (Table 4). The patients continued to have improvement in the outcome measures. As compared with the base-line values, the Oswestry scores changed by a mean of  $-17.3$  in the methylprednisolone group and  $-15.4$  in the placebo group (95 percent confidence

**TABLE 3.** CLINICAL AND FUNCTIONAL OUTCOMES THREE WEEKS AFTER ENROLLMENT AND CHANGES FROM BASE-LINE VALUES, ACCORDING TO TREATMENT GROUP.

OUTCOME MEASURE	THREE WEEKS AFTER ENROLLMENT*		CHANGE FROM BASE LINE†		TREATMENT EFFECT (95% CI)‡
	METHYL- PREDNISOLONE (N = 77)	PLACEBO (N = 80)	METHYL- PREDNISOLONE (N = 77)	PLACEBO (N = 80)	
	Oswestry score	41.6	44.5	$-8.0 \pm 15.3$	$-5.5 \pm 14.3$
Oswestry score $\leq 20$ (% of patients)	19.5	16.3	$18.2 \pm 38.8$	$15.0 \pm 35.9$	$3.2$ ( $-8.6$ to $15.0$ )
Marked or very marked improvement (% of patients)§	—	—	$32.9 \pm 47.3$	$29.5 \pm 45.9$	$3.4$ ( $-11.4$ to $18.2$ )
Visual-analogue pain score for previous week	44.9	49.1	$-21.0 \pm 29.2$	$-12.4 \pm 27.3$	$-8.6$ ( $-17.5$ to $0.3$ )
McGill score					
Present pain intensity	2.2	2.4	$-0.4 \pm 1.3$	$-0.4 \pm 1.2$	$0.0$ ( $-0.4$ to $0.4$ )
Pain-rating index	19.5	21.5	$-8.1 \pm 15.9$	$-4.7 \pm 13.8$	$-3.4$ ( $-8.1$ to $1.3$ )
Sickness Impact Profile					
Overall	16.1	18.4	$-5.5 \pm 7.3$	$-3.0 \pm 9.3$	$-2.5$ ( $-5.1$ to $0.1$ )
Physical dimensions	12.9	13.8	$-5.9 \pm 8.4$	$-3.9 \pm 9.6$	$-1.9$ ( $-4.8$ to $0.9$ )
Psychosocial dimensions	10.8	15.5	$-5.1 \pm 8.8$	$-2.0 \pm 11.0$	$-3.1$ ( $-6.3$ to $0.1$ )
Restricted activity in previous two weeks (no. of days)	8.9	7.9	$-1.0 \pm 3.8$	$-1.8 \pm 4.9$	$0.8$ ( $-0.6$ to $2.2$ )
Finger-to-floor distance (cm)	29.5	33.3	$-6.0 \pm 11.3$	$-1.3 \pm 9.6$	$-4.7$ ( $-8.1$ to $-1.4$ )¶
Positive straight-leg test (% of patients)	77.9	82.5	$-13.0 \pm 37.5$	$-10.0 \pm 34.1$	$-3.0$ ( $-14.3$ to $8.3$ )
Motor deficit (% of patients)	23.4	13.8	$-6.5 \pm 33.8$	$-15.0 \pm 45.3$	$8.5$ ( $-4.1$ to $21.1$ )
Sensory deficits (% of patients)	32.5	41.3	$-29.9 \pm 48.8$	$-12.5 \pm 48.7$	$-17.4$ ( $-32.8$ to $-2.0$ )
Reflex changes (% of patients)	26.0	32.5	$-10.4 \pm 34.7$	$-8.8 \pm 42.7$	$-1.6$ ( $-13.9$ to $10.7$ )

\*Unless otherwise specified, values are means. One patient in the methylprednisolone group was lost to follow-up.

†The change from base line is the difference between the mean value (or proportion of patients) at the three-week visit and the corresponding mean (or proportion) at base line. Plus-minus values are means  $\pm$ SD or proportions  $\pm$ SD. Negative values indicate improvement in the outcome measures, and positive values worsening, except that for the proportion of patients with an Oswestry score of 20 or less and the proportion with marked or very marked improvement, negative values indicate worsening, and positive values improvement.

‡The treatment effect is the difference between the change in the methylprednisolone group and the change in the placebo group. Negative values indicate a positive treatment effect, and positive values a negative effect, except that for the proportion of patients with an Oswestry score of 20 or less and the proportion with marked or very marked improvement, positive values indicate a positive treatment effect, and negative values a negative effect. CI denotes confidence interval.

§Data were missing for one patient in the methylprednisolone group and two patients in the placebo group.

¶ $P=0.006$ .

|| $P=0.03$ .

