

A research synthesis of therapeutic interventions for whiplash-associated disorder (WAD): Part 2 – interventions for acute WAD

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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 evidence supporting 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 clearly defined treatment for acute (less than two weeks), subacute (two to 12 weeks) or chronic (more than 12 weeks) WAD. The present article, the second in a five-part series, evaluates the evidence for interventions initiated during the acute phase of WAD. Twenty-three studies that met the inclusion criteria were identified, 16 of which were randomized controlled trials with 'fair' overall methodological quality (median Physiotherapy Evidence Database score of 5.5). For the treatment of acute WAD, there was strong evidence to suggest that not only is immobilization with a soft collar ineffective, but it may actually impede recovery. Conversely, although exercise programs, active mobilization and advice to act as usual all appeared to improve recovery, it is not clear which of these interventions was the most effective. While there was also evidence supporting the use of pulsed electromagnetic field therapy and methylprednisolone infusion, the evidence was insufficient to establish the effectiveness of either of these treatments. Based on current evidence, activation-based therapy is recommended for the treatment of acute WAD; however, additional research is required to determine the relative effectiveness of various exercise/mobilization programs.

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

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 held that

Une synthèse de la recherche sur les interventions thérapeutiques à l'égard des troubles liés aux coups de fouet cervicaux (TCFC) : Partie 2 – Les interventions en cas de TCFC aigus

Les troubles liés aux coups de fouet cervicaux (TCFC) représentent un problème important en santé publique, associé à des coûts sociaux et économiques substantiels dans le monde industrialisé. De nombreux traitements sont préconisés pour les patients ayant des TCFC, mais souvent, on ne possède pas de données scientifiques probantes en étayant l'efficacité. Les chercheurs ont procédé à une analyse systématique pour évaluer la qualité des preuves associées aux diverses thérapies des TCFC. Ils ont effectué des recherches dans de multiples bases de données (y compris Web of Science, EMBASE et PubMed) pour repérer toutes les études publiées entre janvier 1980 et mars 2009 qui évaluaient l'efficacité de tout traitement clairement défini en cas de TCFC aigu (moins de deux semaines), subaigu (de deux à 12 semaines) ou chronique (plus de 12 semaines). Le présent article, deuxième d'une série de cinq, vise à évaluer les données probantes liées aux interventions amorcées pendant la phase aiguë des TCFC. Les chercheurs ont repéré 23 études respectant les critères d'inclusion, dont 16 étaient des essais aléatoires et contrôlés à la qualité méthodologique globale « modérée » (indice médian de la base de données probantes en physiothérapie de 5,5). Pour traiter un TCFC aigu, des données probantes solides indiquent que non seulement l'immobilisation à l'aide d'un collier cervical souple est inefficace, mais qu'elle pourrait même nuire au rétablissement. Par contre, même si les programmes d'exercice, la mobilisation active et les conseils pour agir semblent tous améliorer le rétablissement, on ne sait pas exactement laquelle de ces interventions est la plus efficace. Des données probantes appuient également l'utilisation d'une thérapie électromagnétique pulsée et d'une infusion de méthylprednisolone, mais elles sont insuffisantes pour établir l'efficacité de ces traitements. D'après les données probantes actuelles, une thérapie fondée sur l'activation est recommandée pour le traitement des TCFC aigus. Cependant, des recherches supplémentaires s'imposent pour déterminer l'efficacité relative de divers programmes d'exercice et de mobilisation.

the majority of whiplash patients recover naturally within a few months of their injury, recent research suggests that recovery is often prolonged, with an estimated 50% of patients still complaining of neck pain one year after injury (4). 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, developing effective therapies that prevent chronicity is of obvious importance.

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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 (which included 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 was 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 (longer 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 WAD may not necessarily be effective when initiated in the subacute or chronic phase. The present article, the second in a five-part series, evaluates the evidence for interventions initiated during the acute (initial two weeks) phase of WAD.

METHOD

The following is a brief summary of the methods used for the current 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 PubMed, 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.
- The 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, and studies were grouped

according to the type of intervention being investigated. For the current article, only studies that investigated interventions initiated during the acute stage (ie, within the first two weeks) 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 quality 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 'good' quality and scores of 4 to 5 were considered '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 using a nonexperimental or uncontrolled design are generally considered to be of lower 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

Sixteen RCTs (plus two follow-up studies) and five non-RCTs were identified that evaluated therapeutic interventions initiated during the acute stage of WAD (ie, within two weeks of injury) and met the inclusion criteria. The median PEDro score of the RCTs was 5.5, with scores ranging from 4 to 8 (Table 1). The most common methodological limitations were a failure to blind patients and/or therapists, with only four studies using at least one of these methods. Furthermore, only four of the studies conducted their analyses on an intention-to-treat basis and only six used blinded assessors. Overall, the studies included in our analysis investigated interventions that covered five different treatment categories: educational interventions, exercise programs, mobilization programs, pharmacological interventions and alternative treatments (including pulsed electromagnetic field therapy [PEMT] and laser acupuncture).

