Chronic Cervical Zygapophysial Joint Pain After Whiplash: A Placebo-Controlled Prevalence Study [Cervical Spine]

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Abstract

Study Design: The authors developed a diagnostic double-blindfolded survey using placebo-controlled local anesthetic blocks.

Objective: To determine the prevalence of cervical zygapophysial joint pain among patients with chronic neck pain (more than 3 months' duration) after whiplash injury.

Summary of Background Data: The prevalence of cervical zygapophysial joint pain after whiplash has been studied by means of comparative local anesthetic blocks. The concern is that such blocks may be compromised by placebo responses and that prevalence estimates based on such blocks may exaggerate the importance of this condition.

Methods: Sixty-eight consecutive patients referred for chronic neck pain after whiplash were studied. Patients with dominant headache were first screened with the use of comparative blocks of the C2-C3 zygapophysial joint. Patients who had positive responses concluded investigations. Those who did not experience pain relief together with the patients with dominant neck pain proceeded to undergo placebo-controlled local anesthetic blocks. Two different local anesthetics and a placebo injection of normal saline were administered in random order and under double-blindfolded conditions. A positive diagnosis was made if the patient's pain was completely and reproducibly relieved by each local anesthetic but not by the placebo injection.

Results: Among patients with dominant headache, comparative blocks revealed that the prevalence of C2-C3 zygapophysial joint pain was 50%. Among those without C2-C3 zygapophysial joint pain, placebo-controlled blocks revealed the prevalence of lower cervical zygapophysial joint pain to be 49%. Overall, the prevalence of cervical zygapophysial joint pain (C2-C3 or below) was 60% (95% confidence interval, 46%, 73%).

Conclusion: Cervical zygapophysial joint pain is common among patients with chronic neck pain after whiplash. This nosologic entity has survived challenge with placebo-controlled, diagnostic investigations and has proven to be of major clinical importance.
Few medical practitioners recognize the entity of cervical zygapophysial joint pain, yet the evidence of the cervical zygapophysial joints being a source of neck pain should be compelling.

The cervical zygapophysial joints are innervated by the medial branches of the cervical dorsal rami. Endowed with a nerve supply, they should, in principle, be a possible source of neck pain. Studies of healthy volunteers have shown that distension of these joints with contrast medium provokes neck pain and referred pain; stimulation to the C2-C3 zygapophysial joint provokes head pain and to the C5-C6 or C6-C7 zygapophysial joints, shoulder girdle pain (Figure 1). Various studies have shown that physicians can relieve patients of their neck pain by anesthetizing their cervical zygapophysial joints with intraarticular injections of local anesthetic by blocking the nerves that supply these joints or by injecting steroids into these joints. However, these studies have not determined the prevalence of cervical zygapophysial joint pain: Is it common or an oddity?

In a study in which single diagnostic blocks were administered to a large sample of patients with posttraumatic neck pain, the authors found the prevalence of cervical zygapophysial joint pain to be between 25% and 65%, depending on whether worst-case or best-case analysis was undertaken. However, single blocks have been shown to have a false-positive rate of 27% and are, therefore, not a reliable tool for epidemiologic studies.

In answer to the question of prevalence, the authors of the current study adopted and validated the paradigm of comparative local anesthetic blocks. This protocol had been advocated by leading experts in the pain field. Local anesthetic blocks can be controlled without the need for sham injections or sham agents. Two local anesthetics are used with different durations of action. True positive responses are ones in which the patient obtains complete relief of pain on both occasions, provided that longer-acting relief occurs when the longer-acting agent is used. Applying this paradigm to a series of consecutive patients with chronic neck pain after whiplash, the authors found the prevalence of cervical zygapophysial joint pain to be 54%.

This prevalence challenges entrenched precepts about the origins of neck pain after whiplash injury as well as beliefs that neck pain is most commonly discogenic, muscular, due to soft-tissue injury or is psychogenic. Furthermore, physicians and surgeons are not accustomed to making a diagnosis of cervical zygapophysial joint pain. For these reasons, they may not accept what appears to be an inordinate prevalence of a relatively unknown condition.

