THE RESPONSE TO EPIDURAL STEROID INJECTIONS IN CHRONIC DORSAL ROOT PAIN*

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ABSTRACT

Thirty-seven patients with long-standing post-herpetic neuralgia and 27 with post-traumatic neuralgia (PTN) were treated with three epidural injections each of methylprednisolone acetate (Depo Medrol) given at weekly intervals. Differential subarachnoid or epidural block was done in all patients and placebo responders were excluded from the study. Mean age, duration of symptoms, and pain intensity measured by visual analogue scale were similar in both groups. Visual analogue scale ratings were reduced one month after treatments from pretreatment values of 84.4 and 78.7 to 9.6 and 15.2 in the post-herpetic and post-traumatic groups respectively, and were further reduced to 4.6 and 11.6 respectively after one year when 89 per cent of patients in the post-herpetic group and 59 per cent of patients in the post-traumatic group were completely pain free. Side effects were minor in all cases. It is suggested that this is the treatment of choice in post-herpetic and post-traumatic neuralgia where steroid administration is not contraindicated.

THE NEURALGIAS associated with previous herpes zoster infection or trauma to segmental spinal nerves are clinically similar, suggesting a common aetiological basis. While the acute lesion manifests itself as an affection of peripheral nerves, inflammation of the dorsal root ganglion is the basic pathological process in both cases.[1] In most cases only a single spinal nerve is involved but occasionally two or more adjacent nerves are affected. Following healing of the acute lesion which occurs within two to six weeks, pain can arise immediately or after several months or even years. It is reputed that in the young these neuralgias persist for only a few weeks, while in patients over 60 years of age moderate to severe pain may continue for more than two months in as many as 50 per cent of patients.[2] The pain is typically intermittent at first, but within a few weeks becomes continuous, burning and radiating within the distribution of the segmental nerves involved in the acute lesion. The latency between the acute lesion and the onset of neuralgia has been ascribed to activation of varicella-zoster virus within dorsal root ganglion cells, at least for those patients who develop post-herpetic neuralgia.[3] This activation may be due to depression of cell mediated immunity, since there is a much higher incidence in patients with neoplastic disease, especially Hodgkin's disease, where 25 per cent of cases have associated neuralgias of segmental nerves.[4]

Episodes of extreme radiating pain triggered by light stimulation of the peripheral nerve endings in the affected segment are common in both conditions, may last for several hours and in severe cases occur repeatedly every day. Despite major advances in the management of the acute lesions, these chronic neuralgias continue to present as a difficult and often intractable clinical problem. Their treatment has included repeated local anaesthetic injections, transcutaneous electrical nerve stimulation, ammonium sulphate injection of nerves, injections of sclerosing solutions such as absolute alcohol and phenol, neurectomy, lateral spinal rhizotomy and various combinations of analgesic and antidepressant drugs.[5-8] All of these have been of questionable value at best, with the number of successes invariably less than the generally accepted rate for placebo responders.

Since the common lesion in both types of neuralgia would seem to be an inflammatory reaction in dorsal root ganglia, it was reasoned that locally applied steroids might be an effective means of reducing this reaction on a long-term basis. Epidural injections of corticosteroids have been used for a number of years since Barry and Kendall[9] first described their use in sciatic nerve root compression. It is clear from the results reported in a variety of lumbosacral pain syndromes that the best response occurs when a significant inflammatory component is pres-

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ent.[1,10-17] A preliminary report of response in patients with post-herpetic, post-traumatic or idiopathic dorsal root pain, to epidural injections of methylprednisolone (DepoMedrol) showed significant reduction in pain only in the post-herpetic and post-traumatic groups.[18]

The present paper describes the results of epidural injections of methylprednisolone in a much larger series of patients with long-standing post-herpetic or post-traumatic neuralgia. The treatment protocol used was identical to that described in the earlier report.[18]