Educational interventions

Two RCTs of good quality (11,12) and one quasirandomized trial (13) investigated the impact of educational interventions initiated during the acute phase of WAD (Table 2). Two of the

TABLE 1
Physiotherapy Evidence Database (PEDro) scores for randomized controlled trials evaluating acute whiplash-associated disorder therapies

Reference, year	PEDro criteria										Total score
	RA	CA	BS	SB	TB	AB	AF	ITT	BC	PVM	
Ferrari et al (11), 2005	✓	✓	✓		✓	✓	✓		✓	✓	8
Pettersson and Toolanen (30), 1998	✓	✓	✓	✓	✓	✓	✓		✓		8
Foley-Nolan et al (31), 1992	✓	✓	✓	✓	✓	✓	✓		✓		8
Vassiliou et al (15), 2006	✓	✓	✓				✓	✓	✓	✓	7
Kongsted et al (12), 2008	✓	✓					✓	✓	✓	✓	6
McKinney et al (14), 1989	✓	✓	✓			✓			✓	✓	6
Kongsted et al (23), 2007	✓	✓					✓	✓	✓	✓	6
Mealy et al (22), 1986	✓	✓	✓			✓			✓	✓	6
Dehner et al (28), 2006	✓		✓				✓		✓	✓	5
Schnabel et al (19), 2004	✓	✓	✓						✓	✓	5
Aigner et al (33), 2006	✓			✓			✓		✓	✓	5
Borchgrevink et al (26), 1998	✓		✓			✓			✓	✓	5
Rosenfeld et al (20), 2000	✓		✓				✓		✓		4
Dehner et al (27), 2009	✓	✓						✓	✓		4
Soderlund (17), 2000	✓		✓						✓	✓	4
Thuile and Walzl (32), 2002	✓		✓						✓	✓	4

AB Assessor blinding; AF Adequate follow-up; BC Between-group comparisons; BS Baseline similarity; CA Concealed allocation; ITT Intention-to-treat analysis; PVM Point estimates and variability reported; RA Random allocation; SB Subject blinding; TB Therapist blinding

studies compared education with advice to act as usual and found conflicting results, with one finding no significant differences between groups (11) and the other finding that patients in the educational group had significantly lower pain ratings six months later (13). Although the study reporting a significant treatment effect was a non-RCT, it is noteworthy that in this study, the educational information was presented in the hospital via a 12 min video, while in the RCT, patients were simply given pamphlets to read at home. Investigating whether the method of delivery affects the impact of educational interventions, Kongsted et al (12) randomly assigned patients to receive either a one-hour information session or an educational pamphlet and reported a nonsignificant trend in favour of those who received the information orally. Evidence regarding the effectiveness of educational interventions is conflicting; however, based on the results of the RCTs, it does not appear that providing educational information during the acute phase provides a significant benefit sufficient to alter outcomes. Nevertheless, further research is needed to determine whether the method of delivery influences the effectiveness of educational interventions.

Conclusions regarding educational interventions in acute WAD: Based on the existing research, it does not appear that providing educational information during the acute phase provides a significant measurable benefit; however, there is some indication that oral and/or video presentation of educational information may be more effective than the distribution of pamphlets.

Exercise programs

Three RCTs and one non-RCT evaluated the effectiveness of exercise programs offered during the acute phase of WAD (Table 3). Two RCTs of good quality (14,15) compared the effect of exercise to immobilization with a soft collar. Both reported exercise was associated with significantly less pain at two and six months, respectively. However, in a follow-up study,

McKinney (16) reported that a comparable percentage of patients in both groups had chronic symptoms two years after injury. In an RCT of fair quality, Soderlund (17) compared an exercise routine aimed at mobilization with an exercise routine aimed at improving kinesthetic sensibility and coordination in addition to mobilization. For the purposes of the present review, mobilization programs were differentiated from exercise programs in that exercise programs had specific treatment aims (eg, strength and endurance) whereas mobilization programs were aimed at simply increasing or maintaining mobility. The authors found that, although patients who performed the additional exercises reported a greater 'ability to reduce pain' (a question relating to coping ability), patients in both groups experienced similar levels of recovery at six months after injury. Finally, in a case series that included 45 patients, Baltaci et al (18) found that mobilization and stabilization exercises were associated with significant recovery at 12 weeks, although it is difficult to determine whether this recovery was due to the exercise program or natural recovery because there was no control group. Given the above results, it appears that exercise programs are superior to immobilization, although long-term recovery may be unaffected by either intervention. Supplemental exercise programs, when added to mobilization programs, were no more effective than mobilization programs alone.

Conclusions regarding exercise programs in acute WAD:

Although long-term recovery may be unaffected by either exercise or immobilization in a soft collar during the acute phase of WAD, it appears that exercise programs are significantly more effective in reducing pain intensity over both the short and medium term. Conversely, supplemental exercise programs added to mobilization programs may not be any more beneficial than mobilization programs alone.