One criticism of the current technique may be that comparative local anesthetic blocks are not reliable because they do not involve a placebo control. This skepticism, however, is contrary to the rigor with which comparative local anesthetic blocks were developed and discussed and the scientific data on which they were based. Nevertheless, if cervical zygapophysial joint pain is to be recognized as a valid nosologic entity, this skepticism needs to be assuaged.

Accordingly, the authors undertook a study to determine the prevalence of cervical zygapophysial joint pain using a stringent, double-blindfolded protocol that incorporated a placebo control. The prevalence was studied in a sample of patients with chronic neck pain after whiplash injury. This condition was selected because it is the most controversial, costly, and perhaps, common form of neck pain.

**Methods**

**Patients.** The study sample consisted of 68 consecutive patients referred to the Cervical Spine Research Unit for assessment of chronic neck pain after whiplash injury. None of the patients had participated in previous studies conducted by this unit. The unit is located in an industrial city, with
a population of 250,000, and has received referrals from a large nearby city (Sydney) and from rural areas as well as from local medical practitioners.

The criteria for referral were that patients must have neck pain of more than 3 months’ duration attributed to a motor vehicle accident. All patients must have consulted a specialist before referral, and only referrals from medical practitioners were accepted. Physicians intending to refer patients to the unit were given written details of the eligibility criteria and copies of an application form. Eligible patients were then seen in order of receipt of completed application forms. In terms of the Quebec Task Force on Whiplash-Associated Disorders classification schedule, patients with Grade 0 were excluded, but patients with any other grade (I-IV) were eligible for inclusion in the current study.

**Ethics.** The study protocol was approved by the hospital and university ethics committees, and informed consent was obtained from all subjects.

**Baseline Clinical Assessment.** A baseline medical assessment was performed, which included a comprehensive medical history and physical examination. Visual analogue scales of pain severity were completed by all patients, and McGill pain questionnaires were administered to all English-speaking subjects. Before intervention, a psychological symptom checklist (SCL-90-R) was administered to all patients by a psychologist. The results of that questionnaire served as a baseline measurement and did not affect progression into the research program.

**Diagnostic Blocks.** Placebo-controlled blocks are not practicable for investigating pain from the C2-C3 zygapophysial joint, because the third occipital nerve, which innervates the C2-C3 zygapophysial joint, has a cutaneous branch. Consequently, numbness or lack of numbness in the cutaneous territory of the third occipital nerve would inform patients as to whether they had received an active or an inactive agent. The medial branches of lower cervical dorsal rami, however, lack a consistent cutaneous distribution. Consequently, patients receive no extraneous clue as to whether they received a local anesthetic or an inactive agent. Therefore, placebo blocks can be applied for joints below C2-C3.

Accordingly, the inception cohort was first screened for C2-C3 zygapophysial joint pain to remove those patients who experienced pain relief from C2-C3 blocks, thereby leaving a sample for whom placebo-controlled lower cervical blocks could be used. A previous study had shown that C2-C3 zygapophysial joint pain was most likely to occur in patients with headache who rated their headache as worse than their neck pain. Accordingly, headache as the major symptom was used as the clinical cue for selecting patients for screening blocks of the third occipital nerve. Patients without headache or for whom neck pain was predominant received placebo-controlled blocks of joints below C2-C3. Those with headache underwent blocks of the third occipital nerve. If such blocks relieved their pain completely, then their investigations were concluded. If, however, third occipital nerve blocks did not relieve their pain, then these patients were given placebo-controlled blocks below C2-C3.

All blocks were performed under image-intensifier guidance using a lateral approach to the medial branches of the cervical dorsal rami, which innervate the target cervical zygapophysial joint (Figures 2A, 2B). The target points and target specificity of cervical medial branch blocks have been established in antecedent studies. Each procedure was performed in the presence of a medically qualified independent observer who corroborated the radiographic position of the operator's needle before injection.