Materials and Methods

Patients

Sixty-three patients, 37 females and 26 males, with a mean age of 51 years (range 22 to 79) who presented with dorsal root pain of more than six months' duration were included in this study. Only patients with known previous herpes zoster (shingles) infection or segmental nerve trauma were included. A number of patients were excluded on the basis of unacceptable risk from steroid medication, such as established peptic ulceration, previous tuberculosis, or diabetes mellitus. Patients with dorsal root pain associated with spinal neoplastic disease, intervertebral disc disease or spinal arthropathies were also excluded, even if previous herpes zoster infection or segmental nerve trauma was also present. Thus the patients included in this study were highly selected on the basis of the above presumptive aetiological factors and the absence of other causes for their pain or contraindications to steroid medication. In every case, one or more other forms of treatment such as analgesics with or without antidepressant drugs, transcutaneous electrical nerve stimulation or repeated local anaesthetic blocks, had been tried and failed to give long-term pain relief.

Initial assessment and diagnostic differential spinal block

All patients were seen in consultation in the Pain-Nerve Block Clinic, a division of the multidisciplinary Pain Clinic at McMaster University Medical Centre. A detailed history of the presenting complaint and a full history were obtained, and a full physical examination was carried out at the initial visit. All past and present medications and other treatments were noted. A psycho-social assessment, including a Minnesota Multiphasic Personality Inventory and a pain questionnaire were completed as appropriate. Routine chest X-ray, full blood count and urinalysis and any specifically indicated laboratory and radiological studies were done. Each patient was assessed as to suitability for steroid medication.

Pain intensity was rated using a visual analogue scale consisting of a 10 cm line marked on the left as "no pain" and on the right as "unbearable pain". This method of pain assessment has been shown to be both simple and reliable.[18,19] Each patient then had the planned procedures explained in detail and an informed consent was obtained. All analgesic and psychotropic medications were stopped, and the patient instructed to complete a daily visual analogue scale rating.

Within one to two weeks after the initial clinic visit, patients were admitted to hospital on a same-day basis, and physical examination was repeated with measurement of visual analogue rating; blood pressure and body weight were noted. A diagnostic epidural differential local block was done with saline and gradually increasing doses of bupivacaine 0.5 per cent plain, injected through a 17-gauge Tuohy needle inserted at the appropriate intervertebral level. In all cases there was a negative placebo response to saline injection and complete relief of pain following dorsal root local anaesthetic block.

The patients were discharged later in the day and instructed to record their visual analogue ratings daily beginning the next day.

Epidural steroid injections

One week later and at weekly intervals thereafter each patient was re-admitted to have epidural injections of methylprednisolone acetate to a total of three injections. The protocol followed was as we have previously reported;[18] namely, 80 mg for a single root, or 60 mg to each of two roots. These were preceded by 1.0 ml bupivacaine 0.5 per cent plain for lumbar and thoracic injections and 0.5 ml for cervical injections to reduce the burning discomfort sometimes experienced with methylprednisolone injections. In all cases, visual analogue ratings were noted before these injections and at one, three, six and twelve months after the final injection in the follow-up visits.

Results

A summary of age and sex of the patients, pre-treatment duration of pain and segmental distribution is given in Table I. There was no significant difference in mean age or duration of

TABLE I

	n	Age	Sex	Pain duration	Distribution		
					cervical	thoracic	lumbar
Post-herpetic	36	54.7 ±13.9	23 F 13 M	4.4 ±3.5	3 8%	25 69%	8 22%
Post-trauma*	27	46.5 ±12.1	14 F 13 M	3.9 ±2.2	0 0%	22 81%	5 19%

*Includes: 11 post-thoracotomy, 7 post-cholecystectomy, 5 post-nephrectomy, 4 nonsurgical trauma.

pain between the post-herpetic (PH) and post-traumatic (PT) groups although the age ranges were different (31 to 79 years in the post-herpetic group and 22 to 59 years in the post-traumatic group). There was an equal sex distribution in the post-traumatic group but female patients accounted for 64 per cent of the patients in the post-herpetic group. Thoracic segments were the most commonly affected, amounting to 69 per cent of post-herpetic patients and 81 per cent of post-traumatic patients. Whereas lumbar segments were nearly equally affected in both groups, cervical involvement was present only in the post-herpetic group. No patient had sacral nerve root involvement. The majority of patients in the post-traumatic group (85 per cent) were post-surgical, comprising 11 post-thoracotomy, seven post-cholecystectomy and five post-nephrectomy neuralgias.

