A research synthesis of therapeutic interventions for whiplash-associated disorder (WAD): Part 5 – surgical and injection-based interventions for chronic WAD

Robert W Teasell MD1,2,3, J Andrew McClure BA1, David Walton PhD candidate4, Jason Pretty BA1, Katherine Salter BA1, Matthew Meyer BA1, Keith Sequeira MD2, Barry Death MD2

Whiplash-associated disorder (WAD) represents a significant public health problem, resulting in substantial social and economic costs throughout the industrialized world. While many treatments have been advocated for patients with WAD, scientific support regarding their effectiveness is often lacking. A systematic review was conducted to evaluate the strength of evidence associated with various WAD therapies. Multiple databases (including Web of Science, EMBASE and PubMed) were searched to identify all studies published from January 1980 through March 2009 that evaluated the effectiveness of any well-defined treatment for acute (less than two weeks), subacute (two to 12 weeks) or chronic (more than 12 weeks) WAD. The present article, the fifth in a five-part series, evaluates the evidence for surgical and injection-based interventions initiated during the chronic phase of WAD. Twenty-five studies were identified that met the inclusion criteria, six of which were randomized controlled trials with ‘good’ overall methodological quality (median Physiotherapy Evidence Database score of 7.5). For the treatment of chronic WAD, there was moderate evidence supporting radiofrequency neurotomy as an effective treatment for whiplash-related pain, although relief is not permanent. Sterile water injections have been demonstrated to be superior to saline injections; however, it is not clear whether this treatment is actually beneficial. There was evidence supporting a wide range of other interventions (eg, carpal tunnel decompression) with each of these evaluated by a single non-randomized controlled trial. There is contradictory evidence regarding the effectiveness of botulinum toxin injections, and cervical discectomy and fusion. The evidence is not yet strong enough to establish the effectiveness of any of these treatments; of all the invasive interventions for chronic WAD, radiofrequency neurotomy appears to be supported by the strongest evidence. Further research is required to determine the efficacy and the role of invasive interventions in the treatment of chronic WAD.

Key Words: Chronic pain; Chronic whiplash-associated disorder; Evidence-based medicine; Injections; Neck pain; Randomized controlled trials

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The term 'whiplash-associated disorder' (WAD) describes the consequences of a whiplash injury, defined as bony and soft tissue injuries of the neck caused by rapid acceleration immediately followed by rapid deceleration of the neck and head (1), almost invariably occurring as a consequence of a motor vehicle collision (MVC). With annual North American incidence rates estimated to be between 70 and 329 per 100,000 people (1,2), whiplash injuries are the most common injury following an MVC (2,3). Although it is widely believed that the majority of whiplash patients recover naturally within a few months of their injury, recent research (4) suggests that recovery is often prolonged, with approximately 50% of patients still complaining of neck pain one year after injury. Moreover, WAD is associated with significant economic costs as a result of lost work productivity, medical care, legal services and other disability-related expenses (5,6). Given the scope and cost of WAD, the identification of effective therapies for patients with whiplash-related injuries, especially chronic WAD, is of obvious importance.

In 1995, the Quebec Task Force (QTF) published its benchmark review (1) of the scientific literature and expert opinion on WAD. One of the primary conclusions of the report was that the majority of therapeutic interventions used in the treatment of WAD had undergone little to no scientific investigation. Accordingly, the QTF emphasized the need for more and higher quality research. More recently, Conlin et al (7,8) conducted a systematic review of the whiplash treatment literature (including studies published from 1993 to 2003) and noted that despite the QTF’s recommendations, “remarkably little quality research” (8) had been published in the area of WAD management.

The objective of the present review is to update and expand on previous work by evaluating the strength of evidence for therapies initiated during the acute (less than two weeks), subacute (two to 12 weeks) and chronic (more than 12 weeks) stages of WAD. Treatments were grouped according to time from injury to assist clinicians in deciding on an appropriate treatment course because therapies that are effective in the treatment of acute and subacute WAD may not necessarily be effective when initiated during the chronic phase. Furthermore, treatments for chronic WAD were divided into two sections: noninvasive interventions, and surgical and injection-based interventions. The present article, the fifth in a five-part series, evaluates the evidence for surgical and injection-based interventions initiated during the chronic phase of WAD.

METHOD
The following is a brief summary of the methods used for the present review. A more detailed explanation of the methodology is provided in the first article of the present series (9). A multistage screening process was conducted to identify all literature that evaluated therapeutic interventions for WAD published from January 1980 to March 2009, regardless of study design. Multiple databases were searched (including MEDLINE, CINAHL, EMBASE, PsycINFO, Web of Science and the Cochrane Central Register of Controlled Trials [CENTRAL]) using the following search terms: whiplash AND (therapy OR treatment OR intervention OR rehabilitation OR surgery OR neurotomy). The literature search was limited to clinical studies written in English that examined adult (18 years of age and older) human populations. A study was deemed eligible for review if it met the following criteria established a priori:

- The purpose of the study was to evaluate the effects of one or more clearly defined treatment protocols for WAD (eg, ‘physiotherapy’ without further elaboration was not considered to be a clearly defined protocol).
- At least 60% of the participants in the study sample must have experienced a whiplash injury resulting from an MVC; alternatively, the sample must have included a distinct and separately analyzed subgroup of MVC-related whiplash patients.
- Evaluation of the treatment effect must have involved measurable outcomes.
- Sample included at least three participants with a whiplash injury.

