Long-term results of cervical epidural steroid injection with and without morphine in chronic cervical radicular pain

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Summary To evaluate the long-term effectiveness of a single cervical epidural steroid injection (CESI) performed with or without morphine, 24 patients, without need of surgery, but suffering for more than 12 months from cervical radicular pain, were included in a prospective and randomised study. The cervical epidural space was injected (C7-D1; 18-ga needle) with an increasing volume (10 ml maximum) of isotonic saline solution to exacerbate the patient's radicular pain. The patients were then randomly allocated to 2 groups: the steroid group (group S, n = 14) received an equivalent volume of 0.5% lidocaine plus triamcinolone acetonide (10 mg/ml) and the steroid plus morphine group (group S + M, n = 10) received the same combination plus 2.5 mg of morphine sulphate. Pain relief was assessed as the percentage of pain decrease on a visual analogue scale on day 1 and at months 1, 3, 6, 8 and 12 after CESI, up to 48 months. Anthropometric data between the 2 groups were similar. The mean volume injected in the epidural space was: 6.6 ± 2.1 and 6.3 ± 1.9 ml in groups S and S + M, respectively, and this volume exacerbated pain in 21 of 24 patients. Despite observing a better transient improvement the day after CESI in the S + M group, long-term results did not differ. The success rate was 78.5% in group S and 80% in group S + M providing pain relief of 86.8 ± 14.7% and 86.9 ± 17.9%, respectively. Pain relief remained stable with time (mean follow-up: 43 ± 18.1 months). These results suggest that a single CESI performed in such cases produces long-lasting pain relief which is not improved when morphine is combined with steroid.

Key words: Epidural; Steroid; Morphine; Cervical pain

Introduction

Cervical epidural steroid injection (CESI) has been proposed in the management of patients with chronic cervical pain (Purkis 1986; Rowlingson and Kirschenbaum 1986; Shulman 1986). This treatment has also been tested in a few patients suffering from spinal stenosis (Shulman 1986) and in a few others with documented compressive lesions (Rowlingson and Kirschenbaum 1986). It has also been proposed for patients suffering from cervical radicular pain (CRP) related to cervical degenerative disease (Purkis 1986) and to cervical radiculopathy (Rowlingson and Kirschenbaum 1986). Yet, CESI techniques are as different as the indications are numerous and the success rate ranges from 40% to 64% (Purkis 1986; Rowlingson and Kirschenbaum 1986; Shulman 1986). However, these results were only analysed retrospectively over varying periods and using different follow-up methods. Thus, in the absence of prospective studies, the real effectiveness of CESI still remains unclear.

On the other hand, results obtained in vitro have shown that opiates might lead to a long-lasting decrease in the excitability of the C fibres (Power et al. 1991). It has also been reported that in patients with recurrent low-back pain, co-administration of morphine and steroids provides better long-lasting pain relief than that induced by each drug alone (Cohn et al. 1986). The present study was thus designed to assess the short-, mid- and long-term effectiveness of a single
CESI performed with or without morphine, in patients with chronic CRP of non-compressive and non-malignant origin whose indications did not require surgery.

Methods

Subjects

After approval of our Ethical Committee, 24 patients were included in a prospective randomised study between January 1986 and January 1991. Exclusion criteria were having undergone cervical spine surgery, malignancy, or having anticoagulant medication. Patients were included after clinical examination and after the systematic investigations including X-ray, myelography and CT scan and electrophysiology had not revealed any pathology. Moreover, each patient had had an ineffective medical treatment for at least 12 months including activity restriction, physiotherapy, and a variety of drugs such as non-steroidal anti-inflammatory agents (NSAID), analgesics, skeletal muscle relaxants, anxiety-relieving and antidepressive drugs. This treatment was considered ineffective since the pain, although temporarily decreased by the treatment, had become permanent, i.e., incessant day and night, for at least 3 months, and had then been considered as intolerable by the patients. The CRP was associated with dysesthesia in a radicular dermatomal distribution and was the only clinical sign in the absence of isolated facet syndromes or motor weaknesses. As surgery was not indicated and since medical treatment remained ineffective, CESI was finally decided for these patients.