Distribution of affected segments

The frequency distribution of affected individual spinal segments is shown in Figure 1 for each group. More than half (55 per cent) of all thoracic segments affected involved T6 and T7 in the post-herpetic PH group (36 per cent of all levels affected). Two other peaks are evident in this group at C2 and L2 in the cervical and lumbar regions respectively. The distribution of affected segments in the post-traumatic PT group reflects the sites of surgical operations, since only 15 per cent involved non-surgical trauma.

Age of onset and duration of symptoms

Figure 2 shows the distribution of onset of symptoms in both groups. In the post-herpetic group, 59 per cent of patients had onset of symptoms in the fifth decade and over. In the post-traumatic group, 74 per cent of patients had onset of symptoms in the fourth decade and over.

The overall mean (±1 S.D.) age of onset of symptoms in the post-herpetic group was 49.78 ± 11.11 with 25 per cent occurring between 30 and 39, 17 per cent between 40 and 49, 42 per cent between 50 and 59, 14 per cent between 60 and 69, and three per cent over 70 years of age. The mean age of onset of symptoms in the post-traumatic group was 41.74 ± 8.32 with 11 per cent occurring between 20 and 29, 15 per cent between 30 and 39, 63 per cent between 40 and 49, and 11 per cent between 50 and 60 years of age.

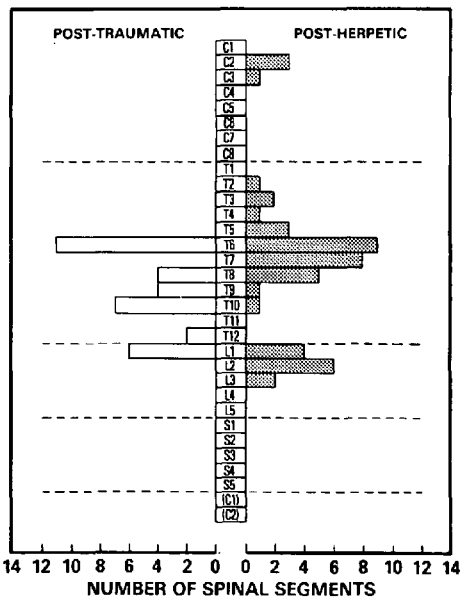

FIGURE 1 Distribution of affected spinal segments for post-herpetic (hatched bars) and post-traumatic (open bars) neuralgias.

Our previous report[18] did not find any relation between duration of symptoms and age; however, in the present larger study, a clear correlation exists for both groups as shown in Figure 3. Up to the age of 40 years, in both groups, the mean duration of symptoms (±1 S.D.) was 1.14 ± 0.5 with no change with age. However, above the

TABLE II
VISUAL ANALOGUE SCALE RATINGS

	Pre-treatment	a	b	c	1 mth	3 mth	6 mth	12 mth
Post-herpetic	84.4	83.7	61.6	36.2	9.6	5.2	5.0	4.6
	±8.2	±8.4	±9.6	±13.0	±10.1	±14.9	±14.6	±8.1
Pain-free (%)					(56)	(83)	(86)	(89)
Post-trauma	78.7	78.4	59.3	38.6	15.2	12.8	10.2	11.6
	±7.7	±7.3	±16.3	±17.3	±14.2	±12.2	±8.4	±17.1
Pain-free (%)					(48)	(56)	(52)	(59)
Mean	81.1	80.7	60.3	37.1	11.9	8.2	7.9	7.8
Total pain-free (%)					(52)	(71)	(71)	(76)