In total, the search procedure yielded 969 citations, 387 of which were duplicates. On screening titles and abstracts for relevance, 121 articles were considered for full review and, after applying inclusion criteria, 83 articles were selected for full review. Information abstracted from studies that met inclusion criteria was organized into tables; studies were grouped according to the type of intervention. For the present article, only studies examining surgical or injection-based interventions initiated during the chronic stage (ie, more than three months postinjury) were included.

All of the included randomized controlled trials (RCTs) were evaluated for methodological quality using a standardized rating scale, the Physiotherapy Evidence Database (PEDro) scale. This evaluation tool was designed specifically for assessing physical therapy research and has been validated for the assessment of RCTs (10). The PEDro scale consists of 10 equally weighted yes/no questions relating to issues of methodological quality and can be accessed at www.pedro.org.au/english/downloads/pedro-scale/. Two independent raters reviewed each article and discrepancies were resolved through consensus or, when that was not possible, by a third rater. Studies with PEDro scores of 9 to 10 were considered to be of ‘excellent’ methodological quality, while scores of 6 to 8 were considered to be of ‘good’ quality, and scores of 4 to 5 were considered to be of ‘fair’ quality. Studies scoring below 4 were judged to be of ‘poor’ quality and were considered to be methodologically equivalent to non-RCTs for the purpose of formulating conclusions. These descriptive terms of quality assessment were used to simplify the interpretation of results; however, it is important to note that these terms are only intended to provide an indication of a study’s rating on the PEDro scale. Non-RCTs were not assigned a PEDro score and were instead given a ‘no score’ designation.

Due to the limited number of studies investigating each of the specific WAD interventions, it was decided that both meta-analytical and levels-of-evidence approaches would be inappropriate. Therefore, a narrative approach was used to summarize the findings and formulate conclusions.

Because studies employing a nonexperimental or uncontrolled design are generally considered to be of inferior quality, these types of studies were only used to formulate conclusions in the absence of RCTs or when the results of
RCTs were conflicting. In addition, when the results of RCTs were conflicting, studies with higher PEDro scores were weighted more heavily.

**RESULTS**

Six RCTs (plus two follow-up studies) and 17 non-RCTs were identified that evaluated surgical or injection-based interventions for chronic WAD (ie, more than three months postinjury), and met the inclusion criteria. The mean PEDro score of the RCTs was 7.5, with scores ranging from 6 to 9 (Table 1). Overall, these RCTs were of high methodological quality, with the only common limitation being failure to conduct analyses on an intention-to-treat basis.

**Injection-based interventions**

**Sterile water injections:** Two studies conducted by Byrn et al (11,12) examined the use of sterile water injections in the treatment of chronic WAD (Table 2). In a pilot case series, Byrn et al (11) treated 10 patients with 0.1 mL intracutaneous sterile water injections into multiple (15 to 25) trigger points. Two months following the initial injections, nine patients reported being completely pain free, although six of these patients received two to four treatments. In a subsequent RCT of good quality, Byrn et al (12) randomly assigned 40 patients to receive subcutaneous injections of 0.3 mL to 0.5 mL of either sterile water or saline in each tender trigger point (range 5–80 injections per patient). Each patient received up to 3 treatments during the first 2 months of the protocol. Patients in the sterile water group reported significantly less mean pain (0.8 versus 2.0, P<0.05) and greater cervical mobility (54° versus 23°, P<0.05) immediately postinjection than those in the saline group; these differences remained significant at the 8-month follow-up (2.4 versus 4.7, P<0.001; and 20° versus –11°, P<0.05, for pain and mobility, respectively). No between-group differences in personality or psychological symptoms were reported.

**TABLE 1**

<table>
<thead>
<tr>
<th>Reference, year, country, PEDro score</th>
<th>RA</th>
<th>CA</th>
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**TABLE 2**

<table>
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<tr>
<th>Reference, year, country, score</th>
<th>Population and methods</th>
<th>Outcome measures</th>
<th>Results</th>
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<tbody>
<tr>
<td>Byrn et al (12), 1993, Sweden, no score</td>
<td>Randomized controlled trial. 40 patients with whiplash-induced neck pain and impaired cervical range of motion of 4–6 years that was refractory to analgesics and physiotherapy were randomly assigned to receive 0.3–0.5 mL subcutaneous injections of either sterile water or saline in each tender trigger point (range 5–80 injections per patient). Each patient received up to 3 treatments during the first 2 months of the protocol</td>
<td>Pain intensity (VAS), mobility of the cervical spine (Myrin goniometer), personality (the Neuroticism, Extroversion and Openness to experience [NEO] personality inventory) and psychological symptoms (Beck Depression Inventory, Spielberger Anxiety Test and Mood Adjective Checklist) were assessed immediately pre- and post-treatment, and at 1, 3 and 8 months after the first treatment</td>
<td>Patients in the sterile water group reported significantly less mean pain (0.8 versus 2.0, P&lt;0.05) and greater cervical mobility (54° versus 23°, P&lt;0.05) immediately postinjection than those in the saline group; these differences remained significant at the 8-month follow-up (2.4 versus 4.7, P&lt;0.001; and 20° versus –11°, P&lt;0.05, for pain and mobility, respectively). No between-group differences in personality or psychological symptoms were reported.</td>
</tr>
<tr>
<td>Byrn et al (11), 1991, Sweden, no score</td>
<td>Case series. 10 patients with ≥6 months whiplash-related neck pain and impaired cervical range of motion were included following a failed course of analgesics and physiotherapy. All tender trigger points received a 0.1 mL intracutaneous injection of sterile water, and patients were encouraged to intensify their physiotherapy treatment. The procedure was repeated in patients whose pain recurred</td>
<td>Pain intensity (VAS) was assessed before the first injection and at unspecified intervals over the following 2 months</td>
<td>8 patients were pain free (VAS = 0) and 2 experienced minimal pain (VAS = 2) immediately following the first injection. Nine of the patients were pain free at the end of the follow-up period, 3 of them after a single treatment, while 6 required 2 to 4 treatments. Significance values were not reported.</td>
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PEDro Physiotherapy Evidence Database; VAS Visual analogue scale