**TABLE 4.** CLINICAL AND FUNCTIONAL OUTCOMES THREE MONTHS AFTER ENROLLMENT AND CHANGES FROM BASE-LINE VALUES, ACCORDING TO TREATMENT GROUP.

OUTCOME MEASURE	AT THREE MONTHS*		CHANGE FROM BASE LINE†		TREATMENT EFFECT (95% CI)‡
	METHYL- PREDNISOLONE (N=77)	PLACEBO (N=79)	METHYL- PREDNISOLONE (N=77)	PLACEBO (N=79)	
	Oswestry score	32.2	34.6	-17.3±20.6	
Oswestry score ≤20 (% of patients)	37.7	41.8	36.4±48.4	40.5±49.4	-4.1 (-19.6 to 11.3)
Marked or very marked improvement (% of patients)§	—	—	55.4±50.1	55.8±50.0	-0.4 (-16.5 to 15.7)
Visual-analogue pain score for previous week	38.9	39.5	-26.5±36.0	-22.5±34.4	-4.0 (-15.2 to 7.2)
McGill score					
Present pain intensity	1.9	1.9	-0.7±1.6	-0.9±1.5	0.2 (-0.3 to 0.7)
Pain-rating index	18.5	18.5	-9.1±18.9	-8.0±19.1	-1.2 (-7.2 to 4.9)
Sickness Impact Profile					
Overall	12.4	13.2	-9.2±10.8	-8.0±14.1	-1.2 (-5.2 to 2.8)
Physical dimensions	9.9	9.4	-8.8±11.6	-8.2±14.3	-0.6 (-4.7 to 3.6)
Psychosocial dimensions	8.7	12.1	-7.2±10.7	-5.3±14.9	-1.9 (-6.1 to 2.2)
Restricted activity in previous weeks (no. of days)	5.9	5.4	-3.9±6.1	-4.2±7.3	0.3 (-1.8 to 2.5)
Finger-to-floor distance (cm)	26.9	27.5	-9.0±13.7	-6.9±13.6	-2.2 (-6.6 to 2.2)
Positive straight-leg test (% of patients)	49.4	53.2	-41.6±52.2	-39.2±49.1	-2.3 (-18.4 to 13.7)
Motor deficit (% of patients)	15.6	12.7	-14.3±42.0	-16.5±51.7	2.2 (-12.8 to 17.1)
Sensory deficits (% of patients)	22.1	20.3	-40.3±56.8	-32.9±52.4	-7.4 (-24.6 to 9.9)
Reflex changes (% of patients)	19.5	27.8	-16.9±44.1	-13.9±52.5	-3.0 (-18.3 to 12.4)

\*Unless otherwise specified, values are means. One patient in each group was lost to follow-up.

†The change from base line is the difference between the mean value (or proportion of patients) at the three-month visit and the corresponding mean (or proportion) at base line. Plus-minus values are means ±SD or proportions ±SD. Negative values indicate improvement, and positive values worsening, except that for the proportion of patients with an Oswestry score of 20 or less and the proportion with marked or very marked improvement, negative values indicate worsening, and positive values improvement.

‡Negative values indicate a positive treatment effect, and positive values a negative effect, except that for the proportion of patients with an Oswestry score of 20 or less and the proportion with marked or very marked improvement, positive values indicate a positive treatment effect, and negative values a negative effect. CI denotes confidence interval.

§Data were missing for three patients in the methylprednisolone group and two patients in the placebo group.

interval for the difference, -9.3 to 5.4;  $P=0.60$ ). Approximately 55 percent of the patients in each group reported marked or very marked improvement. Fourteen of the 43 patients (33 percent) in the methylprednisolone group who were not working at base line because of their sciatica returned to work within three months, as compared with 18 of 41 patients (44 percent) in the placebo group.

The results of the secondary analyses (data not shown) were very similar to those shown in Tables 3 and 4. None of the changes in the outcome measures at the three-month visit differed significantly between the study groups.

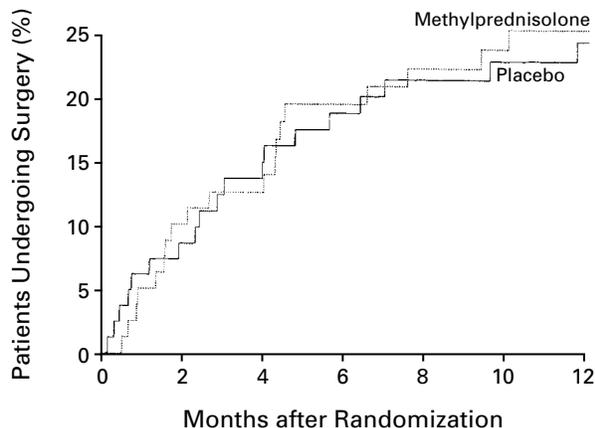
When asked at the end of the trial to guess what type of injection they had received, 18 of 69 patients (26 percent) in the methylprednisolone group and 25 of 71 (35 percent) in the placebo group thought they had received the placebo, and 29 patients (42 percent) in the methylprednisolone group and 32 (45 percent) in the placebo group said they did not

know. Responses were not available for nine patients in each group.