Mobilization programs

In total, seven RCTs and three quasirandomized trials assessed the relative effectiveness of active mobilization, advice to 'act

TABLE 2
Summary of studies evaluating educational interventions for acute whiplash-associated disorder (WAD)

Reference, year, country, score	Population and methods	Outcome measures	Results
Kongsted et al (12), 2008, Denmark, PEDro score = 6	Randomized controlled trial. 182 participants with mild, acute WAD complaints were randomly assigned to receive either a 1 h educational session with a specially trained nurse (n=119) or an educational pamphlet (n=63). Both groups received the same information, the only difference being the method of delivery	Neck disability (Copenhagen Neck Functional Disability Scale) and average neck pain and headache (on a scale from 0 to 10) were assessed at baseline and at 3 months, 6 months and 12 months postintervention	After 3 months, 6 months and 12 months, 60%, 58% and 66% of the total sample had recovered, respectively. Although a greater proportion of those who received oral advice were considered to be recovered at 12 months (70% versus 58%), group differences were not significant on any of the outcome parameters
Ferrari et al (11), 2005, Canada, PEDro score = 8	Randomized controlled trial. 112 patients presenting to an emergency department with acute WAD received nonstandardized treatments. At discharge, experimental group patients received a 1-page evidence-based pamphlet offering reassurance and emphasizing mobilization and continuation of normal activities; control group patients received a standard, nondirective discharge information sheet	Subjective global improvement (patients who chose 'all better' were considered recovered), symptom severity, extent of limitations in daily activities, employment status and health resource use were assessed at 2 weeks and 3 months postinjury	At 2 weeks, 7.3% of the experimental group and 8.8% of the control group reported recovery; at 3 months, 21.8% of the experimental group and 21.0% of the control group reported recovery. No significant differences were found between the groups at any time
Oliveira et al (13), 2006, USA, no score	Quasirandomized trial. 126 patients presenting to an emergency department with acute WAD received unspecified standard care or standard care plus a 12 min educational video. The video, which was viewed in the emergency department, emphasized the psychophysiological aspects of chronic pain and included education about the physiology and course of whiplash injury; treatment within (rest and immobilization) and after 48 h (gradual return to activity); physical and emotional triggers of pain; and instruction on stretching exercises and breathing relaxation. All patients received analgesics as needed	The Short Musculoskeletal Function Assessment and a survey assessing medication and medical service usage were conducted by phone at 1 month, 3 months and 6 months postinjury	Compared with the standard care group, the video group had less pain at 1 month, 3 months and 6 months (P<0.001). Medical service usage and medication use were also lower for the video group at 6 months (P<0.001)

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as usual' and immobilization initiated during the acute phase of WAD (Table 4). As mentioned previously in the present review, mobilization programs were differentiated from exercise programs in that exercise programs had specific treatment aims whereas mobilization programs were aimed at simply increasing or maintaining mobility.

Four of the RCTs (two of good quality and two of fair quality) and two of the non-RCTs compared the use of mobilization exercises with immobilization using a soft collar, with three of the RCTs reporting that mobilization was associated with significantly greater reductions in pain at the time of follow-up, ranging from eight weeks to three years (19-22). Furthermore, Mealy et al (22) also reported that mobilization was associated with improved cervical range of motion (ROM) at eight weeks after injury. In contrast, in an RCT of good quality, Kongsted et al (23) reported that patients who performed mobilization exercises and patients immobilized with a soft collar had similar outcomes in terms of pain, disability and work capability at one year after injury. It should be noted, however, that a large proportion of patients in the soft collar group reported poor compliance with the study protocol. A subsequent analysis showed that patients who actually wore the collars as frequently as was stipulated had a significantly higher risk of being disabled and/or having altered work ability compared with patients in the mobilization group. Similarly, neither of the non-RCTs found significant differences between mobilization and immobilization with a soft collar in terms of pain or cervical ROM (24,25).

In addition to comparing active mobilization with immobilization, Kongsted et al (23) included a third trial condition in which patients were advised to act as usual (ie, remain active but within the limits of pain). Although the authors found that all three groups experienced similar levels of recovery, almost one-half of the patients in the act-as-usual group sought other interventions. In fact, a large percentage of patients in all three treatment groups used cointerventions, making it difficult to isolate and determine the effect of each individual treatment. Two other RCTs of fair quality also investigated the effectiveness of advising patients to act as usual. Comparing advice to act as usual versus immobilization with a soft collar, Borchgrevink et al (26) found that advice to remain active was associated with significantly better recovery in terms of a wide range of outcomes, including neck pain, headache, memory and concentration. Dehner et al (27) compared advice to act as usual to active (joint mobilization, soft tissue and trigger point treatments) and passive (heat, massage and electrotherapy) physical therapy and found that both types of therapy were associated with lower median periods of disability. However, it should be noted that 65% of the participants in the act-as-usual group used other neck interventions during the study period or were lost to follow-up. In terms of reducing pain at two months after injury, active therapy was significantly more effective than passive therapy (27).

