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Management of chronic pain in whiplash injury

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We investigated the response of chronic neck and shoulder pain to decompression of the carpal tunnel in 38 patients with whiplash injury. We also determined the plasma levels of substance P (SP) and calcitonin gene-related peptide (CGRP), which are inflammatory peptides that sensitise nociceptors. Compared with normal control subjects, the mean concentrations of SP (220 *v* 28 ng/l; $p < 0.0001$) and CGRP (400 *v* 85 ng/l; $p < 0.0005$) were high in patients with chronic shoulder and neck pain before surgery. After operation their levels fell to normal. There was resolution of neurological symptoms with improvement of pain in 90% of patients. Only two of the 30 with chronic neck and shoulder pain who had been treated conservatively showed improvement when followed up at two years.

In spite of having neuropathic pain arising from the median nerve, all these patients had normal electromyographic and nerve-conduction studies. Chronic pain in whiplash injury may be caused by 'atypical' carpal tunnel syndrome and responds favourably to surgery which is indicated in patients with neck, shoulder and arm pain but not in those with mild symptoms in the hand. Previously, the presence of persistent neurological symptoms has been accepted as a sign of a poor outcome after a whiplash injury, but our study suggests that it may be possible to treat chronic pain by carpal tunnel decompression.

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Whiplash injury is a challenging condition to treat since the underlying pathology is poorly understood. The prognosis is adversely affected in the presence of persistent neurological signs, which are often not typically radicular. Many patients suffer disability because of chronic pain which affects their daily work and leisure activities. Some clinicians, members of the insurance industry and defence lawyers have advanced the concepts of secondary gain and compensation neurosis in such patients.[1-4] In some the cause of chronic neck and shoulder pain has been ascribed to carpal tunnel syndrome[5] and Ide et al[6] recently described entrapment of the brachial plexus and of peripheral nerves, including the median nerve at the carpal tunnel, after whiplash injury. They stated that nerve entrapment may cause severe symptoms and their persistence is associated with a poor outcome. Neurophysiological studies are normal in nerve entrapment caused by whiplash injury.[5,6] Chronic pain after whiplash injury has been thought to arise from the posterior facet joints[7] and also from damage to discs and ligaments.[8]

Pain is elicited by A-delta and C nociceptor fibres. Chronic pain may be caused by inflammatory factors which sensitise nociceptors in association with microneural damage. Sensory neurones projecting to laminae I and II of the superficial dorsal horn express the nociceptor peptides, calcitonin gene-related peptide (CGRP) and substance P (SP).[9,10] The latter is a sensory peptide and plays an important role in pain sensation while CGRP is a powerful vasodilating agent found in small sensory neurones and co-localised with SP. It is also a neurotransmitter and plays a significant part in sensory transmission.

In this prospective study we have investigated the levels of SP and CGRP before and after surgery for chronic neck and shoulder pain after whiplash injury. The clinical and functional outcomes after decompression of the median nerve at the carpal tunnel were also evaluated.

Patients and Methods

We treated 38 patients with chronic pain after whiplash injury by decompression of the carpal tunnel. A further 30 with similar signs and symptoms were treated conservatively and they served as a control group. The mean follow-up was for 18 months (12 to 24). There were ten men and

28 women in the surgical group with a mean age of 37.5 years. In the control group there were 12 men and 18 women with a mean age of 34.2 years. All the patients had been either drivers or passengers and stated that they had been wearing seat-belts. They all had developed symptoms and signs of atypical carpal tunnel syndrome as a result of the injury. They had peripheral symptoms within the area of the median nerve in addition to pain in the neck and shoulder. Routine clinical and neurological examination included assessment of the range of movements of the neck, focal tenderness, and changes in sensation and power in the upper limb. All patients had received physiotherapy in the form of either exercises for the release of nerve tension or cervical traction, and some had undergone acupuncture. Many had had osteopathic treatment and some used a transcutaneous electrical nerve-stimulator. All took non-steroidal anti-inflammatory drugs and had worn a cervical collar for a period of one to three weeks. After one year of conservative treatment the patients were assessed using a visual analogue scale. Tapping and compression of the median nerve at the wrist were carried out to elicit referred pain in the shoulder and neck. A local anaesthetic test was performed by infiltrating 0.5% bupivicaine around the median nerve at the most tender site, usually 2.5 cm proximal to the distal wrist crease, which caused temporary resolution of pain in the shoulder and neck. All patients had plain radiography and six had MRI of the cervical spine. An independent clinician (RW) carried out these assessments.