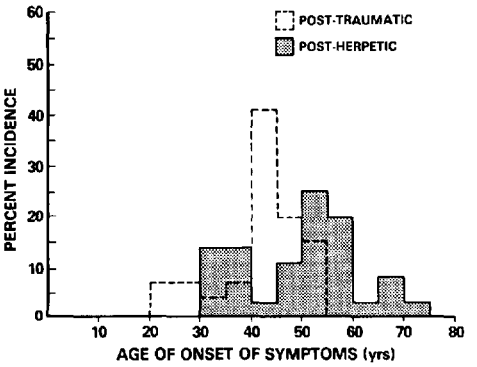

FIGURE 2 Percentage incidence of onset of symptoms with age for post-herpetic (hatched bars) and post-traumatic (open bars) neuralgias.

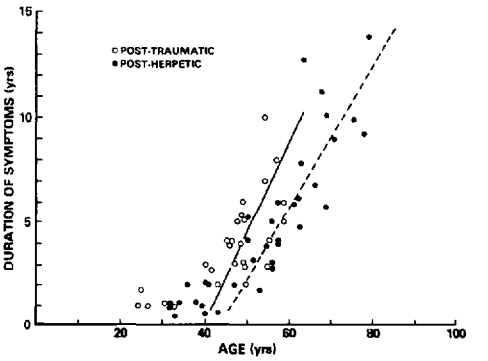

FIGURE 3 Duration of symptons before treatment plotted against age at time of initial assessment, for post-herpetic (closed circles) and post-traumatic (open circles) neuralgias. The linear regression lines for post-traumatic (solid line) and post-herpetic (broken line) patients over 40 years of age are shown.

age of about 40 years, duration of symptoms (S) increased linearly with age (A) in both groups. In the post-herpetic group, the linear correlation shown in Figure 3 is given by $S = 0.31A - 13.19$ while that for the post-traumatic group is given by $S = 0.44A - 17.4$.

Response to epidural steroids: visual analogue scale pain ratings

The mean visual analogue scale ratings (±1 S.D.) are presented for both groups in Table II. Mean pretreatment values were similar. There was a small but statistically insignificant reduction in visual analogue ratings one week after the diagnostic local anaesthetic block (Column a), but a highly significant reduction ($P < 0.01$) following steroid injections (Columns b, c, *et seq.*). The reduction in visual analogue scale ratings in the post-herpetic group one month after the last of the three epidural steroid injections was 89 per cent of pretreatment values, with 56 per cent of patients completely pain free (zero visual analogue rating) at that time. For the post-traumatic group, the reduction in visual analogue rating after one month was 81 per cent of pre-treatment values with 48 per cent of patients pain free. Further reductions were recorded after 3, 6, and 12 months in the post-herpetic group and after one year 89 per cent of patients were pain free. In the post-traumatic group, at one year there was a small but insignificant increase in visual analogue ratings compared with those at six months; however, significantly fewer patients (59 per cent) were pain free after one year in the post-traumatic group, compared with the post-herpetic group at that time. Figure 4 summarizes the reduction in pain levels in both groups, with percentage of patients free of pain at one year indicated.

Side effects and complications of steroid injections

The most common side effects noted were mild weight gain and elevation of affect. Table III shows a summary of the mean change in body

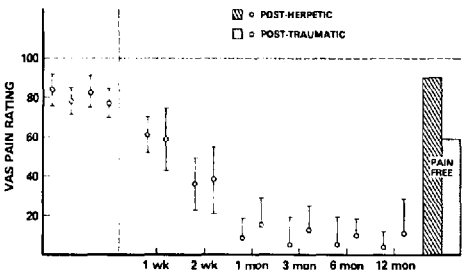

FIGURE 4 Mean visual analogue scale ratings ± 1 S.D. after steroid injections (vertical broken line) are shown for post-herpetic (heavy circle) and post-traumatic (light circle) neuralgias. The percentage of patients pain-free after one year is indicated for each group.

