Rheumatology 1999;38:1255–1259

A randomized, double-blind, placebo-controlled trial of sclerosing injections in patients with chronic low back pain

E. Dechow[1], R. K. Davies[1], A. J. Carr[2] and P. W. Thompson[1,3]

[1]Rheumatology Unit, Studland Centre, Poole Hospital NHS Trust, Longfleet Road, Poole, Dorset BH15 2JB, [2]Outcomes Research Unit, Kings College Hospital, East Dulwich Grove, London SE22 and [3]Bone and Joint Research Unit, Medical College, Royal London Hospital, Turner Street, London E1, UK

Abstract

Objective. To determine the clinical efficacy of sclerosing injections in patients with chronic low back pain.

Methods. Randomized, double-blind, placebo-controlled trial of three, once weekly injections of dextrose–glycerine–phenol with lignocaine *vs* saline plus lignocaine in patients with mechanical back pain of more than 6 months' duration. All patient assessments were performed blind by an experienced physiotherapist. The injections to the ligaments of the L4–5 and L5–S1 lumbar motion segments were given by an orthopaedic physician experienced in the technique, blinded to the nature of the injection solution according to a standard protocol. Demographic and clinical data, the short-form McGill Pain Questionnaire, the modified Somatic Pain Questionnaire, the Zung Depression Inventory, Oswestry Disability Scale and the modified Schober method of measuring spinal flexion were undertaken at 0, 1, 3 and 6 months.

Results. Seventy-four patients [mean (S.D.) age 45(11) yr, female:male ratio 1:1, median pain duration >10 yr] were recruited and there were no drop-outs over the study period. There were no statistically significant differences in patient characteristics between the placebo and treatment groups at baseline or for any measure at follow-up.

Conclusions. Three, weekly sclerosant injections alone may not be effective treatment in many patients with undifferentiated chronic back pain. Patient selection and combination with other treatment modalities may be factors in determining treatment success.

KEY WORDS: Sclerosing injections, Chronic low back pain, Pain questionnaires.

Sclerosing injections have been used in patients with chronic low back pain since the 1950s. They are advocated particularly in patients with clinical features of 'spinal instability' [1–5]. The rationale for their use is based on two premises. First, that the laxity of the ligaments and fascia supporting the lumbar motion segments is responsible for many cases of chronic low back pain [6] and second, that the injection of substances which initiate an inflammatory response will strengthen these ligaments and consequently reduce back pain [7, 8].

There are a number of reports suggesting that sclerosing injections are a safe and effective treatment for low back pain [9, 10], but we have identified only two randomized, controlled clinical trials, both undertaken in the Sansum Medical Clinic in Southern California (Ongley *et al.* [11] and Klein *et al.* [12]). They included different amounts of manipulative therapy and local anaesthesia in treatment protocols for treatment and control groups. The results are therefore difficult to interpret.

A number of adverse events including paralysis and death were reported with the use of early proliferative agents such as psyllium seed oil and zinc sulphate [13–15]. These events occurred following inadvertent intrathecal injection. The most commonly used solution amongst current practitioners is a mixture of glucose, glycerine and phenol which has been demonstrated to be safe.

At present, sclerosing injections are provided by Poole Hospital NHS Trust and purchased by general practitioners. They are popular but not cheap as they are classed as day case surgery and require three injection sessions at weekly intervals. We therefore designed a study to evaluate their effectiveness in patients with undifferentiated chronic low back pain.

Submitted 18 November 1998; revised version accepted 13 July 1999.

Correspondence to: P. W. Thompson, Rheumatology Unit, Studland Centre, Poole Hospital NHS Trust, Longfleet Road, Poole, Dorset BH15 2JB, UK.

Methods

Subjects

Patients with low back pain of more than 6 months' duration were recruited from those referred by their general practitioner to the Departments of Rheumatology and Orthopaedic Surgery in East Dorset. In order reliably to detect a 50% or greater difference in reported pain or disability between the placebo and active group as seen in the previous studies ($\beta = 90\%$, $\alpha = 0.05$) a total of 34 patients in each group was needed.

The inclusion criteria included males and females aged 18–71 yr with mechanical low back pain of more than 6 months' duration. Patients were excluded if they were pregnant or contemplating pregnancy, had evidence of nerve root entrapment, unresolved litigation, severe co-existing disease or body weight greater than 20 kg over their ideal.

Patients were randomly allocated (random number list) to placebo or active treatment.

The study had local Ethics Committee approval.