Pain Res Manage Vol 15 No 5 September/October 2010
TABLE 3
Summary of studies evaluating botulinum toxin A (BTXA) trigger point injections for chronic whiplash-associated disorder (WAD)

<table>
<thead>
<tr>
<th>Reference, year, country, score</th>
<th>Population and methods</th>
<th>Outcome measures</th>
<th>Results</th>
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<tbody>
<tr>
<td>Braker et al (15), 2008, Israel, PEDro score = 9</td>
<td>Randomized controlled trial. 20 patients with cervical myofascial pain, 2–48 weeks after a whiplash injury, were randomly assigned to receive either 200 units of BTXA or placebo (injected equally into four trigger points)</td>
<td>Pain intensity (VAS and verbal rating scale), quality of life (Short-Form 36 Health Survey), cervical ROM and intensity of tender pain-evoked mechanical pressure pain (using an algometer) were assessed at 3, 6, 9, 12 and 24 weeks after injection. A global assessment of treatment efficacy was also rated by physicians at 24 weeks</td>
<td>Although the BTXA group consistently made larger improvements, between-group differences were nonsignificant with the exception that a greater percentage of patients in the BTXA group achieved a 50% reduction in pain intensity at 24 weeks (70% versus 11%, P&lt;0.05)</td>
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<tr>
<td>Padberg et al (16), 2007, The Netherlands, PEDro score = 9</td>
<td>Randomized controlled trial. 40 patients with chronic WAD were randomly assigned to receive either 100 units of botulinum toxin (Botox®) or placebo (saline) in 2 mL syringes</td>
<td>Pain intensity (VAS) and cervical ROM were assessed at baseline and at 12-week follow-up</td>
<td>After 12 weeks, no significant differences were found between the two groups</td>
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<tr>
<td>Freund and Schwartz (13), 2000, Canada, PEDro score = 7</td>
<td>Randomized controlled trial. 30 patients with WAD for 26 months refractory to conservative treatment were divided into two groups: 15 received 100 units BTXA diluted to 100 units/1 mL saline, and 15 received 1 mL saline delivered to the five most tender cervical trigger points</td>
<td>Neck, head and shoulder pain intensity (VAS), cervical ROM, and the Verno-Mior Function Index were assessed at baseline and at 2 and 4 weeks post-treatment</td>
<td>At 4 weeks, patients in the treatment group had better cervical ROM (343±17.8° versus 308±12.9°, P&lt;0.01), and less neck, head and shoulder pain (10±1.3 versus 14.1±2.1, P&lt;0.01) than those in the placebo group. Although not significant, a greater percentage of patients in the treatment group showed improvement in subjective function (20% versus 8%)</td>
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<td>Juan (14), 2003, Spain, no score</td>
<td>Case series. 31 patients with WAD for ≥3 months were included after a failed course of conservative treatment. A dose of 50 to 75 units of BTXA diluted to 100 units/1 mL saline was injected into each patient’s tender superficial muscles. Patients also received information on home exercise</td>
<td>Neck pain intensity (VAS), cervical ROM and the Neck Pain Disability Index were assessed initially, and at 1, 4 and 8 weeks after injection</td>
<td>In total, 77.4% of patients responded positively to the treatment. Significant improvements were seen in terms of both pain intensity (from 6.6±2.1 to 4.8±2.1, P&lt;0.05) and cervical ROM (P&lt;0.05). Although not significant, neck pain disability also trended toward improvement</td>
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*Allergan Inc, USA. PEDro Physiotherapy Evidence Database; ROM Range of motion; VAS Visual analogue scale

Conclusions regarding sterile water injections in chronic WAD: Although there is evidence that sterile water injections are more effective than saline injections, methodological concerns prohibit definitive support for sterile water injections as beneficial for reducing whiplash-related symptoms.