Finally, two studies investigated issues related to length of or type of immobilization. In an RCT of fair quality, Dehner et al (28) compared patients who were immobilized with a soft collar for either two or 10 days and reported no significant

TABLE 3
Summary of studies evaluating exercise programs for acute whiplash-associated disorder (WAD)

Reference, year, country, score	Population and methods	Outcome measures	Results
Vassiliou et al (15), 2006, Germany, PEDro score = 7	Randomized controlled trial. 200 patients with WAD for less than 48 h were prescribed an NSAID and an antihistamine. Immobilization group patients wore a soft collar continuously for the first 7 days postinjury, after which they could seek treatment at their discretion. Physiotherapy group patients had 10 sessions during the first 2 weeks postinjury, which included heat application, lymphatic drainage and massage; active resistance exercises were performed daily at home. Collar use was permitted for the first 2 days	Primary outcomes were pain intensity and disability (on a scale from 0 to 10). The secondary outcome was the proportion of patients with residual pain (defined as pain severity of less than 1 of 10). Assessment was conducted during the first treatment week, and at 6 weeks and 6 months postinjury	Although between-group differences were not significant during the first week, patients in the physiotherapy group reported significantly less pain (1.5 ± 2.3 versus 2.7 ± 2.8 , $P < 0.01$) and disability (1.3 ± 2.2 versus 2.5 ± 2.7 , $P < 0.01$) at 6 months. These differences were maintained at 6 months in terms of both pain (1.2 ± 2.1 versus 2.3 ± 2.6 , $P < 0.001$) and disability (1.1 ± 1.2 versus 2.0 ± 2.4 , $P < 0.001$). Furthermore, more physiotherapy patients (81.9%) than immobilization patients (62.7%) reported no pain at 6 months ($P < 0.01$), but not at 6 weeks
Soderlund (17), 2000, Sweden, PEDro score = 4	Randomized controlled trial. 59 patients with acute WAD were included. Control group patients were instructed to complete arm, neck and breathing exercises at least 3 times daily; alternate rest with activity; protect their neck from cold; walk daily; maintain good posture; avoid lifting; and refrain from collar use. Patients in the experimental group completed the same exercise program, complemented by the addition of exercises to improve kinesthetic sensibility and neck muscle coordination	The Pain Disability Index, Self-Efficacy Scale, CSQ, cervical ROM, cervicothoracic posture and kinesthetic sensibility were assessed at baseline, and at 3 months and 6 months follow-up	Although both groups showed improvement over time, the two groups did not differ significantly in terms of any of the outcome measures. However, patients in the experimental group reported a greater increase in perceived ability to decrease pain ($P < 0.01$), although this result is based on a single item on the CSQ
McKinney et al (14), 1989, Northern Ireland, PEDro score = 6	Randomized controlled trial. 247 patients with acute WAD received mobilization advice ($n=66$), physiotherapy ($n=71$) or rest ($n=33$). Those in the rest group were given general advice to mobilize after 10 to 14 days of rest. Physiotherapy included multimodal therapy and active and passive repetitive movements (10 h over 6 weeks). Mobilization advice (one 30 min session) included a demonstration of neck exercises	Neck pain intensity (VAS) and cervical ROM (assessed with a goniometer) were assessed initially, and at 1- and 2-month review sessions. Lateral flexion was used as a proxy for full ROM	Although patients in the physiotherapy and advice groups did not differ with respect to pain intensity or cervical ROM at any time, both groups demonstrated greater improvement than those in the rest group in terms of mean ROM (64 ± 12.9 and 64.1 ± 12.7 versus 55.1 ± 14.8 , $P < 0.01$) and median pain severity (1.9 and 1.8 versus 3.0, $P < 0.01$) at the 2-month follow-up session
McKinney (16), 1989, Northern Ireland	Follow-up study. A 2-year follow-up to the McKinney et al (14) study	The presence of symptoms and time to recovery were recorded at 2 years postinjury via a mailed follow-up questionnaire	The proportion of patients without persistent symptoms did not differ significantly between the physiotherapy (56%) and rest (54%) groups; however, a significantly greater proportion of advice group patients (77%) were symptom free at 2 years ($P < 0.05$) compared with those in the physiotherapy and rest groups
Baltaci et al (18), 2003, Turkey, no score	Case series. 45 patients with WAD of unspecified duration completed an individualized program (3 weeks, 3 day per week) of passive mobilization based on the Cyriax approach. Mobilization was complemented with a home exercise program consisting of arm and shoulder movements while holding a 0.5 kg weight	Pain intensity (VAS) was assessed before treatment, and at 3 weeks, 6 weeks and 12 weeks postinjury. Cervical ROM was assessed before and after treatment	Pain intensity was significantly reduced at both the 3-week ($P < 0.05$) and 6-week ($P < 0.05$) follow-ups. Cervical ROM increased 10° in flexion, 20° in extension, 15° in right lateral flexion, 10° in left lateral flexion, 15° in right rotation and 10° in left rotation from pre- to post-treatment; significance levels were not reported

CSQ Coping Strategies Questionnaire; NSAID Nonsteroidal anti-inflammatory drug; PEDro Physiotherapy Evidence Database; ROM Range of motion; VAS Visual analogue scale

differences between these two groups in terms of pain, disability or ROM. Similarly, Gennis et al (29) compared rest with or without a soft collar for two weeks and found that both groups experienced comparable levels of recovery.

Conclusions regarding mobilization in acute WAD: Although there is some conflicting evidence, it appears that immobilization with a soft collar is less effective than active mobilization and no more effective than advice to act as usual. In contrast, there is strong evidence that active mobilization is associated with reduced pain intensity and limited evidence that mobilization may also improve ROM, although it is not clear whether active mobilization is any more effective than advice to act as usual.