Investigations were initiated at the segmental level suggested by the distribution of the patient's pain with use of the maps of referred pain from cervical zygapophysial joints described by Dwyer et al. For patients with unilateral pain, blocks were performed on the side of their pain. For patients with bilateral pain, blocks were commenced unilaterally on the side on which their pain was worse or arbitrarily if they were unable to specify a dominant side of pain.
Each patient was allocated randomly to receive either a short-acting local anesthetic (lidocaine 2%) or a long-acting local anesthetic (bupivacaine 0.5%) for the first block. If a patient obtained no pain relief from the first block, then the series was restarted at another, usually adjacent, level. This iteration was repeated until pain relief was obtained or until all relevant joints were excluded as the source of neck pain. If a patient obtained relief from the first block at any level below C2-C3, then he or she received two more blocks, separated by intervals of at least 1 week. On the second occasion, these patients were allocated randomly to receive either normal saline or the local anesthetic that they did not receive for their first block. On the third occasion, they received the remaining agent. All procedures involved the injection of 0.5 mL of solution onto each of the two target nerves, regardless of which agent was used.

The patient and the operator were blindfolded to the order of administration of the agents until the series of blocks was completed. The patient's responses to these blocks were assessed by the operator by way of telephone interview on the evening of or day after the block. The patients were asked to report how much their pain was relieved and for how long the relief lasted. A positive response was recorded only if the patient reported complete or profound pain relief after the injection. Minor or partial relief, consistent with the usual fluctuation of the patient's pain, was considered a negative response.

Regarding the placebo-controlled blocks, a positive diagnosis was recorded only if the patient's pain was relieved completely and reproducibly by each of the local anesthetic blocks but not by the placebo injection. All other responses were considered negative. A diagnosis of C2-C3 zygapophysial joint pain was made if the patient's pain was completely and reproducibly relieved by two different local anesthetic blocks and provided that the patient correctly discriminated the longer acting of the two local anesthetics used. All other responses were considered negative.

To determine whether there were clinical cues that might reliably predict the outcome of diagnostic blocks, the authors compared the demographic characteristics, mode of accident, history of pain, and clinical examination findings of patients with a true-positive diagnosis with those of patients who failed to meet the diagnostic criteria.

**Results**

All of the 68 eligible patients referred for assessment consented to participate. The study population consisted of 42 women and 26 men aged 41 ± 10 years (mean ± SD). Pain had been present for an average of 54 months (range, 7 months to 44 years). In 63 cases, pain had developed within 3 days of the accident; in only one case did the patient's current pain develop after more than 3 months. At the time of enrollment, only 25% of the patients were employed in the same capacity as before the motor vehicle accident responsible for their neck pain, whereas 34% were unemployed because of their injuries.

Most of the patients had been drivers (n = 48, 68%) or passengers (n = 18, 26%) in cars at the time of the accident. Of the four remaining patients, one was a pedestrian who had been struck by a motor vehicle; one was a motorcyclist and the other a bicyclist, both of whom suffered hyperextension injuries; and one had fallen off the back of a moving truck. Of those who were in a car at the time of the accident, 59% were struck from the rear, 29% from the front, and 12% from the side.

All patients presented with neck pain. Thirty patients presented with unilateral pain only, 24 had bilateral pain but were able to identify a dominant side, and the remaining 14 experienced equal bilateral pain. For 41 patients, neck pain was the dominant symptom. The other 27 patients had neck pain as well, but headache was their dominant symptom (Figure 3). Besides neck pain and headache, the patients reported numerous associated symptoms (Table 1).
All study patients satisfied the Quebec Task Force classification criteria for Grade II whiplash-associated disorder, that is, they all reported neck pain, stiffness, or tenderness and exhibited musculoskeletal signs. All patients were tender to palpation over at least one level of the cervical spine posteriorly. But all but nine patients (87%) exhibited a limited range of cervical motion in at least one direction.