Botulinum toxin A injections: Three RCTs and one non-RCT examined the use of botulinum toxin A (BTXA) injections in the treatment of chronic WAD (Table 3). In an RCT of good quality, Freund and Schwartz (13) randomly assigned 30 patients to receive either 100 units of BTXA or saline injected into five trigger points. Patients in the BTXA group experienced significant reductions in pain intensity four weeks after treatment, while those in the placebo group showed no such improvement. Similarly, Juan (14) followed 31 patients treated with 50 to 75 units of BTXA and found that pain and ROM improved significantly. In contrast, two RCTs of excellent quality (15,16) compared the effectiveness of BTXA with saline injections and found that BTXA was no more effective than placebo in reducing pain intensity at three and six months following treatment, respectively. However, it is noteworthy that while Padberg et al (16) did not find a trend in favour of the treatment group, Braker et al (15) found that those treated with BTXA reported consistently better outcomes than those in the placebo group, a trend that did not reach significance. Braker et al (15) injected 200 units of BTXA while Padberg et al (16) only injected 100 units, implying that higher doses may be required (although Juan [14] suggested otherwise). In addition, Braker et al (15) actively sought to reduce the time from injury to treatment, with an unreported number of patients receiving treatment during the subacute phase of WAD. Although this suggests that earlier treatment may have some benefit, findings from the subacute WAD literature have not confirmed this postulation (17,18).

Conclusions regarding BTXA injections in chronic WAD: There is contradictory evidence regarding the effectiveness of BTXA injections during the chronic stage of WAD.

Corticosteroid injections: One RCT and three non-RCTs evaluated the effectiveness of corticosteroid injections in the treatment of chronic WAD (Table 4). In a triple-blinded RCT of good quality, Barnsley et al (19) randomly assigned patients to receive intra-articular facet joint injections of either a corticosteroid (5.7 mg betamethasone) or an anesthetic (0.5% bupivacaine). The authors found no significant between-group differences, with a median time to return of 50% pre-injection pain levels of only three and 3.5 days for those in the corticosteroid group and the anesthetic group, respectively. In contrast, in one of two retrospective case series (20,21), Slipman et al (21) reported that, in a retrospective sample of 18 WAD patients with persistent daily headaches, intra-articular injections of a corticosteroid (0.8 mL Celestone Soluspan [betamethasone; Schering-Plough, USA] and 0.2 mL of 1% Xylocaine [lidocaine; AstraZeneca UK Ltd]) reduced the frequency of headaches in 61% of patients, although statistical significance was not reported.
In another retrospective case series, Slipman et al (20), 2001, USA, ns reported on 22 patients who underwent fluoroscopically guided cervical selective nerve root blocks using the same corticosteroid solution. Patients received an average of 2.1 injections and treatment was administered in conjunction with a physiotherapy program. Although 59% of patients experienced a transient steroid effect following treatment, there were no measurable benefits associated with this treatment at follow-up (an average of 33 weeks post-treatment).

Finally, in a case series involving 43 WAD patients with both a positive impingement sign and a positive analgesic block response of a painful shoulder, Chauhan et al (22) evaluated the effectiveness of subacromial space corticosteroid (40 mg Depo-Medrone [methylprednisolone acetate; Pfizer Inc, USA]) injections. In addition to the injection, patients also participated in a 12-week physiotherapy program designed to correct scapulothoracic rhythmic dysfunction and strengthen the rotator cuff muscles. The authors reported that 79% of patients showed ‘significant’ or ‘moderate’ shoulder pain relief. However, it was not clear whether the steroid injection, the physiotherapy or the combination of the two interventions were responsible for this improvement. Moreover, given that the authors failed to report several pertinent details (including statistical significance and the assessment procedure), the overall value of this study is limited.

Conclusions regarding corticosteroid injections in chronic WAD: Corticosteroid intra-articular and selective nerve root block injections did not appear to be effective for relieving pain in patients with chronic WAD. Based on the results of a case series (22), subacromial space corticosteroid injections combined with physiotherapy may be effective for patients with late-onset shoulder pain; however, further research is needed.

Tropisetron trigger point injections: One case series examined the effect of tropisetron, a 5HT3 receptor antagonist, in patients with chronic WAD (Table 5). Ettlin (23) followed 20 patients who received a total of 73 sessions of trigger point injections. In 84% of the sessions, pain relief of greater than two weeks in 52% of the sessions and more than two months in 10% of the sessions. It should be noted, however, that the duration of relief following treatment was highly variable, both within and between individuals. Furthermore, because this study was not blinded and failed to include a control group, it is difficult to assess the true benefit of tropisetron.

Conclusions regarding tropisetron trigger point injections in chronic WAD: Although one case series reported that tropisetron injections temporarily relieved whiplash-related pain, the evidence is not strong enough to demonstrate the effectiveness of this treatment.
Dextrose and lidocaine intra-articular injections: One case series examined the use of ‘joint regeneration’ therapy (theorized to strengthen the zygapophysial joint capsule) during the chronic phase of WAD (Table 6). Hooper et al (24) administered intra-articular injections of dextrose and lidocaine to 18 patients and found that pain and disability improved significantly at two-, six- and 12-month follow-up. However, because this study was unblinded, failed to include a control group and permitted patients to participate in conterventions (during and after the treatment), it is not clear whether the observed improvement could be attributed to the experimental treatment.

Conclusions regarding dextrose and lidocaine intra-articular injection therapy in chronic WAD: Although the results of one small case series suggested that ‘joint regeneration’ (dextrose and lidocaine intra-articular) therapy may reduce whiplash-related pain and disability, the evidence is not strong enough to establish the effectiveness of this treatment.