Pharmacological interventions

A single study was identified that investigated a pharmacological intervention initiated during the acute phase of WAD (Table 5). In an RCT of good quality, Pettersson and Toolanen (30) examined the use of methylprednisolone, a drug with both neuroprotective and anti-inflammatory effects. The authors reported that treatment with methylprednisolone was associated with a significant reduction in disabling symptoms, total number of sick days and sick leave profile at six months after injury. However, on review of the study's results, it appears that these differences were largely accounted for by a small number of outliers. Thus, although the results from this study suggest that methylprednisolone is effective in the treatment of WAD,

TABLE 4
Summary of studies evaluating simple mobilization exercises for acute whiplash-associated disorder (WAD)

Reference, year, country, score	Population and methods	Outcome measures	Results
Dehner et al (27), 2009, Germany, PEDro score = 4	Randomized controlled trial. 70 patients with acute whiplash injuries were randomly assigned to receive either 'active physical therapy' (joint mobilization, soft-tissue treatment, trigger point treatment, posture training and electrotherapy) or 'passive physical therapy' (moist heat application, classic massage and electrotherapy). Therapy began 1 week after random assignment and was provided 3 times per week for 7 weeks	Outcome measures included average pain scores (VAS) and ROM deficit assessed with a two-legged goniometer. Assessments were made at baseline and at 2 months postinjury. The period of disability was also documented after 2 months	Participants in the active physical therapy group made significantly greater improvements in pain scores compared with participants in the passive group (50.5 versus 39.2, $P < 0.05$). Neither group showed deficits in ROM after 2 months
Kongsted et al (23), 2007, Denmark, PEDro score = 6	Randomized controlled trial. 458 participants with acute WAD who were considered to be at high risk of developing chronic WAD were randomly assigned into 3 groups: immobilization in neck collar, act as usual or active mobilization (ie, mechanical diagnosis and therapy)	Primary outcome measures assessed at baseline and 1 year included self-reported intensity of headache and neck pain (on a scale of 0–10), the Copenhagen Neck Functional Disability Scale and work capability	At the 1-year follow-up, 48% of patients reported considerable neck pain, 53% reported disability and 14% were still sick listed. However, no significant differences were found between the 3 groups
Dehner et al (28), 2006, Germany, PEDro score = 5	Randomized controlled trial. 70 patients were randomly assigned to either 2- or 10-day immobilization with a soft cervical collar within 24 h of a whiplash injury. After 7 days, all patients started a standardized physiotherapy program	At baseline and at 2 months and 6 months, pain and disability scores were assessed using VASs and ROM was assessed using a goniometer	No significant differences were detected between patients immobilized for 2 days and those immobilized for 10 days
Schnabel et al (19), 2004, Germany, PEDro score = 5	Randomized controlled trial. 200 patients with WAD for less than 48 h were prescribed NSAIDs. 97 patients were advised to wear a soft collar day and night for 1 week. 103 patients received instructions from a physiotherapist (2 to 5 visits during the first week) on exercises for mobilization of the affected regions	Symptom prevalence and VAS mean 1-week pain intensity and disability were recorded at baseline and 6 weeks postinjury	Patients in the exercise group reported significantly lower mean pain intensity (1.6±2.2 versus 1.0±1.8) and disability (1.6±2.2 versus 0.9±1.7) as well as a significantly lower prevalence of neck pain (45% versus 28%), headache (27% versus 14%), shoulder pain (34% versus 16%) and absence of symptoms (44% versus 65%) than those in the collar group at 6 weeks
Rosenfeld et al (20), 2000, Sweden, PEDro score = 4	Randomized controlled trial. 97 patients with acute WAD were randomly assigned to receive early (within 96 h) versus delayed (at 2 weeks) treatment and active versus standard treatment. Active treatment included small-range, small-amplitude neck rotations 10 times every waking hour; individual programs were added for patients who experienced no improvement within 20 days. Standard treatment included written material advising rest for the first 2 weeks, followed by active movement 2 to 3 times daily. The written material outlined the benefits of soft collar use	Neck, head and shoulder pain intensity (VAS) and cervical ROM (inclinometer) were measured at baseline and at 6 months	Active treatment (early or delayed) was associated with a significantly greater reduction in pain (−22.5 versus −3.2), but not ROM, compared with standard treatment ($P < 0.001$). Although active treatment tended to be more effective when it was initiated within 96 h of injury and standard treatment tended to be more effective when it was initiated 2 weeks postinjury, there was no significant difference between early and delayed treatment when considered independent of treatment type
Rosenfeld et al (21), 2003, Sweden	Follow-up study. A 3-year follow-up to the Rosenfeld et al (20) study. Follow-up article received a PEDro score of 8 due to clearer reporting of subject and therapist blinding, and an intention-to-treat analysis of the 3-year follow-up data	Sick leave for the 6 months preceding the 3-year follow-up was reported, in addition to the outcomes reported in Rosenfeld et al (20)	Active treatment was associated with a greater reduction in pain intensity and a shorter duration of sick leave than standard treatment ($P < 0.05$). Improvement in cervical ROM favoured active versus passive treatment
Borchgrevink et al (26), 1998, Norway, PEDro score = 5	Randomized controlled trial. 201 patients with acute WAD received a 5-day prescription of NSAIDs and instructions for self-training exercises to be initiated immediately. Patients were randomly assigned to an 'act-as-usual' group (no sick leave or collar) or an immobilization group (14 days of sick leave and collar use)	The following outcomes were assessed immediately following treatment and at 6 weeks and 6 months postinjury: Pain and headache intensity (VAS), pain localization and associated symptoms, cervical and shoulder ROM, and cognitive symptoms	Patients in the 'act-as-usual' group had significantly less neck pain ($P < 0.01$); pain during daily activities ($P < 0.05$); fewer headaches ($P < 0.01$), memory and concentration problems ($P < 0.001$); and fewer painful regions ($P < 0.01$) than patients in the immobilization group at 6 months. Neck and shoulder ROM did not differ between groups
Mealy et al (22), 1986, Ireland, PEDro score = 6	Randomized controlled trial. 61 patients with acute WAD received active treatment or immobilization. Immobilization consisted of 2 weeks of soft collar use, followed by gradual mobilization. Active treatment consisted of ice, heat and passive mobilization, and home neck exercises performed within the limit of pain	Pain intensity (VAS) and cervical ROM (goniometer) were assessed at baseline and at 4 weeks and 8 weeks after sustaining injury	The active treatment group experienced significantly less pain than the control group at 4 (2.9±.6 versus 5.1±.5) and 8 (1.7±.4 versus 3.9±.6) weeks ($P < 0.05$), and significantly greater cervical ROM (34.1±1.5 versus 29.6±1.6) at 8 weeks ($P < 0.05$)