TABLE III
SIDE EFFECTS OF EPIDURAL STEROIDS

Wt gain (Kg)	Mean BP (mm Hg)	Affect	Appetite
2.6±0.4	5.2±0.6	↑	↑
(0–6.9)	(2.5–7.5)		
82%		89%	76%

COMPLICATIONS OF 252 INJECTIONS

CSF tap	3	(0.01%)
Blood tap	2	(0.01%)
Hypotension	16	(25%) m̄ 4.4 ± 1.2 mm HG
Spinal headache	1	

weight and blood pressure with the number of patients showing these side effects expressed as a percentage. More than 80 per cent of patients gained weight by a mean of 2.6 ± 0.4 kg and 60 per cent of patients showed slight increase in mean blood pressure of 5.2 ± 0.6 mm Hg. These were transient and had usually returned to pretreatment levels by the third month after the final injection. Appetite was increased in about three-quaters of patients.

A total of 252 injections were given to the 63 patients and the complications of these amounted to 2.4 per cent. Puncture of the dura mater occurred on three occasions, a blood tap on two occasions and spinal headache on one occasion (associated with dural puncture). Hypotension occurred relatively frequently in six per cent of all injections but in 25 per cent of patients and only occurred during diagnostic local anaesthetic blocks. This was readily reversed in all cases by increasing the rate of intravenous infusion of Ringer Lactate. The mean drop in blood pressure was 4.4 ± 1.2 mm Hg. No recordable change in blood pressure was noted following steroid injections.

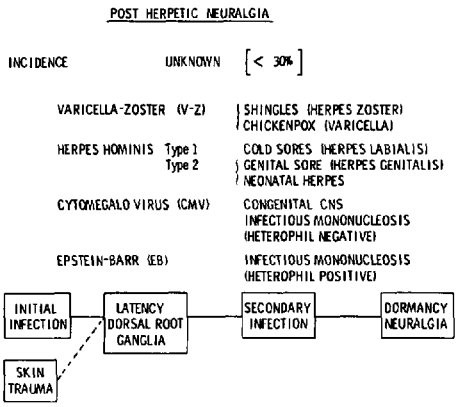

FIGURE 5 Herpes virus group with a suggested mechanism for a common inflammatory process in post-herpetic and post-traumatic neuralgias.

DISCUSSION

The response to a series of three-weekly epidural injections of methylprednisolone in patients with post-herpetic or post-traumatic neuralgia, confirms an earlier preliminary report.[18] Further, the side effects of these injections were minor, although frequent. The rate of freedom from pain of 89 per cent in the post-herpetic group and 59 per cent in the post-traumatic group, is much greater than the generally accepted placebo response rate of around 30 per cent. It is noteworthy that all patients were given a differential intrathecal or epidural spinal block before treatment and only those showing a nil placebo response to saline injection were included. Thus, it seems reasonable to conclude that these rates of freedom from pain reflect, in this highly selected group of patients, a true therapeutic response without significant placebo effects.

The intractability of these neuralgias and the variability of their natural history, make long-term effects difficult to assess. The reported data were obtained after only one year, but some patients were followed up for more than three years and there does not seem to be a significant relapse rate. The fact that in all cases these patients obtained relief of their pain following steroid injections makes this procedure worthy of serious consideration for this type of patient.

The mechanism of the action of methylprednisolone plus the small volume of bupivacaine in these conditions is not known. Reduction of the inflammatory response in nerve roots, lysis of

adhesions and interrupted sympathetic reflex activity have been suggested as possible effects of steroids administered by this route.[18] The rationale for using local anaesthetic was to reduce the burning sensation from steroid injection into the epidural space. However, it is possible that the series of weekly local anaesthetic injections, could have reduced the sympathetic component of these neuralgias.[20,23] However, repeated local anaesthetic injections without steroid usually offer only transient relief. The action of methylprednisolone, like other glucocorticoids, is probably anti-inflammatory. Varicella-Zoster virus is neurophilic and during the acute lesion enters the spinal dorsal roots, ganglia, and dorsal horns of the spinal cord, remaining in these sites in a dormant state. The latent period between the acute infection and subsequent neuralgia can vary from a few weeks to several years, and likely is due to reactivation of latent virus.[3] The inflammatory lesion may be focal or diffuse within the dorsal horns and ganglia and is characterized by round cell infiltrates and fibrosis. Similar lesions have been reported for post-traumatic spinal pain syndromes,[1] suggesting that these also may have a viral or inflammatory basis. The presence of the herpes virus group is common in the skin of healthy subjects and, thus, skin trauma involving segmental nerves could offer a route for these neurophilic viruses to the dorsal spinal structures. A summary of this group of virus with a suggested mechanism of reactivation is shown in Figure 5. The higher incidence of herpes zoster in patients with neoplastic disease, particularly Hodgkin's disease, suggests that a significant factor in reactivation may be immune deficiency.