Epidural blood patch therapy
An intriguing case series (25) examined the effectiveness of epidural blood patch (EBP) therapy in patients with chronic WAD and a suspected cerebrospinal fluid (CSF) leak (Table 7). Ishikawa et al (25) assessed 66 chronic WAD patients with a suspected CSF leak and found evidence of a CSF leak in 37 patients. Following a two-week ‘control’ period in which patients participated in conventional therapies, 36 patients received the experimental therapy (EBP), which was repeated up to three times if symptoms did not improve (with a mean of 2.2 procedures). The authors reported that, while no symptom improvement was noted during the control period, pretreatment symptoms (headache, memory, dizziness, visual impairment, cervical pain, nausea and auditory symptoms) were significantly reduced one week following treatment. Furthermore, these improvements were maintained for up to six months. Although the authors concluded that their findings implicated a CSF leak in the etiology of chronic WAD, there is no way of knowing if this was, in fact, the case. To our knowledge, a consistent relationship between whiplash injuries and CSF leaks has yet to be established and, hence, interpretation of this study is difficult.

Conclusions regarding EBP therapy in chronic WAD: While the results of one case series (25) suggested that EBP therapy may be an effective treatment for chronic WAD involving a suspected CSF leak, the association of a CSF leak with chronic WAD has never been established.
Surgical interventions

Radiofrequency neurotomy: One RCT of good methodological quality, two follow-up studies and five non-RCTs examined the use of radiofrequency neurotomy (RFN) in the treatment of chronic WAD (Table 8). Following a successful pilot project in which 70% of those who underwent lower cervical medial branch neurotomies achieved complete pain relief for at least six months (26), Lord et al (27) randomly assigned 24 patients (selected on the basis of response to placebo-controlled diagnostic blocks) to undergo either active or sham radiofrequency procedures. Twenty-seven weeks following surgery, seven patients (58%) in the active group reported being pain free, compared with only one patient (8%) in the control group. Furthermore, the median time to the return to 50% of the preoperative level of pain was found to be significantly greater for patients in the active group (263 days) than for patients in the control group (8 days). Interestingly, patients who reported complete pain relief also exhibited resolution of preoperative psychological distress, as measured by the Symptom Checklist 90-R (28). Finally, in a follow-up of patients included in both the pilot project and the RCT (26,27), McDonald et al (29) reported on 28 patients who underwent lower cervical medial branch neurotomies, 18 of whom obtained complete pain relief for at least 90 days; the median duration of relief for these patients was 421 days. It should be noted that Lord et al (26) performed 10 third occipital neurotomies for the treatment of C2 to C3 zygopophyssial joint pain during their pilot project and found that the rate of technical failure was considerably higher for this procedure, with only three of 10 patients achieving long-lasting pain relief. Consequently, Lord et al recommended that RFN should not be used to treat C2 to C3 zygopophyssial joint pain until technical difficulties (such as inadequate coagulation) are resolved.

While these results suggest that RFN is an effective treatment for chronic whiplash, a number of methodological concerns have been noted (30). First, there is some indication that blinding may have been compromised in that 42% of patients in the active treatment group developed complications (lasting pain and/or numbness) following surgery, which may have revealed the treatment assignment. Second, significantly more patients in the control group reported being involved in injury-related litigation at baseline than patients in the experimental group (83% versus 33%, respectively). Although this may have biased results in favour of the treatment group, there is some evidence that litigants and nonlitigants do not differ significantly in terms of success, duration of relief or satisfaction with RFN procedures (27,31). Despite these criticisms, the study by Lord et al (27) is considered to be a breakthrough in the treatment of chronic WAD and received a PEDro score of 8, indicating high methodological quality.

In investigating the effect of repeated RFN, Husted et al (32) identified 21 patients who underwent multiple (two to seven) RFNs and found that the rate of success and the duration of relief were consistent following each procedure – in total, 39 of 41 surgeries were successful, with a mean duration of relief of 11.5 months. It should be noted, however, that this study involved a self-selected group of patients who were satisfied with their initial treatment and who had decided to repeat the procedure, raising the possibility of placebo effects. In another case series involving 40 patients, Prushansky et al (33) investigated the effect of RFN using a large number of outcomes and reported that, in addition to reductions in pain intensity, treatment with RFN was associated with improvement in pain-related disability, cervical ROM, isometric cervical muscle strength and cervical pressure pain threshold; however, 30% of the study’s participants were excluded because they were lost to follow-up. Finally, in a case series involving 14 patients, Liliang et al (34) examined the effectiveness of pulsed radiofrequency lesioning. By using multiple cycles at lower temperatures, this technique does not cause thermal tissue damage to adjacent nerve roots and is virtually painless. The authors reported 86% of patients at one-month follow-up and 64% of patients at one-year follow-up experienced significant pain relief.

Conclusions regarding RFN for chronic WAD: Although relief may not be permanent, there is strong evidence that RFN is effective in reducing pain in patients with chronic WAD. Moreover, it appears that the procedure can be repeated with a similar probability of success. Nevertheless, further research is needed to determine which patients are most likely to obtain significant relief from this highly invasive procedure.

Occipital nerve decompression: One case series (35) examined the use of greater occipital nerve decompression to relieve chronic whiplash-related headaches in 13 patients undergoing a total of 18 procedures (Table 9). While none of the patients reported achieving complete pain relief, 13 (72%) of the operations resulted in greater than 50% relief for at least three months following the procedure. Unfortunately, this study was not blinded, did not include a control group, did not report statistical significance and used a carefully selected sample of patients. Consequently, it is not clear on the basis of this study whether neurolysis of the greater occipital nerve actually had a beneficial effect on whiplash-related headache.