The patients were contacted by telephone in June 1996 to determine whether they had undergone back surgery since the end of the trial and, if so, the date of the surgery. Nine patients who had not had surgery within three months after enrollment could not be contacted (six in the methylprednisolone group and three in the placebo group). Data for these patients were censored at the date of the three-month visit. On the basis of the survival analysis, the cumulative probability of undergoing back surgery in the 12 months after randomization was 25.8 percent in the methylprednisolone group and 24.8 percent in the placebo group ( $P=0.90$  by the log-rank test) (Fig. 1).

## DISCUSSION

Our results are consistent with those of previous studies, which have suggested that the benefits, if any, of epidural corticosteroid injections for sciatica



**Figure 1.** Cumulative Probability of Back Surgery in 158 Patients with Sciatica Randomly Assigned to Treatment with Methylprednisolone or Placebo.

due to herniated nucleus pulposus are only short term.<sup>17</sup> Although there were no significant differences between the study groups in functional improvement as assessed by the Oswestry scores or in the proportion of patients reporting marked or very marked improvement at three weeks, six weeks, or three months, during the first six weeks of the trial, the patients who received epidural corticosteroid injections reported less leg pain than those who received placebo. In addition, 4 patients (5 percent) in the methylprednisolone group withdrew during the first six weeks of the trial because of lack of efficacy, as compared with 11 patients (14 percent) in the placebo group. In the absence of data on the patients' views of these outcomes, it is difficult to draw conclusions about their clinical importance.

To facilitate the interpretation of the magnitude of the treatment effect, effect sizes were calculated as suggested by Kazis et al. (the mean change in the methylprednisolone group minus the mean change in the placebo group, divided by the pooled standard deviation of the base-line means).<sup>32</sup> As guidelines for interpreting the size of the treatment effect, Cohen defined a value of 0.20 as a small effect, a value of 0.50 as a moderate effect, and a value of 0.80 as a large effect.<sup>33</sup> For leg pain, methylprednisolone injections had an effect size of 0.40 at three weeks and 0.50 at six weeks. With the exception of the effect size for the finger-to-floor distance at three weeks (0.30), the effect sizes of the outcome measures, including the Oswestry score, were small (less than 0.20). All the measures that we assessed improved over the course of the study, and at three months, there were no differences between the two treatment groups in any of the measures. Thus, we found that epidural corticosteroid injections do not afford

long-term advantages over placebo and that many patients with sciatica have improvement over time without specific treatment.

Our primary analysis, in which data obtained at the time of withdrawal were imputed to subsequent evaluations, assumed that no improvement occurred after withdrawal. This assumption was made more frequently for the placebo group (from which 22 patients withdrew) than for the methylprednisolone group (from which 13 patients withdrew). The natural history of back pain and sciatica is such, however, that most patients have spontaneous improvement over time. Thus, if any bias had been introduced by data imputation, it would have led us to overestimate the benefit of methylprednisolone injections.

Previous studies have reported that only 10 to 15 percent of patients with sciatica require surgical decompression.<sup>2</sup> The observation that as many as 25 percent of the patients enrolled in this trial underwent surgery within 12 months may be explained by the fact that to be eligible for the study, patients had to have had symptoms for a minimum of 1 month. The similar probability of surgery at 12 months in the two study groups (25.8 percent in the methylprednisolone group and 24.8 percent in the placebo group) underscores the absence of any long-term efficacy of epidural corticosteroid injections.

In our view, the absence of a therapeutic effect of epidural methylprednisolone injections cannot be explained by differences in the use of concurrent interventions in the two groups. There were minimal differences in the numbers of patients who received concurrent pharmacologic or nonpharmacologic treatments that were not allowed by the protocol and in the types of such treatments. In addition, it is unlikely that the small volume (1 ml) of saline injected into the epidural space in the placebo group caused a distention of the epidural structures that was sufficient to have a therapeutic effect.

In conclusion, we found that epidural injections of methylprednisolone, as compared with saline injections, afforded mild-to-moderate improvement in leg pain and sensory deficits and reduced the need for analgesics. However, the injections had no effect on functioning or the need for subsequent surgery.

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