TABLE 4 – CONTINUED

Summary of studies evaluating simple mobilization exercises for acute whiplash-associated disorder (WAD)

Reference, year, country, score	Population and methods	Outcome measures	Results
Crawford et al (24), 2004, United Kingdom, ns	Quasirandomized trial. 108 patients with WAD for less than 48 h were given a soft collar and NSAIDs on presentation. The early mobilization group was given an advice sheet detailing a self-mobilization exercise program to be initiated immediately. The immobilization group was advised to wear a soft collar for 3 weeks and told to mobilize using the same exercise advice sheet. Physiotherapy was prescribed as a cointervention for both groups, at the discretion of the clinicians	Neck pain (VAS), total neck movement and disability for activities of daily living (score derived by authors) were assessed at baseline and at 3 weeks, 12 weeks and 52 weeks postinjury. Return to work time also was recorded	There were no differences in pain scores or total range of movement between the two groups at 1 year; however, those in the mobilization group did return to work significantly sooner than those in the collar group (17 versus 34 days; $P < 0.05$). Both groups experienced improvement in neck pain and cervical ROM at the 3-week follow-up; however, those in the collar group had greater impairment at baseline
Gennis et al (29), 1996, USA, ns	Quasirandomized trial. 250 patients presenting to the emergency department with acute WAD received either a soft collar or no collar and advice to rest. All patients were given analgesics as required during the 2-week intervention period	Pain intensity (VAS) and categorical improvement (recovered, improved or deteriorated) was assessed at baseline and 6–12 weeks postinjury	No significant between-group differences were identified for pain intensity, recovery, improvement or deterioration
Pennie and Agambar (25), 1990, United Kingdom, ns	Quasirandomized trial. 135 patients with acute WAD received active treatment or immobilization. 74 patients used a collar for 2 weeks before beginning a program of mobilization exercises. Patients who had not improved by 6 weeks were referred for physiotherapy. Active treatment consisted of intermittent halter traction (2 days per week for 10 min), advice on sleeping posture, and instruction to perform neck and shoulder exercises between clinic visits	Subjective global improvement, total neck mobility (goniometer), and neck, arm, head and back pain (VAS) were assessed at baseline and at 6–8 weeks and 5 months postinjury	There were no significant differences between groups for cervical ROM, subjective improvement or pain in any of the anatomical locations at 6–8 weeks or 5 months

ns No score; NSAID Nonsteroidal anti-inflammatory drug; PEDro Physiotherapy Evidence Database; ROM Range of motion; VAS Visual analogue scale

TABLE 5

Summary of a study evaluating a pharmacological intervention for acute whiplash-associated disorder (WAD)

Reference, year, country, score	Population and methods	Outcome measures	Results
Pettersson and Toolanen (30), 1998, Sweden, PEDro score = 8	Randomized controlled trial. 40 acute WAD patients who sought treatment within 8 h of injury were randomly assigned to receive a methylprednisolone infusion (bolus at 30 mg/kg/h for 15 min and maintenance at 5.4 mg/kg/h for 23 h) or a placebo. All patients also had a cointervention including soft collar use for 1–2 weeks, physiotherapy and analgesics	Presence of disabling symptoms severe enough to prevent the patient from returning to work, number of sick days in the 6-month period before and after the injury, and sick-leave profile for 6 months after injury	There was a significant difference between the actively treated patients and the placebo group in terms of disabling symptoms ($P < 0.05$), total mean number of sick days (4.7 versus 51.7, $P < 0.01$) and sick-leave profile ($P < 0.01$), all of which favoured the actively treated group

PEDro Physiotherapy Evidence Database

further study using a larger sample size is needed before any definitive conclusions can be drawn regarding the clinical significance of this intervention.

Conclusions regarding pharmacological interventions in acute WAD: While there is some evidence that methylprednisolone infusion is effective in improving recovery from WAD, further research using larger sample sizes is needed before firm conclusions can be drawn regarding the clinical benefit of this intervention.