Twenty-eight patients (41%) also satisfied the criteria for Grade III whiplash-associated disorder, that is, they had neck symptoms and neurologic signs. Fifteen patients exhibited reduced sensation in a region of the upper limb, 2 patients exhibited weakness of at least one muscle group of the upper limb, and 11 patients exhibited both reduced sensation and weakness. However, none of these patients satisfied the criteria for the diagnosis of radiculopathy. Their neurologic symptoms were not dermatomal or myotomal and were usually intermittent. These features are common among whiplash patients and are caused by mechanisms other than nerve root compression.

All patients had undergone cervical spine radiography before entering the study, and the films made available were reviewed by one of the authors. Otherwise, a radiologist's report was accepted for the purposes of determining the presence or absence of any abnormalities. There were only three reports of fracture or dislocation of the cervical spine. One of the motorcyclists had crush fractures of the C5 and C6 vertebral bodies after his accident in 1948 and experienced degenerative changes. One patient had a separation of the C7 spinous process and another had separation of the C7 and T1 spinous processes. These three patients' conditions satisfied the Quebec Task Force criteria for Grade IV whiplash-associated disorder. However, the radiologically apparent fractures were considered unlikely to account for the chronic pain experienced by each of these patients, because their injuries had healed before presentation to this unit. The only other abnormalities detected were age-related degenerative changes in six cases.

Eleven patients withdrew from the study. The reasons for withdrawal were obtained by mail to determine whether there was a consistent factor responsible for their decisions. The replies and the patient characteristics are summarized in Table 2. Another five patients did not complete the investigations. Of these, two patients had experienced adverse reactions to lidocaine, which precluded further use of amide local anesthetics; one patient's pain completely resolved after the first diagnostic block; one patient had another motor vehicle accident and suffered multiple injuries that prevented traveling; and the remaining patient was lost to follow-up. As a group, those who withdrew or who did not complete the investigation did not differ significantly from the rest of the cohort regarding gender, age, employment status, accident characteristics, or psychological profiles. Likewise, the duration, distribution, quality, and severity of their pain; the location of tenderness; and the presence of restricted neck movements did not differ significantly from that of the remaining patients.

Fifty-two patients completed the investigations. Of these, 22 presented with dominant headache and underwent third occipital nerve blocks. Eleven responded and satisfied the criteria for C2-C3 zygapophyiscal joint pain. This response rate constituted a prevalence of C2-C3 zygapophyiscal joint pain of 50% (95% confidence interval [CI], 29%, 71%) among patients with chronic neck pain and dominant headache after whiplash injury.

The remaining 11 patients with dominant headache, along with the 30 patients who presented with dominant neck pain, subsequently underwent placebo-controlled blocks of cervical zygapophyiscal joints below C2-C3. Of these 41 patients, 20 satisfied the criteria for the diagnosis of cervical zygapophyiscal joint pain. They obtained complete relief of their neck pain after each of the local anesthetic injections but no relief after injection of normal saline. This constitutes a proportion of 49% (95% CI, 33%, 64%) of patients with chronic neck pain after whiplash that did not stem from C2-C3.
Overall, 31 of the 52 patients who completed the investigation had cervical zygapophysial joint pain at C2-C3 or at lower levels. Therefore, among all those for whom the condition was sought, the prevalence of cervical zygapophysial joint pain was 60% (95% CI, 46%, 73%).

The most common levels for symptomatic joints were C2-C3 and C5-C6 (Figure 4). Further investigation of the positive cases has revealed that five of these patients have more than one symptomatic joint. Three patients had C2-C3 zygapophysial joint pain bilaterally, one of whom also had C5-C6 and contralateral C6-C7 zygapophysial joint pain. One patient had C2-C3 and ipsilateral C4-C5 zygapophysial joint pain. The remaining patient had C2-C3 and ipsilateral C5-C6 joint pain.