CESI procedure

After verbal consent, epidural injection was performed by the same anaesthetist (L.C.) in an induction anaesthetic room. An intravenous line (glucose 5%) was inserted and vital signs such as electrocardiogram and blood pressure were monitored. After local infiltration with 1% lidocaine, an 18-ga epidural needle was introduced in sterile conditions into the C7 T1 interspace, with the patient lying on his painful side. The epidural space was identified with the saline loss-of-resistance technique. An increasing volume of isotonic saline was then injected over a 10-sec period to try to exacerbate the patient's radicular pain. If this bolus triggered the CRP, the injection was then stopped and the volume exacerbating the pain was noted. In the absence of pain exacerbation, the maximum volume of bolus injected was 10 ml. An identical volume of saline for washing the epidural space was injected 10 min later. The patients were then randomly allocated into 2 groups to receive the same volume containing 1% lidocaine as solvant and the total dose of triamcinolone acetonide was volume-dependent, whereas the dose of morphine was the same for each patient. Successful epidural deposition of the agents was indicated by transient numbness in one or both hands. The patients were kept in intensive care for 24 h where electrocardiogram and pulse oximetry were monitored. Morphine-induced side effects were treated by incremental doses of naloxone hydrochloride injected intravenously.

Evaluation criteria

Before the CESI, the patients had complained of a permanent intolerable pain that they themselves rated at 100 mm on a visual analogue scale (VAS). This was the pain control value. After the CESI, the patients were asked to again rate their pain on the VAS. The effectiveness of the treatment was evaluated as the percentage of pain decrease on the VAS. This was recorded on day 1 and months 1, 3, 6, 8 and 12 after CESI during a complete clinical examination. At the end of the last examination, all patients received a VAS scale and a graph plotting pain against time. They were informed that we would phone them 18, 24, 36 and 48 months after treatment in order to follow-up pain evolution. The results were rated according to the pain decrease on the VAS: decreases of 100, 75–99, and 51–74 mm were termed complete, excellent and good results, respectively. Decreases of 25–50, 25, and 0 mm were termed fair, poor and failure, respectively. The overall follow-up period was at least 12 months.

Morphine-induced side effects (pruritus, nausea, vomiting, dizziness, urinary retention, respiratory depression and cardiovascular instability) were noted.

The medical treatment was analysed at the same periods and then compared to the pre-operative status.

Return to work and work status were also analysed.

TABLE I

CHARACTERISTICS OF PATIENTS SUFFERING FROM CERVICAL RADICULAR PAIN FROM NON-COMPRESSIVE ORIGIN AND TREATED EITHER WITH STEROIDS (GROUP S) OR WITH STEROIDS + MORPHINE (GROUP S + M)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group S</th>
<th>Group S + M</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>24</td>
<td>14</td>
</tr>
<tr>
<td>Age (M/F)</td>
<td>47.7±8</td>
<td>50.16±8.9</td>
</tr>
<tr>
<td>Follow-up (months)</td>
<td>43±18.1</td>
<td>48.4±18.6</td>
</tr>
<tr>
<td></td>
<td>(12-68)</td>
<td>(12-68)</td>
</tr>
</tbody>
</table>

TABLE II

SHORT- AND MID-TERM PAIN RELIEF RESULTS OF A SINGLE CERVICAL EPIDURAL INJECTION OF EITHER STEROIDS ALONE (GROUP S, n = 14) OR STEROIDS + MORPHINE (GROUP S + M, n = 10) PERFORMED IN 24 PATIENTS SUFFERING FROM CERVICAL RADICULAR PAIN BUT WITH NO COMPRESSIVE LESIONS

<table>
<thead>
<tr>
<th>Pain relief</th>
<th>1 Day</th>
<th>1 Month</th>
<th>3 Months</th>
<th>6 Months</th>
<th>8 Months</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S</td>
<td>S + M</td>
<td>Total</td>
<td>S</td>
<td>S + M</td>
<td>Total</td>
</tr>
<tr>
<td>Complete</td>
<td>5</td>
<td>3</td>
<td>8</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Excellent</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>6</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Good</td>
<td>6</td>
<td>3</td>
<td>9</td>
<td>10</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>% Success</td>
<td>95.8</td>
<td>75</td>
<td>79.2</td>
<td>79.2</td>
<td>79.2</td>
<td>79.2</td>
</tr>
<tr>
<td>Fair</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Poor</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>None</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
TABLE III
EVALUATION OF DRUG CONSUMPTION IN THE 24 PATIENTS BEFORE AND 3 MONTHS AFTER CESI