Alternative treatments

PEMT: The effectiveness of PEMT was examined in two RCTs, although only one specified that therapy was initiated during the acute phase (Table 6). In an RCT of good quality, Foley-Nolan et al (31) randomly assigned patients to wear soft collars fitted with either an active or inactive PEMT device. Patients in the active PEMT group reported less pain at two and four weeks, and greater cervical ROM at 12 weeks; however, the groups were no longer significantly different in terms of pain intensity at 12 weeks after treatment. Similarly, Thiule

and Walzl (32) reported a significantly greater reduction in pain and improvement in cervical ROM among patients who received PEMT compared with those who received medication alone. Unfortunately, because Thiule and Walzl (32) failed to report the duration of follow-up or the time from injury to the initiation of therapy, their results could not be used in formulating conclusions about the effectiveness of PEMT for acute WAD.

Conclusions regarding PEMT in acute WAD: Although there is some evidence that PEMT decreases pain intensity and increases cervical ROM over the short term, the evidence is insufficient to support the use of this treatment with confidence.

Laser acupuncture: One RCT of fair quality investigated the use of laser acupuncture as a treatment for acute WAD (Table 7). Aigner et al (33) compared treatment with laser acupuncture combined with cervical collar use versus treatment with a collar and placebo laser and found no significant short- or long-term differences between the two treatment groups. Although there were some technical variables associated with the use of laser

TABLE 6
Summary of studies evaluating pulsed electromagnetic field therapy (PEMT) for acute whiplash-associated disorder (WAD)

Reference, year, country, score	Population and methods	Outcome measures	Results
Thiule and Walzl (32), 2002, Austria, PEDro score = 4	Randomized controlled trial. 92 patients with WAD of undefined duration were randomly assigned to receive NSAIDs, a muscle relaxant and PEMT (increasing intensity twice daily for two weeks), or medication only	Mean pain intensity in three areas (neck, head, shoulder and arm; rated on a scale of 1–10) and cervical ROM (flexion/extension, rotation and slope) were assessed at baseline and after treatment	Patients who received PEMT experienced a significantly greater reduction in mean pain (with a mean decrease across all three regions of 2.8 versus 0.7, $P < 0.05$) and significantly more improvement in cervical ROM (with a mean increase across all three regions of 21.7° versus 15.83°, $P < 0.05$)
Foley-Nolan et al (31), 1992, Ireland, PEDro score = 8	Randomized controlled trial. 40 patients with acute WAD were prescribed analgesics and NSAIDs and instructed to wear a collar for 8 h/day for 12 weeks, removing the collar periodically to perform neck exercises. Treatment group patients received PEMT via a diathermy generator incorporated into the collar. The control group wore facsimile collars. Patients in either group who were dissatisfied with their progress at 4 weeks were referred to a physiotherapy program	Pain intensity (VAS), analgesic consumption, cervical ROM (graded as full, two-thirds normal, one-third normal or absent) and subjective assessment of improvement were assessed at baseline and over the course of treatment at 2, 4 and 12 weeks	Compared with the control group, the PEMT group had less pain at 2 (3.8 versus 6.0) and 4 (2.5 versus 5.0) weeks ($P < 0.05$) (but not at 12 weeks) and greater cervical ROM at 12 weeks (4.5 versus 4.0, $P < 0.05$), which was a reversal from baseline. The PEMT group also consumed fewer analgesics at 2, 4 and 12 weeks ($P < 0.05$), and reported better subjective progress at 2 and 4 weeks ($P < 0.01$)

NSAID Nonsteroidal anti-inflammatory drug; PEDro Physiotherapy Evidence Database; ROM Range of motion; VAS Visual analogue scale

TABLE 7
Summary of a study evaluating laser acupuncture for acute whiplash-associated disorder (WAD)

Reference, year, country, score	Population and methods	Outcome measures	Results
Aigner et al (33), 2006, Austria, PEDro score = 5	Randomized controlled trial. 50 patients with acute WAD were prescribed a muscle relaxant and an analgesic, and wore a collar for 1–2 weeks with an effort toward gradual reduction in collar use. The treatment group received laser acupuncture 3 times per week for up to 3 weeks; the control group received sham laser acupuncture	Cervical ROM (goniometer), duration of collar use, sick leave, medication use, and duration of pain and subjective symptoms were assessed after the last acupuncture treatment and 8–12 months postinjury	No significant differences were reported between the two groups on any of the outcome measures. Although both groups improved in terms of cervical ROM, results marginally favoured the control group. Significance levels were not reported

PEDro Physiotherapy Evidence Database; ROM Range of motion

acupuncture that may not be fully accounted for (eg, strength of the laser and duration of irradiation), it does not appear that this intervention is beneficial for patients with acute WAD.

Conclusions regarding laser acupuncture in acute WAD:

Laser acupuncture does not appear to be any more effective than placebo in the treatment of acute WAD.

DISCUSSION

In total, 23 articles that evaluated interventions initiated within the first two weeks following a whiplash injury were identified. The results of the current review support both the consensus recommendations of the QTF (1) and the evidence-based recommendations of Conlin et al (7,8) – activation-based therapies initiated during the acute phase appear to be the most effective means of reducing the duration and severity of whiplash-associated neck pain, ROM deficits and disability.