Assessment methods

Subjects were asked to complete a screening questionnaire that combined demographic characteristics with information about previous and present history and current medication and completed the following specific outcome tools: the short-form McGill Pain Questionnaire [16] which includes a summation of affective and sensory word scores (total word score), a 10 cm visual analogue scale (VAS) and a present pain intensity score; the pain drawing grid of Margolis [17]; the Modified Somatic Perception Questionnaire (MSPQ) [18]; the modified Zung Depression Inventory [19]; the Oswestry Disability Scale [20] which covers self-reported difficulty with a range of activities of daily living; and a physical examination that included the modified Schober [21] method of measuring spinal flexion.

Patients were assessed by an experienced physiotherapist blinded to the treatment groups prior to treatment and at 1, 3 and 6 months following the treatment. After written informed consent they were randomly allocated to either the treatment group or the control group. The treatment group received three, once weekly injections of a solution of 5 ml of dextrose 25%, glycerine 25% and phenol 2.4% made up to 100 ml with sterile water combined with 5 ml of 1% lignocaine. The control group received three, once weekly injections of 5 ml of the normal saline solution combined with 5 ml of 1% lignocaine.

Procedure

Injections were given according to established procedure by an experienced operator [11]. A rigid $3'' \times 20$G, $3'' \times 22$G or occasionally $3.5'' \times 20$G needle was used. All injections were made from a single insertion into the following sites: tip of the spinous process of L4 and L5 and associated supraspinous and interspinous ligaments; apophyseal joint capsules at L4–5 and L5–S1; attachment of the iliolumbar ligaments at the transverse processes of L5; attachment of the iliolumbar and dorsolumbar fascia to the iliac crest; and attachments of the long and short fibres of the posterior sacroiliac ligaments and the sacral and iliac attachments of the interosseous sacroiliac ligaments. The majority of patients received light intravenous sedation with midazolam.

Baseline results were compared using Mann–Whitney and *t*-tests. Mean scores for the questionnaire results and lumbar flexion for the measurements at baseline, 1, 3 and 6 months were compared using one-way analysis of variance (ANOVA).

Results

Seventy-four patients were recruited and there were no drop-outs over the study period. There were no statistically significant differences between the placebo and treatment groups at baseline (Table 1). All patients receiving compensation had had their claims settled.

Figure 1 shows the mean and standard errors for the short-form McGill Pain Questionnaire (VAS, total word scores and present pain intensity) and the pain drawing grid by Margolis. There was a trend downwards in both groups over the study period, but this did not reach statistical significance. Figure 2 shows the mean and standard errors for the MSPQ scores, the Zung Depression Inventory, the Oswestry Disability Questionnaire and lumbar flexion. There was a trend downwards for MSPQ that did not reach statistical significance, but no change in depression or self-reported disability. There was a trend to increased spinal flexion in both groups, but this did not reach statistical significance. There were no significant differences between the placebo and treatment groups for any measure over the 6-month follow-up.

TABLE 1. Demographic data for the placebo and treatment groups at baseline expressed as numbers, mean (S.D.) or percentages. There were no statistically significant differences between the means (*t*-test) or percentages (Mann–Whitney) for any parameter

	Placebo	Treatment
n	38	36
Age (yr)	46 (11)	44 (11)
Female:male	18:20	20:16
Duration of pain		
< 5 yr	12	8
5–10 yr	5	10
> 10 yr	21	18
Weight (kg)	71 (13)	73 (16)
Height (m)	1.72 (0.08)	1.71 (0.09)
Lumber flexion (m)	0.052 (0.013)	0.049 (0.015)
Work related	16%	14%
Compensation	5%	17%
Back surgery	11%	11%
Receiving benefits	32%	39%
Currently employed	50%	52%
Current smoker	34%	33%
Other treatments	8%	11%
Taking analgesics	63%	67%