Of the 27 patients (71%) who had electromyography (EMG) and nerve-conduction studies, all had normal results. The effects of pain on their daily activities were recorded.

Determination of SP and CGRP. Approval of the Ethical Committee was obtained. In the 38 patients blood was taken before operation, and at 13 days and six weeks after surgery. None had heart disease or hypertension. A control group for this part of the study consisted of healthy subjects with no injuries and were randomly chosen by age and gender.

Plasma obtained from centrifuged blood (5 ml) collected in EDTA aprotinin tubes was stored at -80°. Commercially available enzyme-immunoassay kits (Peninsula Laboratories, Merseyside, UK) were used to measure the plasma SP (EIA 7451) and CGRP (EIA 6012). The lowest detectable concentration for plasma CGRP was 0.04 ng/l, and there was no cross-reaction with SP, vasoactive intestinal polypeptide or calcitonin. The lowest detectable concentration for SP was 0.03 ng/l[3] and there was no cross-reaction with neurokinin (A, B) or neuropeptide K.

To obtain standard curves, known amounts of peptides were incubated with their specific antibodies. Biotinylated-labelled peptide, added as a tracer, formed immobilised primary antibody/biotinylated-labelled peptide complexes. The complexes were then allowed to bind to streptavidin-conjugated horseradish peroxidases. Any excess biotinylated-labelled peptides and peroxidases were washed away. Tetramethyl benzidine dihydrochloride, when reacted with conjugated horseradish peroxidases, produces a colour intensity (absorbance) that can be read at 450 nm and from which a standard curve can be derived. The intra- and interassay coefficients of variation were 6.3% and 7.2% for CGRP and 12.4% and 8.3% for SP, respectively.

Statistical analysis. The results were expressed as the mean, median and standard deviation. The non-parametric Mann-Whitney U test was used throughout. A p value of 0.05 was the criterion for statistical significance.

Results

Levels of neurotransmitters. In the patients the mean plasma concentration of SP (220 ± 161 ng/l) before operation was significantly higher ($p < 0.00001$) than that of the 11 normal control subjects (28 ± 29 ng/l). By 13 days after operation, it was reduced (59 ± 63 ng/ml) but was still greater than that for the normal control subjects ($p < 0.005$). Six weeks after operation, the concentration (19 ± 21 ng/l) was not notably different. Similarly, before surgery, in the patients the mean plasma concentration of CGRP (400 ± 140 ng/ml) was significantly higher ($p < 0.0005$) than that of the 11 normal control subjects (85 ± 62 ng/ml). At 13 days after operation, it was decreased (142 ± 140 ng/ml) but still significantly higher ($p < 0.05$) but by six weeks after operation there was no notable difference (65 ± 99 ng/ml). The results are shown in Table I. Hypoaesthesia to light touch and pin prick was present in the distribution of the median nerve in the forearm and hand on the affected side in all patients before operation. This recovered in 33 (87%) within three to four weeks after surgery. In the conservatively treated control group, 28 (93%) still showed hypoaesthesia at follow-up.

Testing of muscle power was performed according to the MRC grading. There was weakness of the pronator teres, the thenar muscles, and the long flexors of the index and middle fingers, which are all innervated by the median nerve. The power of these muscles was between grade 2+ and grade 4. This returned to normal (grade 5) in 36 patients (95%) after operation. Muscle power ranged from grade 3+ to grade 4 for 28 of the control patients (93%). The muscles supplied by the axillary, musculocutaneous, ulnar and radial nerves had grade-5 power.

The Jamar dynamometer was used to compare the grip strength on the affected with the normal side. Table II gives the results.

Before operation paraesthesiae were referred distally into the fingers in 36 patients on tapping over the median nerve 2.5 cm proximal to the wrist crease on the affected side. This recovered in 33 (87%) after surgery. There was proximal referral of paraesthesiae in 35 patients (92%) and this disappeared in 34 (89%) after operation.