Despite substantial evidence that activation-based therapies are the most efficacious treatment options for patients with acute WAD, the relative effectiveness of exercise programs, active mobilization and advice to act as usual remains unclear. There are several reasons for this. First, the majority of activation-based therapies have been compared with immobilization and not other activation-based interventions. Second, exercise is often investigated as one aspect of a

broader treatment regimen; for example, some exercise programs incorporate multiple forms of exercise (eg, stretching and gradual resistance) and/or therapeutic elements (such as heat application and reassurance that whiplash injury is usually of relatively short duration). Finally, given the degree of recovery that occurs naturally following a whiplash injury, it can be difficult to determine whether an observed improvement is due to the intervention or to natural recovery, which is especially true regarding advice to act as usual, in which the intervention may function more by allowing natural recovery to take place. Conversely, one trial did compare mobilization and advice with a physiotherapy program and, although no significant differences were found at either one or two months after treatment, a significantly greater percentage of patients in the mobilization group reported being symptom free two years after injury (14,16). This suggests that simple mobilization exercises and advice to remain active may produce better long-term results than more formal physiotherapy exercise programs, although the latter are superior to no treatment. Furthermore, it may be that certain exercises, such as strengthening exercises, only serve to slow recovery when compared with simple mobilization exercises, suggesting that remaining active is critical but attention is needed to ensure exercise programs are not too aggressive because more aggressive programs may aggravate healing tissues.

TABLE 8
Summary of evidence for acute whiplash-associated disorder (WAD) therapies

Intervention	Conclusions
Educational	Based on the existing research, it does not appear that providing educational information during the acute phase provides a significant measurable benefit; however, there is some indication that oral and/or video presentation of educational information may be more effective than the distribution of pamphlets
Exercise programs	Although there is some conflicting evidence, it appears that immobilization with a soft collar is less effective than active mobilization and no more effective than advice to act as usual. In contrast, there is strong evidence that active mobilization is associated with reduced pain intensity and limited evidence that mobilization may also improve range of motion, although it is not clear whether active mobilization is any more effective than advice to act as usual
Mobilization	There appears to be strong evidence that immobilization with a soft collar is less effective than active mobilization and no more effective than advice to act as usual. In contrast, active mobilization appears to be associated with reduced pain intensity, although it is not clear whether active mobilization is any more effective than advice to act as usual
Pharmacological	While there is some evidence that methylprednisolone infusion is effective in improving recovery from WAD, further research using larger sample sizes is needed before firm conclusions can be drawn regarding the clinical benefit of this intervention
Pulsed electromagnetic field therapy	Although there is some evidence that pulsed electromagnetic field therapy decreases pain intensity and increases cervical range of motion over the short term, the evidence is insufficient to support the use of this treatment with confidence
Laser acupuncture	Laser acupuncture does not appear to be any more effective than placebo in the treatment of acute WAD

Immobilization of the neck using a soft cervical collar has repeatedly been shown to be ineffective at best. At worst, this technique may impede natural recovery by promoting prolonged neck stiffness through inhibiting movement and discouraging patients from taking an active role in their own recovery. While the ineffectiveness of soft collars has long been recognized clinically, researchers often use cervical collars as a control condition. In light of the substantial evidence demonstrating the ineffectiveness of soft collars for the treatment of acute WAD, the ethics of immobilizing patients with a soft collar as a control treatment warrants serious reconsideration. Not only is knowingly providing inefficacious treatment ethically questionable, but comparing experimental treatments with a therapy that may be harmful offers little scientific value. Alternatively, directly comparing active treatments with one another avoids the ethical dilemma of prescribing a cervical collar and offers an opportunity to explore which particular neck exercise regimens are most effective in treating acute WAD.

In addition to activation-based treatments, there is also some evidence suggesting that both PEMT and methylprednisolone infusion may improve recovery over the short term; however, the literature supporting both of these interventions was limited. In contrast, it has been demonstrated that laser acupuncture and educational interventions are ineffective in improving recovery from acute WAD. It should be noted, however, that some evidence suggests that verbal and/or video presentation of educational information may be more effective than the distribution of pamphlets. Further complicating this issue, several of the studies that were described as providing advice to act as usual also contained aspects of educational intervention. Clearly, further research is needed to clarify whether providing patients with educational information, either alone or in conjunction with other interventions, is beneficial during the acute 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 did 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.

According to Dufton et al (34), the longer the delay between injury and the commencement of therapy, the greater the risk that patients will go on to develop chronic symptoms. Moreover, interventions initiated during the subacute phase do not appear to be effective in reducing whiplash-related symptoms (see part 3 in this series [35]). Given this evidence, it seems to be very important that patients begin therapy as soon as possible after sustaining their injury. Nevertheless, a large percentage of patients with whiplash-related injuries recover naturally over a relatively short period of time. This highlights the need for research of a controlled design that allows one to make a clear distinction between treatment-related improvement and natural recovery, particularly for interventions initiated during the acute phase. Based on the results of the current review, activation-based therapy appears to be the most efficacious approach when managing acute WAD (Table 8). However, further research is needed to determine the optimum protocol (eg, duration and intensity) for activation-based treatments as well as which form of activation-based therapy offers the greatest benefit for patients with acute WAD.

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