Conclusions regarding occipital nerve decompression in chronic WAD: On the basis of one case series (35), there was limited evidence that greater occipital nerve decompression may be effective in reducing whiplash-related headache, although further research using more rigorous methodology is needed before definitive conclusions can be drawn.

Carpal tunnel decompression: One case series evaluated the effectiveness of carpal tunnel decompression in the treatment of chronic whiplash-related neck and shoulder pain (Table 10). The rationale given for this intervention is that entrapment of the brachial plexus and peripheral nerves, including the median nerve at the carpal tunnel, may be a cause of pain following whiplash injury (36). Alpar et al (36) compared 38 WAD patients who underwent carpal tunnel decompression surgery with 30 patients treated as usual. At a mean follow-up time of 18 months, neck and shoulder pain had ‘resolved’ in 95% of the surgery patients, but only in 7% of the controls. However, because this study was not blinded and did not report statistical significance, it is difficult to draw any meaningful conclusions on the basis of this study.

Conclusions regarding carpal tunnel decompression in chronic WAD: Although there was limited evidence that carpal tunnel decompression may be effective in reducing
Table 8: Summary of studies evaluating radiofrequency neurotomy (RFN) for chronic whiplash-associated disorder (WAD)

<table>
<thead>
<tr>
<th>Reference, year, country, score</th>
<th>Population and methods</th>
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<tr>
<td>Lord et al (26), 1995, Australia, PEDro score = 8</td>
<td>Randomized controlled trial. 24 patients with ≥3 months pain in one or more cervical zygapophysial joints (excluding C2–C3) that was refractory to conventional therapy were randomly assigned to one of two treatment groups. 12 patients received percutaneous RFN, and 12 received a sham neurectomy. Patients received treatment only for their most painful joint</td>
<td>Pain intensity (VAS), the McGill Pain Questionnaire and yes/no questions regarding pain during activities were assessed at baseline and at a 3-month follow-up. Time to return of 50% preoperative pain level was also assessed via telephone contact</td>
<td>6 of 12 control group patients and 3 of 12 active treatment patients experienced return of pain immediately after the operation. Significantly different median times elapsed before pain returned to the 50% preoperative level: 263 days in the active treatment group compared with 8 days in the sham treatment group (P&lt;0.05)</td>
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<td>Husted et al (32), 2008, USA, ns</td>
<td>Case series. 22 patients with chronic WAD who had previous success with RFN but whose symptoms had returned were included in this study to receive another RFN treatment. One patient was lost to follow-up</td>
<td>Success of treatment was quantified as greater than 50% relief of pain following the operation</td>
<td>Repeat treatment was considered to be a success in 95% of patients and a failure in 1%. The mean duration of relief was 11.5 months, which is not significantly different from the duration of relief following initial treatment</td>
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<td>Liliang et al (34), 2008, Taiwan, ns</td>
<td>Case series. 14 patients with chronic WAD underwent pulsed radiofrequency lesioning of the cervical medial branches. The procedures were performed in 2 cycles of 180 s after localization under fluoroscopy guide</td>
<td>Primary outcome measures included pain intensity (VAS) and medicare requirements. Outcomes were assessed at 1, 6 and 12 months after the procedure</td>
<td>12, 11 and 9 patients reported a greater than 60% reduction in pain at the 1-, 6- and 12-month follow-ups, respectively. Medicine requirements were also decreased in 13, 12 and 10 patients at the 1-, 6- and 12-month follow-ups, respectively</td>
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<td>Prushansky et al (33), 2006, Israel, ns</td>
<td>Case series. 40 patients with chronic WAD (whose pain remained after receiving conservative treatments) underwent cervical RFN in various locations</td>
<td>Pain intensity (VAS), the Neck Disability Index, cervical range of motion, isometric cervical muscle strength, cervical pressure pain threshold, Symptom Checklist 90-R and subjective report of improvement were assessed at baseline and approximately 1 year after the intervention</td>
<td>Compared with baseline, patients showed significant improvement on each of the outcome measures, including pain intensity (32±30 versus 52±25), neck disability (17.2±9.7 versus 22.5±8.9) and cervical range of motion (251.3±68.2 versus 212±67.5), each significant at P&lt;0.001. Collectively, improvement was noted in 70% of patients at the 1-year follow-up, with 80% satisfied with the procedure</td>