Direct pressure applied for five seconds over the median nerve 2.5 cm proximal to the distal wrist crease produced

Table I. Mean (SD; median) plasma concentrations of SP and CGRP in 38 patients with whiplash injury, measured before and after surgery, and in 11 normal control subjects

	Whiplash injury			
		Postop		Normal
	Preop	13 days	6 weeks	control group
SP (ng/l)	220 ± 161 (200)*	59 ± 63 (25)†	19 ± 21 (9.5)	28 ± 29 (20)
CGRP (ng/l)	400 ± 140 (460)‡	142 ± 140 (100)§	65 ± 99 (20)	85 ± 62 (100)

* $p < 0.00001$
† $p < 0.005$
‡ $p < 0.0005$
§ $p < 0.05$

Table II. Results of the Jamar test (kg/force) in the surgical (38 patients) and control (30 patients) groups

	Surgical group		Conservatively-treated control group	
	Affected side	Unaffected side	Affected side	Unaffected side
Before surgery	38.9	47.8	37.8	49.6
After surgery (6 weeks)	46.2	49.2	36.9	46.8

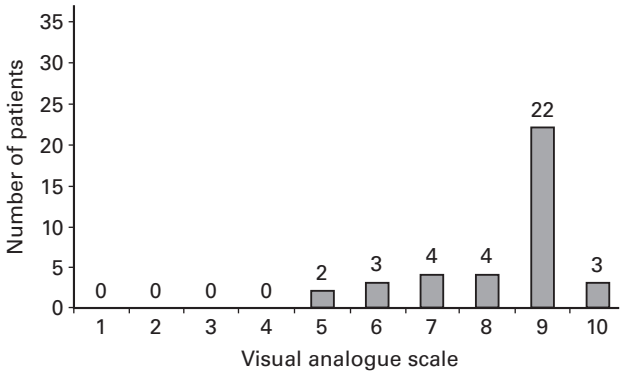

Fig. 1a

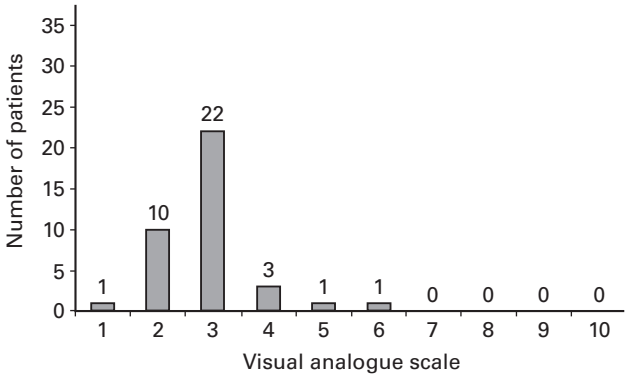

Fig. 1b

Visual analogue scale to assess the severity of pain in 38 patients with whiplash injuries a) before and b) after surgery.

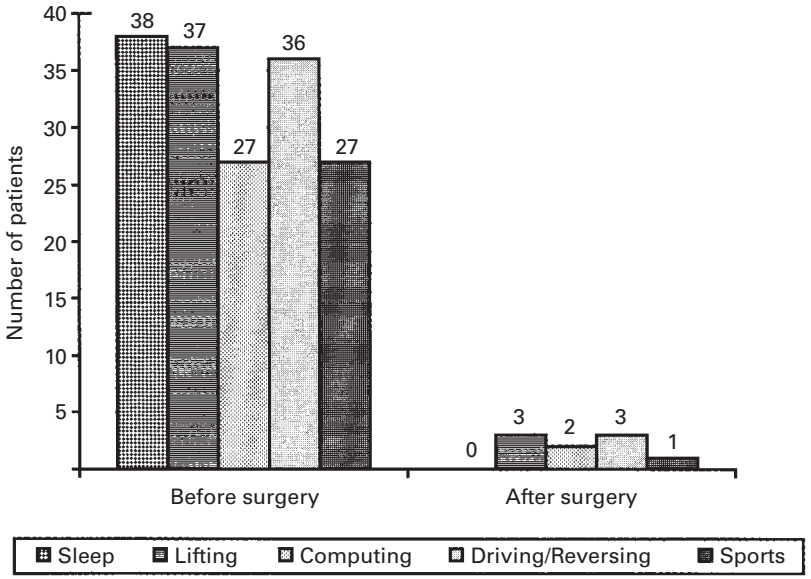

Fig. 2

Improvement in the activities of daily living of 38 patients with whiplash injury before and after surgery at follow-up at two years.

pain which was referred proximally to the neck, shoulder or the interscapular region in 34 patients (89%). This disappeared in 33 patients after operation (87%). The Floyd nerve-tension test[11] in the upper limb was positive in all patients before surgery, and became negative in 34 (89%) after operation. The test was positive in 28 of the patients treated conservatively (93%). The neck and shoulder pain resolved in 36 patients (95%) after operation.