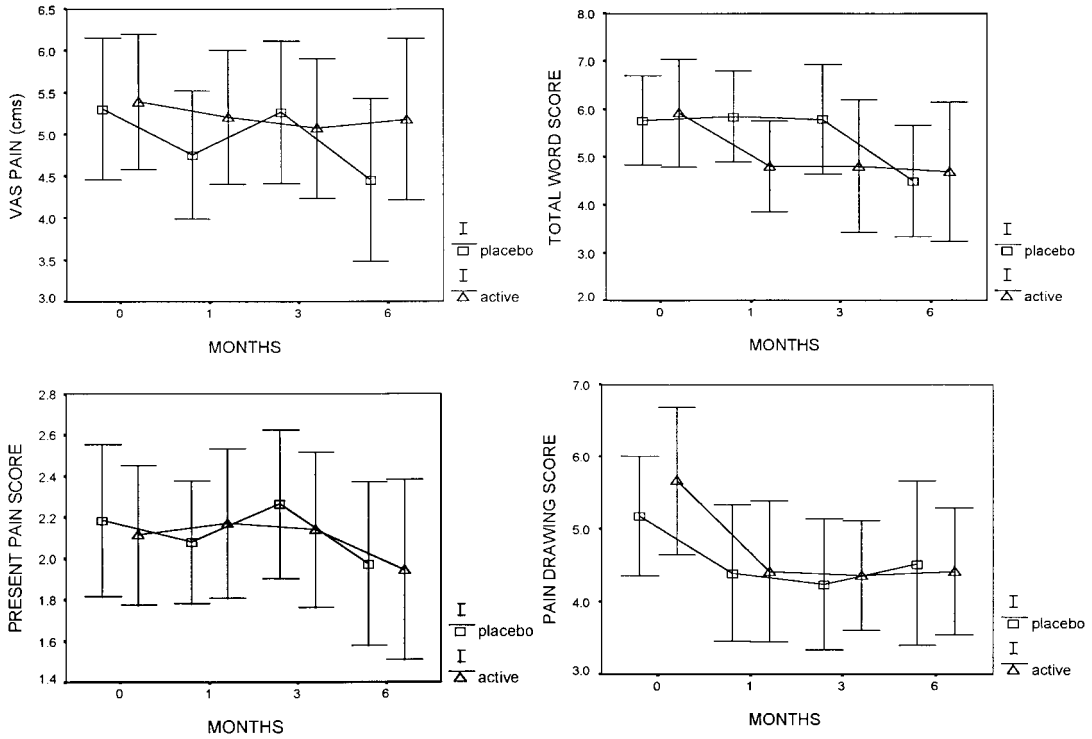

FIG. 1. Means and standard errors in bars over time for treatment and placebo groups for the visual analogue pain scale, present pain score and total word score of McGill, and pain drawing score of Margolis.