There were no statistically significant differences between those patients with a true-positive diagnosis and those who failed to meet the diagnostic criteria with regard to their demographic characteristics (including age, gender, litigation, and employment status), mode of accident (including the patient's position in the vehicle, the direction of forces, and the estimated collision speed), history of pain (duration, distribution, quality as measured by the McGill Pain Questionnaire, and severity as measured by a visual analogue scale), clinical examination findings (restricted movements and location of maximum tenderness), and psychological profiles as measured by a psychologist using the SCL-90-R. Patients with a positive diagnosis were more likely to be female, to have had a rear-end collision, and to have restricted neck movement in at least one direction.

However, none of these differences reached statistical significance and none was found to be a useful predictor of the outcome of double-blindfolded, placebo-controlled diagnostic blocks.

**Discussion**

The protocol followed in the current study was stringent and reliable. Antecedent studies have shown that cervical medial branch blocks are a valid means of identifying painful cervical zygapophysial joints. Clinical studies have shown that that 0.5-mL aliquots of local anesthetic do not spread consistently to anesthetize structures other than the target cervical medial branch, and anatomic studies have shown that the cervical zygapophysial joints are the only structures innervated by the medial branches of the cervical dorsal rami that might be considered a source of chronic pain. Consequently, complete pain relief after a cervical medial branch block can only be interpreted as indicating that the joint supplied by the nerves blocked is the source of the patient's pain.

In the current study, these blocks were performed under stringent double-blindfolded, controlled conditions. Agents were delivered into strictly defined, predetermined target points under radiographic control, monitored by the operator and a separate observer. Neither the operator nor the patient knew the order of administration of the agents until all procedures had been completed and until all responses had been recorded.

Each patient received two local anesthetics and normal saline, allocated randomly. Three injections were used, because in the assessment of spinal pain, a placebo-controlled study cannot be conducted using one injection of local anesthetic and one of placebo. It is necessary in the first instance to establish if the target joint is putatively painful. There is no point to blocking a painless joint with normal saline. To establish that a joint is painful, the first block must be with a local anesthetic. It is impractical to then use placebo as the second agent, because a mischievous patient would know that the second agent is always the dummy. Therefore, once a putatively painful joint is found using the first local anesthetic block, second and third blocks are required in which local anesthetic and normal saline are assigned randomly. This maintains the blindfolding of the patient without contravening contemporary ethics requirements for informed consent.
In the current study, two different local anesthetics were used, but the duration of effect was not a diagnostic criterion. To be classed as true-positive responders, patients only had to experience complete relief with each active agent and but no relief with normal saline. The way in which duration of relief correlates with response to normal saline is complex, and details are addressed elsewhere.24

The significant feature of the current study is that cervical zygapophysial joint pain emerged as very common. Of the 41 patients eligible for placebo-controlled blocks who completed the investigation, 49% satisfied the diagnostic criteria. The 95% CI is the appropriate statistic to adjust for sample size, and in the current study, the 95% CI of the 49% prevalence estimate is 33-64%.

This estimate, however, pertains only to the prevalence of zygapophysial joint pain below C2-C3. To determine the overall prevalence of cervical zygapophysial joint pain, the prevalence of pain from C2-C3 should be added, which in the current study was 50% of patients with dominant headache.

Unfortunately, for anatomic reasons, placebo controls are not feasible for C2-C3 pain because the nerve that supplies this joint has a cutaneous branch. Nevertheless, the prevalence of C2-C3 zygapophysial joint pain as determined by comparative local anesthetic blocks is not discordant with the prevalence of lower cervical zygapophysial joint pain as determined by placebo-controlled blocks.

Overall, 31 of 52 patients who completed investigation had cervical zygapophysial joint pain at C2-C3 or below. This constitutes an overall prevalence of 60% (95% CI, 46%, 73%). A worst-case analysis requires that all patients who withdrew or who did not complete investigations are assumed not to have cervical zygapophysial joint pain. This means that the worst-case prevalence is 31 of 68, or 46% (95% CI, 34%, 57%). However, the patients who withdrew did not differ in any clinical or demographic respect, thus there is no reason to believe that all would have exhibited negative results. Therefore, the worst-case prevalence must be an underestimate.