At follow-up at two years only two of the control group had improvement of their neurological symptoms. The remaining 28 (93%) continued to experience these problems and had chronic pain in the shoulder and neck. There was no recurrence of pain or other symptoms in the surgically-treated group at the end of follow-up.

There was no evidence of fracture or dislocation on radiographs. Ten patients (27%) showed loss of cervical lordosis. Three had narrowing of the disc space at the C4/5 levels with no arthritis of the facet joints. Six patients had MRI of the cervical spine which showed no abnormality.

The visual pain analogue scale showed the subjective assessment of pain before (Fig. 1a) and after (Fig. 1b) surgery. The activities of daily living improved considerably after surgery because of relief from pain (Fig. 2).

Discussion

Chronic pain in the shoulder and neck is common after a whiplash injury. The cause of the neurological symptoms remains uncertain in the presence of normal neurophysiological investigations and findings on imaging of the neck and shoulder. These symptoms are not typical of radicular pain and, although some are similar to those of the carpal tunnel syndrome, pain in the shoulder and neck pain is not characteristic of entrapment of the median nerve at the wrist. In our study, 27 patients (71%) had a normal EMG. Alpar[5] reported that of 225 patients with whiplash injury only 3% had abnormal EMG changes. Ide et al[6] also found normal neurophysiological investigations in patients with symptoms and signs of irritation of the brachial plexus and entrapment of peripheral nerves after a whiplash injury. We feel that in a whiplash injury the median nerve may be injured by stretching of the neck due to the extension, flexion and vertical components of the force.

The characteristic features of atypical carpal tunnel syndrome are referral of dysaesthesia to the shoulder and neck on tapping over the median nerve proximal to the wrist, increase in pain in the shoulder and neck by direct pressure on the same area and disappearance or improvement of the shoulder and neck pain on infiltration of this site with 6 ml of 0.5% bupivicaine. These features suggest that chronic shoulder and neck pain after whiplash injury may arise from the median nerve at the level of the wrist and that the pain is referred proximally. The nerve pain is thus not felt at the site of its origin[12] It has been shown that pain from the median nerve may be experienced in the neck and shoulder.[13]

The EMG and nerve-conduction studies are normal because most of the fibres which constitute a peripheral nerve are A-delta fibres of small diameter and unmyelinated C fibres. Standard nerve-conduction studies assess function in the large and myelinated fibres and thus only test a few of those which constitute a peripheral nerve. Such studies are therefore unsuitable as an aid in the diagnosis of this condition.[14,15] There is evidence that neurotransmitters such as SP and CGRP are released in the dorsal horn with other agents which sensitise nociceptors. When impulses arrive from C-fibre afferents, SP is released[16] and the plasma levels of neurotransmitter peptides are elevated[10]

Our patients with an isolated whiplash injury had high plasma levels of pain neurotransmitters which fell to normal levels after decompression of the median nerve at the wrist. The plasma levels of SP are also raised in other painful conditions,[17-20] and those of CGRP are altered in soft-tissue injuries,[21] in chronic pain[22] and infection.[23]

Carpal tunnel decompression is indicated in patients who have chronic neck, shoulder and arm pain after a whiplash injury. Changes in the plasma levels of neurotransmitter peptides and independent clinical and functional outcomes confirm the benefits of this treatment. The relief from pain and restoration of normal muscle power are evidence that any decrease in muscle power is due to inhibition of pain. Jamar dynanometric studies may not be helpful in the assessment of individual muscle weakness. The presence of a normal EMG and nerve-conduction studies should not deter surgeons from offering carpal tunnel decompression to patients with chronic pain in the shoulder and neck after a whiplash injury.

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