One other possible explanation of the effect of repeated injections of methylprednisolone in relieving these neuralgias, is that polyethylene glycol 4000, the preservative used, may be mildly neurolytic. These glycols are metabolized to oxalic acid, which has corrosive properties. The "c" fibre activity predominates in both neuralgias and these small neurones lie at the periphery of the dorsal root ganglion. Thus any minor neurolytic effect would presumably depress "c" fibre activity, while more central segmental sensory neurones would be unaffected. A recent paper by Perkins and Hanlon[22] reported that in five patients with post-herpetic neuralgia, up to 50 per cent pain relief was obtained after methylprednisolone 80 mg was injected epidurally at the affected segments. In this small series, local anaesthetics were also used, but differential spinal block was apparently not done, so that inclusion of placebo responders seems likely and would have reduced the overall long-term response. A further seven patients in their study had acute herpes and were relieved of pain by these injections for more than five months.

Thus far the only preventative measures which have been shown to reduce the incidence of post-herpetic neuralgia, are repeated injections of local anaesthetic,[22] and oral steroids given during the acute phase,[21] where post-herpetic neuralgia was reduced from 73 to 30 per cent. However, this is complicated by the fact that the incidence of post-herpetic neuralgia may vary from 10 per cent in young patients to more than 50 per cent in patients over 60 years of age.[2] Supplements of vitamin B12 may also be of some benefit in minimizing neural damage in the acute phase but are unlikely to be of benefit in chronic neuralgia. It seems reasonable to conclude, from the limited evidence available, that the use of prolonged or repeated local anaesthetic block with administration of oral steroids during the acute phase, may significantly reduce the incidence of these distressing neuralgias.

In the present study, the use of repeated epidural injections of methylprednisolone resulted in marked relief of pain in patients with post-herpetic or post-traumatic neuralgia. A hypothesis is presented to explain the similarity of these two chronic spinal pain syndromes by invoking a common inflammatory aetiology. The safety of the procedures with the absence of significant side effects makes this the treatment of choice when there is no contra-indication to steroid administration.

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RÉSUMÉ

Trente-sept patients souffrant de névralgie post-herpétique de longue durée et vingt-sept de névralgie post-traumatique ont été traités avec trois injections épidurale chacun d'acétate de méthyl prednisolone administrées à une semaine d'intervalle. Un bloquage différentiel sous-arachnoidien ou épidural fut effectué d'abord chez tous ces malades et ceux qui étaient soulagés par le placebo ont été exclus de l'étude. L'âge moyen, la durée des symptômes et l'intensité à la douleur mesurée par représentation graphique étaient identiques dans les deux groupes. La cote d'évaluation sur l'échelle graphique fut diminuée au mois après traitement, à partir des valeurs initiales de 84.4 et 78.7 jusqu'à 9.6 et 15.2 dans les groupes post-herpétique et post traumatique respectivement et à 4.6 et 11.6 respectivement aprés un an alors que 89 pour cent des patients du groupe post-herpétique et 59 pour cent des patients du groupe post-traumatique étaient complétement guéris. Les effets secondaires ont été mineurs dans tous les cas. Ce travail semble indiquer que le traitement proposé est le traitement de choix dans la névralgie d'origine herpétique et traumatique lorsque les stéroides ne sont pas contre-indiqués.