<table>
<thead>
<tr>
<th>Drug consumption</th>
<th>NSAID</th>
<th>Analgesics</th>
<th>Anxiety-relieving</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before (n)</td>
<td>After (n)</td>
<td>Before (n)</td>
</tr>
<tr>
<td>Permanent or episodic</td>
<td>24</td>
<td>4</td>
<td>24</td>
</tr>
<tr>
<td>Never</td>
<td>0</td>
<td>20</td>
<td>0</td>
</tr>
</tbody>
</table>

| P < 0.001 | P < 0.001 | P < 0.05 |

Statistical analysis
Results were expressed as means ± SD and were compared using the non-parametric U Mann-Whitney test. Qualitative results were compared using the exact probability test (Fisher test). Results were considered as significant when P < 0.05.

Results
The anthropometric data of the 2 groups are listed in Table I. No difference between the S and S + M groups was noted. The mean follow-up periods and the mean volume injected were also similar: 44.8 ± 18.6, and 40.4 ± 19.8 months and 6.6 ± 2.1 and 6.3 ± 1.9 ml in groups S and S + M, respectively. The mean dose of triamcinolone acetonide was not significantly different: 66 ± 21 and 63 ± 19 mg for S and S + M, respectively. The initial saline injection exacerbated radicular pain in 21 patients, whereas a maximum volume of 10 ml gave no pain in 1 patient in group S and in 2 patients in group S + M.

Sixteen patients had stopped work over 3 months, 6 were retired (5 and 1 in groups S and S + M, respectively) and 2 (1 in each group) had been unemployed for more than 1 year.

Side effects
CESI was uneventful for all patients in group S, whereas the addition of morphine produced minor side effects in all but 1 patient. Pruritus was observed in 9, nausea in 4, dizziness in 3 patients. Such adverse side effects were immediately treated with incremental doses of naloxone injected intravenously and, as a result, vomiting, urinary retention, respiratory depression and cardiovascular instability were not observed.

Analgesia
The durations of short- and mid-term pain relief are listed in Table II. Although a higher proportion of complete and excellent results was observed in group S + M the day after CESI (P < 0.03), there was no other difference between the 2 groups after this period. Three months after CESI, complete and excellent results were observed to the same degree: 71.4% and 70% in groups S and S + M, respectively. A pain decrease of more than 50 mm was observed in 78.5% and 80% of the cases corresponding to a decrease on the VAS of 86.82 ± 14.7 mm and 86.88 ± 17.9 mm in groups S and S + M, respectively, when compared to the 100 mm control value. Two patients had a 51 and 52 mm decrease in pain. As shown in Table II and illustrated in Fig. 1a,b, the improvement no longer varied 3 months after CESI. The two fair results were in group S.

No poor results were noted. The 3 failures were the 3 patients in whom pain was not exacerbated by the saline rapid injection test. They reported no change in pain from 1 to 12 months after treatment. On the other hand, pain was exacerbated in the 21 remaining patients, and 17 of these (80.8%) had a decrease in pain greater than 75 mm.

![Fig. 1](image-url)
Regarding long-term evolution (Fig. 1a,b), pain relief remained stable for 48 months (n = 11) and in some cases for more than 60 months (n = 9).

The intensity of the medical treatment decreased significantly 3 months after CESI (Table III) and remained unchanged over subsequent periods. Thirteen patients having more than 89% pain relief stopped taking NSAID or analgesics after CESI. Four patients having relief ranging from 75% to 89% needed analgesics from time to time 3 months after CESI. The medical treatment was not strongly altered by CESI in patients having fair results after CESI.

All the 16 working patients returned to work whatever the result obtained after CESI. No correlation was found between pain relief and absenteeism: 17 patients returned to work 1 month after CESI. One patient from group S + M returned to work after the third month despite a 51% pain relief. The 2 unemployed patients reported 52% and 80% relief from pain respectively. Two of the retired people gained no benefit from CESI, 1 obtained a fair result, and 3 got more than 75% pain relief 3 months after CESI.