Having used a separate sample of consecutive patients, the authors have confirmed their previous experience with this condition, but with use of placebo controls rather than with comparative local anesthetic blocks only. For patients with chronic neck pain after whiplash injury, cervical zygapophysial joint pain is extraordinarily common. As a diagnostic entity it cannot be ignored.

Establishing a diagnosis of cervical zygapophysial joint pain allows appropriate treatment to be directed specifically to the symptomatic joint. However, the treatment of cervical zygapophysial joint pain is still in its infancy. Encouraging reports of treatment using intraarticular steroids in uncontrolled studies18,22,29,37 were not supported by a recent randomized, double-blindfolded, controlled trial of this therapy.7 Outcome studies evaluating percutaneous radiofrequency medial branch neurotomy have reported only modest results,21,30-34,36 but may have been compromised by technical problems.11 A pilot study of an amended radiofrequency procedure yielded encouraging results22 and a randomized double-blindfolded controlled trial is in progress.

References


**Keywords:**

neck pain; placebo effect; prevalence; whiplash; zygapophysial joint
Figure 1. Maps showing the typical distribution of pain referred from each of the cervical zygapophyssal joints when stimulated in normal volunteers (modified from Dwyer et al).

Figure 2. Lateral radiographs showing needles in position on the target points for cervical medial branch blocks. A, A needle in position to block the third occipital nerve as it crosses the C2-C3 zygapophysial joint. B, A needle in position to block the C4 medial branch where it crosses the waist of the ipsisegmental articular pillar.
Figure 3. Flow diagram showing the number of patients included in each stage of the investigation protocol. TON = third occipital nerve.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Neck pain</td>
<td>100</td>
</tr>
<tr>
<td>Headache</td>
<td>88</td>
</tr>
<tr>
<td>Disturbance of concentration and/or memory</td>
<td>71</td>
</tr>
<tr>
<td>Paresthesia in upper limb</td>
<td>68</td>
</tr>
<tr>
<td>Weakness or heaviness in arms</td>
<td>68</td>
</tr>
<tr>
<td>Dizziness</td>
<td>53</td>
</tr>
<tr>
<td>Visual disturbance</td>
<td>42</td>
</tr>
<tr>
<td>Back pain</td>
<td>18</td>
</tr>
</tbody>
</table>

Table 1. Prevalence of Symptoms and Associated Features for 68 Consecutive Patients With Chronic Pain After Whiplash Injury
Table 2. Demographic Features and Reasons for Patients’ Withdrawal From Study

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Gender</th>
<th>Reason for Withdrawal</th>
</tr>
</thead>
<tbody>
<tr>
<td>31</td>
<td>F</td>
<td>Attempting other means of treatment</td>
</tr>
<tr>
<td>34</td>
<td>F</td>
<td>Could not afford to travel</td>
</tr>
<tr>
<td>38</td>
<td>M</td>
<td>Not enough pain because of a change in work practices</td>
</tr>
<tr>
<td>43</td>
<td>F</td>
<td>Not enough pain</td>
</tr>
<tr>
<td>43</td>
<td>F</td>
<td>Son became very ill</td>
</tr>
<tr>
<td>44</td>
<td>M</td>
<td>No reason given</td>
</tr>
<tr>
<td>48</td>
<td>F</td>
<td>Too much back pain to travel, awaiting operation</td>
</tr>
<tr>
<td>52</td>
<td>M</td>
<td>Underwent cervical neurosurgery</td>
</tr>
<tr>
<td>52</td>
<td>M</td>
<td>No reason given</td>
</tr>
<tr>
<td>59</td>
<td>F</td>
<td>Concurrent medical condition that prevented travel</td>
</tr>
<tr>
<td>66</td>
<td>M</td>
<td>No reason given</td>
</tr>
</tbody>
</table>

Figure 4. The distribution of symptomatic cervical zygapophysial joints by segmental level in 31 patients with cervical zygapophysial joint pain (a total of 38 positive joints).