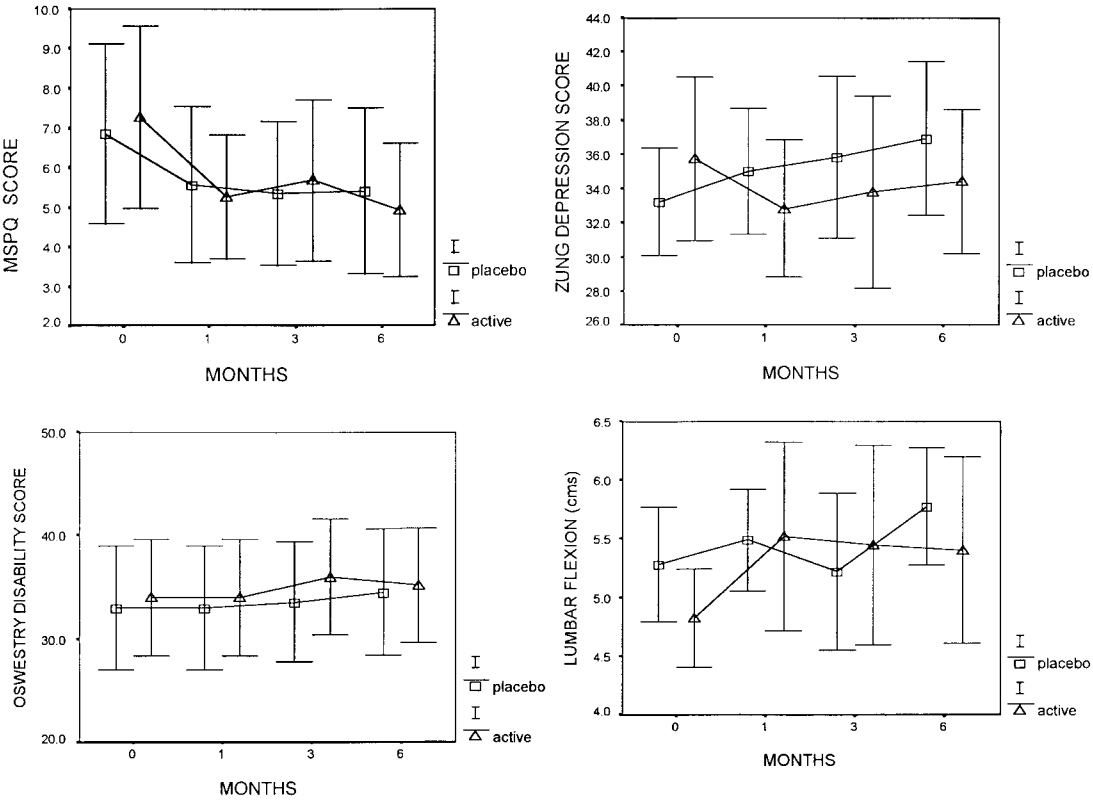

FIG. 2. Means and standard errors in bars over time for treatment and placebo groups for the Oswestry Disability score, Modified Somatic Perception Questionnaire score, Zung Depression score and lumbar flexion by the modified Schober method.

Patients with symptoms of longer than 10 yr were significantly older and heavier than those with a shorter history, but there were no significant differences between placebo and treatment groups for any measurement parameter when analysed according to age group (<5 yr, 5–10 yr or >10 yr).

There were no significant differences in the results when analysed without the patients who were receiving compensation.

A few subjects reported a transient increase in back pain following the injections, but there were no differences between the treatment and control groups and no other significant adverse reactions.

Discussion

Our findings suggesting that sclerosing injections are of no greater benefit than placebo in the treatment of patients with chronic low back pain appear at odds with the studies of Ongley and Klein and the clinical experience of many physicians both in Europe and North America [22].

The reasons for this discrepancy may be related to patient selection (see [11, p. 37]), radiological, racial or social differences between the trial centres, technical differences in the treatment programmes, or insensitivity of the assessments.

Our patients represent a heterogeneous population with undifferentiated chronic low back pain. They were not specifically identified as likely to benefit from sclerosing therapy, for example clinical features of 'spinal instability' were not sought (defined clinically as episodic severe exacerbations of pain and muscle spasm following minor movement). Many patients were not considered ideal candidates for sclerosing injections by the operator at the time of the treatment for a variety of reasons relating to technical difficulties, deconditioning, patients relying on invalidity benefit, excessive psychological stress, etc. even though they technically fulfilled the inclusion criteria. Therefore, the group of patients recruited into our study was likely to respond poorly to any single intervention in keeping with the relatively poor prognosis in the group of patients in the UK today. These factors may also account for the surprising lack of a significant placebo effect in our study compared with the Californian trials. These patients may be better suited to functional restoration or pain management programmes.

The patients in the Californian studies showed a spectrum of radiological and imaging disorders characteristic of the heterogeneous nature of patients with chronic mechanical back pain. We have not assessed these parameters in our subjects and it is possible that differences exist. Furthermore, there are likely to be racial, social and geographical differences between Southern California and Dorset that might influence the response to the interventions.

Our study compared sclerosant injections with placebo. The Ongley and Klein protocols were more complicated involving several procedures. Patients underwent infiltration of lignocaine into specific sites followed by spinal manipulation and injection of triamcinolone into the gluteus medius origin. In the Klein study both placebo and treatment groups received the same protocol but the placebo group in the Ongley study received a smaller dose of lignocaine (10 ml of 0.5% compared with 60 ml 0.5%) and a sham manipulation. In both studies there followed six weekly ligament injections of either sclerosant mixture or placebo according to the protocol described previously. All patients were taught flexion and extension exercises and were encouraged to continue at subsequent visits. In both studies there were significant improvements in both treatment and placebo groups. The magnitude of the improvement was greater in the Ongley study which made a comparison of the complete regimen than in the Klein study where both treatment and placebo groups received manipulation, corticosteroid injections and exercises. While comparison is difficult the differences in results suggest that the complete regimen is more effective than the component parts. While we have been unable to demonstrate improvement with sclerosant injections alone, their combination with manipulation, corticosteroids and exercise appears to be beneficial. Furthermore, it may be that six weekly injections are required before a benefit can be demonstrated.

We aimed to use similar outcome measures to the Californian studies in order to allow reasonable comparison. They evaluated pain using an 8 cm VAS scale, the pain drawing grid of Margolis and the disability questionnaire of Roland and Morris [23]. Both the latter and the Oswestry Disability Questionnaire are validated tools of self-reported disability in patients with back pain and have been used and evaluated more frequently than other scales [24]. Thus, it seems unlikely that differences in outcome assessments could explain the differences between the three trials.