Discussion

We performed the CESI procedure in patients suffering from non-malignant chronic cervical radicular pain, of which the etiology remained undetermined. Since they were no compressive lesions, these patients did not require surgical treatment, so the mechanism accounting for CRP was postulated to be a form of 'irritation'. Using a process of elimination, Purkis (1986) suggested that this diagnosis might be related to cervical spine osteoarthritis and that in such cases CESI might be a good indication. Assuming that pain is related to a purely inflammatory process, injection of steroids could indeed be relevant regarding both their analgesic (Johansson et al. 1990) and anti-inflammatory actions (Winnie et al. 1972). We have attempted to define this postulated diagnosis of an 'irritative' inflammatory process more accurately by injecting a rapid bolus of saline in the epidural space close to the painful site. Since epidural injection of fluid increases epidural pressure (Usubiaga et al. 1967), we thought that this might result in a mechanical stretching of the nerve root. If so, this process could induce a radiating pain in cases of nerve root irritation, as experimentally demonstrated by others (Bogduk and Cherry 1985). This was the rationale for the first phase of our injection technique. The second phase consisted in re-injecting the epidural space with saline with the aim of 'breaking' some peridural adhesions associated with either the initial osteoarthritis (Revel et al. 1988) or with the chronic inflammatory state causing nerve root entrapments (Rydevik et al. 1984). In addition, since inflammatory substances tend to leak after mechanical or chemical irritation of a nerve root (Murphy 1977), this saline re-injection might also wash out exudates from the epidural space. The third phase was the procedure and consisted in injecting a personalised dose of steroids using a volume equivalent to that having eventually exacerbated the pain. A local anaesthetic was used only as a transient block to test that the agent had really reached the appropriate site of action.

Using such a technique, a single injection significantly improved pain relief in 79% of patients. It is likely that these results are better than those reported in the literature. Indeed, the reported efficacy of CESI ranges from 40% (Shulman 1986) to 62.5% (Purkis 1986). However, as far as complete and excellent results are concerned (i.e., a pain decrease of more than 75 mm on the VAS), the results of this study come close to those of Rowlingson and Kirschenbaum (1986): 17 of our 24 patients (70.8%) and 16 of their 25 (64%), respectively. Both the small size of each group and the lack of accuracy of the evaluation criteria could account for at least a 10% discrepancy in the results observed. On the one hand, a placebo group (i.e., patients having needle insertion but no fluid or no treatment injection) would have been of value in assessing the real efficacy of CESI; unfortunately the Ethics Committee did not allow us to use such a method. On the other hand, a placebo effect has already been quantified ranging from 0% to 27% for chronic lumbar pain (Sayle-Creer and Swerdlow 1969; Yates 1978; Busch and Hillier 1991), and it is likely that this effect had little influence on the final results. Taking this into account, it is clear that several variables might shift the VAS evaluation up or down. However, the fact that we found a good relationship between the pain decrease score and the need for a specific medical treatment is a strong argument in favour of the real long-lasting efficacy of CESI. No conclusion can be drawn in this study about return to work, as all patients including the failure case returned to work.

The failures were observed in the first month (Fig. 1a,b), usually within 10 days after injection, and were observed in the same patients who had no pain exacerbation with the saline injection. It is likely that these patients were probably suffering from nerve root fibrosis rather than inflammation, and it is well known that in such cases, steroids (Rowlingson and Kirschenbaum 1986) or morphine (Tasker 1984) are of minor interest. Repeated injections might be of value in such patients, although conflicting results are reported in the literature. Purkis (1986) showed that repeated injections increased the success rate from 31.2% to 62.5%, although this was not confirmed by Shulman (1986).

Regarding the use of morphine, Cohn et al. (1986) reported a long-lasting analgesia using epidural steroids.
plus morphine in patients suffering from recurrent low-back pain. In the present study, the addition of morphine did not improve the results obtained with steroids alone. This may be accounted for by different indications, different injection sites, and also differences in pain mechanism. Although injection of steroids alone was totally uneventful and can be performed as an outpatient procedure, the addition of morphine induced adverse effects contraindicating this procedure for such patients. Thus, in our opinion, the addition of morphine did not seem to provide any benefit in our patients.

We conclude that in patients suffering from chronic CRP unrelated to a compressive or malignant origin and not needing surgery, a single CESI could be helpful when medical treatment remains ineffective. It produces excellent and complete long-term results in 70.8% of cases. Although morphine produces a better transient improvement the day after CESI, the long-term follow-up is not altered.

References