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<td>Sapid and Gorup (31), 2001, USA, ns</td>
<td>Cohort study. 46 patients with ≥5 months of whiplash-induced headache, neck pain and shoulder pain were referred following a failed course of conservative treatment. 28 patients were litigant while 18 patients were nonlitigant. All patients had successful diagnostic medial branch nerve blocks before undergoing therapeutic RFN</td>
<td>Pain intensity (VAS), medication use and self-reported symptom improvement were obtained at baseline, 2 weeks and 1 year post-treatment</td>
<td>Compared with baseline, both litigants and nonlitigants experienced a significant reduction in pain intensity (from 8.2±1 to 3.6±1.8, P&lt;0.05), and had reduced medication use by 50%, however, between-group differences were not significant</td>
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<td>McDonald et al (29), 1999, Australia</td>
<td>Follow-up study. This study was a follow-up of 2 previous studies (Lord et al, 1995 [26] and 1996 [27]). Of the 28 patients who underwent RFN between C3–C4 and C6–C7, 11 were from Lord et al 1995 (26), 14 were from Lord et al 1996 (27) and 3 were new. Most patients received repeat procedures once their pain returned</td>
<td>The primary outcome measure was time to return of 50% preoperative pain level. Pain intensity (VAS) and the McGill Pain Questionnaire were assessed at baseline and at 3- and 12-month follow-ups or when pain returned</td>
<td>Pain refractory to the initial treatment (less than 30 days relief) did not respond to a second treatment. Recurrent pain that was relieved by the initial treatment for at least 90 days was relieved by repeat procedures for at least 90 days: median pain relief per procedure in this group (n=11) was 218.5 days; the range of cumulative duration of relief was 14 months to 5.4 years, as a result of 4 shorter-lasting procedures and 2 longer-lasting procedures</td>
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<td>Wallis et al (28), 1997, Australia</td>
<td>Secondary analysis. This study used a subset of the patients included in Lord et al 1996 (27). Only the 17 patients with a single painful joint were retained for analysis. The authors reasoned that any untreated painful joints could negatively influence the patient’s psychological profile</td>
<td>Pain intensity (VAS), the McGill Pain Questionnaire, the Symptom Checklist 90-R and yes/no questions regarding pain during activities were assessed at baseline and at 3 months post-treatment</td>
<td>6 of 9 patients receiving the active treatment and 3 of 8 receiving the sham neurotomy experienced complete resolution of psychological distress, total pain relief and full restoration of function</td>
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<td>Lord et al (26), 1995, Australia, ns</td>
<td>Case series. 19 patients with WAD for ≥3 months were diagnosed with cervical zygapophysial joint pain through comparative local anesthetic blocks. 10 patients underwent therapeutic third occipital neurectomy and 10 underwent lower cervical medial branch neurectomy. 28 procedures were performed for treatment of 21 joints</td>
<td>The primary outcome measure was duration of complete pain relief, defined as absolutely no pain in the targeted region. Progress was recorded at 3 and 12 months follow-ups, or when the pain returned</td>
<td>3 of 10 patients who underwent third occipital neurectomy and 7 of 10 patients who underwent lower cervical medial branch neurotomy obtained complete pain relief for clinically useful periods (6 months to 2 years). Ataxia was a regular side effect of third occipital neurotomy</td>
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ns No score; PEDro Physiotherapy Evidence Database; VAS Visual analogue scale
Cervical discectomy and fusion: Two case series examined the effectiveness of cervical discectomy and fusion for chronic WAD (Table 11). Algers et al (37) followed 20 patients who underwent discectomy and an anterior cervical fusion and reported that results were 'unsatisfying', although 55% of patients reported at least some reduction in headache and neck pain. Conversely, in a case series involving 44 patients selected on the basis of response to diagnostic blocks, Long et al (38) performed posterior cervical fusion of C1, C2, C3 and C4 in various combinations. Bony fusion was achieved in 95% of patients, with 79% obtaining complete pain relief and another 14% obtaining satisfactory relief. Moreover, pain intensity was reported to be significantly reduced for up to four years, although statistical results were not reported.