Finally, the power of our study was calculated to not miss a 50% difference between placebo and treatment groups with confidence. It is possible that we have missed a smaller improvement that would be clinically significant. We chose the 50% level because of the large placebo response seen in the other studies.

In summary, following three, weekly sclerosant injections to the lumbar spinal ligaments we have been unable to demonstrate improvement in pain, self-reported function, somatization, depression or spinal flexion in patients with undifferentiated chronic back pain. The results might be explained in terms of differences in patient selection, underlying pathology, social circumstances, additional treatment modalities or insufficient power of the study. Further research is needed to identify which components of the regimens are most effective and whether there are subgroups of patients who are more likely to respond to these safe treatments.

Acknowledgements

The authors thank the staff of the Pain Relief Clinic at Poole Hospital, Drs Richard Ellis and Nigel North,

Salisbury Hospital for clinical and statistical advice and the patients who took part. The study was funded by the South and West Region Research and Development Programme (Project Grant R/21/9.95/Thompson).

References

1. Hackett GS. Ligament and tendon relaxation treated by prolotherapy, 3rd edn. Springfield: Charles C. Thomas, 1958.
2. Neff F. Back pain and disability. W Med 1960;1:12–7.
3. Myers A. Prolotherapy treatment of low back pain and sciatica. Bull Hops Joint Dis 1961;22:48–55.
4. Peterson TH. Injection treatment for back pain. Am J Orthop 1963;5:320–5.
5. Coplans CW. The conservative treatment of low back pain. In: Helfet AJ, Gruebel DM, eds. Disorder of the lumbar spine. Philadelphia: J.B. Lippincott, 1978.
6. Banks AR. A rationale for prolotherapy. J Orthop Med 1991;13:54–9.
7. Klein RG, Dorman TA, Johnson CE. Proliferant injections for low back pain: histological changes of injected ligaments and objective measurements of lumbar spinal mobility before and after treatment. J Neurol Orthop Med Surg 1989;10:123–6.
8. Liu YK, Tipton CM, Matthes RD, Bedfork TG, Maynard JA, Walmer H. An *in situ* study of the influence of a sclerosing solution in rabbit medial collateral ligaments and its junction strength. Connect Tissue Res 1983;11:95–102.
9. Dorman TA. Treatment for spinal pain arising in ligaments using prolotherapy: a retrospective survey. J Orthop Med 1991;13:54–9.
10. Schwartz RG, Sagedy N. Prolotherapy: a literature review and retrospective study. J Meurol Orthop Med Surg 1991;12:220–33.
11. Ongley MJ, Klein RG, Dorman TA, Eek BC, Hubert LJ. A new approach to the treatment of chronic low back pain. Lancet 1987;2:143–6.
12. Klein RG, Eed BC, Delong B, Mooney V. A randomised-double blind trial of dextrose–glycerine–phenol injections for chronic low back pain. J Spinal Dis 1993;6:23–33.
13. Hunt WE, Baird WC. Complications following injections of sclerosing agents for precipitating fibro-osseous proliferation. J Neurosurg 1961;18:461–5.
14. Keplinger JE, Bucy PC. Complications following injections of sclerosing agents—report of a case. J Am Med Assoc 1960;73:1333–6.
15. Schnieder RC, Williams JI, Liss L. Fatality from treatment with sclerosing agent to precipitate fibro-osseous proliferation. J Am Med Assoc 1959;170:1768–72.
16. Melzac R. The short-form pain questionnaire. Pain 1987;30:191–7.
17. Margolis RB, Raymond CT, Krause SJ. A rating system for use with patient pain drawings. Pain 1986;24:57–65.
18. Main CJ. The modified somatic perception questionnaire. J Psychosom Res 1983;27:503–14.
19. Zung WWK. A self-rated depression scale. Arch Gen Psychiat 1964;32:63–70.
20. Fairbanks JCT, Davies JB, Couper J, O'Brien JP. The Oswestry low back pain disability questionnaire. Physiotherapy 1980;66:271–3.
21. Williams R, Blinkley J, Bloch R. Reliability of the modified–modified Schober and double inclinometer methods for measuring lumbar flexion and extension. Phys Ther 1993;73:26–37.
22. Dorman TA. Prolotherapy: a survey. J Orthopaed Med 1993;15:49–50.
23. Roland MR, Morris RM. A study of the natural history of low back pain. Spine 1983;8:145–50.
24. Beurskers AJ, De Vet HC, Koke AJ *et al.* Measuring functional status in patients with low back pain. Spine 1995;20:1017–28.