Conclusions regarding cervical discectomy and fusion in chronic WAD: Only two low-quality case series (37,38) reported on cervical discectomy and fusion; however, it is not clear whether this procedure provides substantial relief for patients with chronic WAD.

DISCUSSION

In total, 25 studies were identified that examined surgical and injection-based interventions initiated during the chronic phase of WAD (more than three months). While a few of the included RCTs were of good overall quality, the majority of the studies were small, uncontrolled nonrandomized trials or case series. Moreover, with the exception of research evaluating botulinum toxin injections, none of the interventions were investigated by more than one RCT. This highlights the wide range of surgical and injection-based interventions used to treat chronic WAD, but it also means that many of the conclusions reached in the present review are based on limited evidence and, as such, should be viewed with some caution.

Based on the results of one high-quality RCT and several non-RCTs, there is strong evidence that RFN is effective in reducing whiplash-related pain. Furthermore, the success of
TABLE 12
Summary of evidence for surgical and injection-based therapies for chronic whiplash-associated disorder (WAD)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Conclusions</th>
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<tr>
<td>Sterile water injections</td>
<td>Although there is evidence that sterile water injections are more effective than saline injections, methodological concerns prohibit definitive support for sterile water injections as beneficial for reducing whiplash-related symptoms.</td>
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<td>Botulinum toxin injections</td>
<td>There is contradictory evidence regarding the effectiveness of botulinum toxin injections during the chronic stage of WAD.</td>
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<td>Corticosteroid injections</td>
<td>Corticosteroid intra-articular and selective nerve root block injections did not appear to be effective for relieving pain in patients with chronic WAD. Based on the results of a case series, subacromial space corticosteroid injections combined with physiotherapy may be effective for patients with late-onset shoulder pain; however, further research is needed.</td>
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<td>Tropisetron injections</td>
<td>Although one case series reported that tropisetron injections temporarily relieve whiplash-related pain, the evidence is not strong enough to demonstrate the effectiveness of this treatment.</td>
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<td>Intra-articular dextrose and lidocaine injections</td>
<td>Although the results of one small case series suggested that ‘joint regeneration’ (intra-articular dextrose and lidocaine) therapy may reduce whiplash-related pain and disability, the evidence is not strong enough to establish the effectiveness of this treatment.</td>
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<td>Epidural blood patch therapy</td>
<td>While the results of one case series suggested that epidural blood patch therapy may be an effective treatment for chronic WAD involving a suspected cerebrospinal fluid leak, the association of a cerebrospinal fluid leak with chronic WAD has never been established.</td>
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<td>Radiofrequency neurotomy</td>
<td>Although relief may not be permanent, there is strong evidence that radiofrequency neurotomy is effective in reducing pain in patients with chronic WAD. Moreover, it appears that the procedure can be repeated with a similar probability of success. Nevertheless, further research is needed to determine which patients are most likely to obtain significant relief from this highly invasive procedure.</td>
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<td>Occipital nerve decompression</td>
<td>On the basis of one case series, there was limited evidence that greater occipital nerve decompression may be effective in reducing whiplash-related headache, although further research using more rigorous methodology is needed before definitive conclusions can be drawn.</td>
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<tr>
<td>Carpal tunnel decompression</td>
<td>Although there was limited evidence that carpal tunnel decompression may be effective in reducing whiplash-related pain, the evidence was insufficient to determine the effectiveness of this procedure.</td>
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<tr>
<td>Cervical discectomy and fusion</td>
<td>Only two low-quality case series reported on cervical discectomy and fusion; however, it is not clear whether this procedure provides substantial relief for patients with chronic WAD.</td>
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</table>

RFN in a significant number of chronic WAD patients suggests that the etiology of pain may often be due to cervical facet joint injuries. While this conclusion is consistent with the findings from Conlin et al (8), a more recent review (30) deemed the RCT by Lord et al (27) to be ‘scientifically inadmissible’; however, the criteria for dismissing this study appear to be relatively minor and do not justify this extreme position. Nevertheless, RFN has been implemented slowly and with some reluctance, perhaps because clinical experience has not generated sufficient enthusiasm, anticipated benefits do not outweigh potential risks, or the effect is not permanent. Considering the invasive nature of this procedure and some uncertainty regarding which patients will actually benefit, further research is needed.

Several other treatments were evaluated and supported by single, small, nonrandomized trials, most of which were case series: tropisetron injections, intra-articular dextrose and lidocaine injections, EBP therapy, subacromial and selective nerve root block corticosteroid injections, occipital nerve decompression and carpal tunnel decompression. While some of these trials represent promising innovations in the treatment of chronic WAD, further research is needed to determine the effectiveness of these interventions. There is also evidence that sterile water injections are superior to saline injections, although this evidence does not convincingly demonstrate the effectiveness of sterile water injections in treating whiplash-related symptoms.

There is conflicting evidence regarding the effectiveness of botulinum toxin injections. While only one of three RCTs (13) found that BTXA injections were associated with significant benefit compared with placebo, one of the other trials (15) reported a consistent trend in favour of BTXA over placebo. Additional research is needed to establish the effectiveness of this intervention. Similarly, cervical discectomy and fusion was evaluated in two case series with conflicting results. Furthermore, it does not appear that intra-articular corticosteroid injections are beneficial during the chronic stage of WAD.

The present review was limited by several methodological concerns. First, because of the small number of studies in the whiplash literature, the criteria for inclusion were quite broad. All studies were included regardless of study design, as long as 60% of the sample experienced a WAD and they included a sample of at least three participants with a whiplash injury. This may have resulted in the inclusion of some studies of lower scientific merit; however, such studies were only used to formulate conclusions in the absence of superior RCTs, and these limitations were noted in the conclusions themselves as well as in the discussion. Second, there are limitations with the quality assessment process used in the current review to evaluate the methodological quality of RCTs. For example, it is possible that an RCT with significant between-group differences at baseline that does not blind patients, therapists or assessors could still have a PEDro score of 6 and be considered a study of good methodological quality despite these significant limitations. Again, these issues were noted in relevant conclusions and study descriptions. Nevertheless, these measures do not negate the need for readers to be ‘critical consumers’ of the material presented.

Another limitation that should be noted is that conclusions based on the studies included in the present review may not be generalizable to all patients with WAD. Patients who agree to undergo invasive interventions have likely already
failed to benefit from more conservative treatments and may experience a greater degree of distress from their symptoms than patients who do not seek out such treatments. This may be particularly true of patients who participate in studies investigating surgical procedures – one can assume that they are chronic whiplash patients who are more severely affected.

Due to the cost and risk associated with surgical and injection-based interventions, it is of particular importance that these procedures are rigorously evaluated. The need for high-quality research is highlighted by the fact that such invasive interventions are the most likely to elicit placebo responses (39). Unfortunately, the majority of studies included in this review were non-RCTs with small sample sizes, generic inclusion criteria, poor methodological design (eg, inadequate length of follow-up) and poor reporting quality (eg, no statistical findings reported). Collectively, these limitations precluded firm conclusions regarding the effectiveness of any surgical or injection-based intervention for patients with chronic WAD. There are overall positive results examining RFN and mixed results for botulinum toxin injections (Table 12). Further research is needed to determine which interventions are most effective for individuals with chronic WAD refractory to more conventional treatment.

REFERENCES


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