LITERATURE REVIEW

CHRONIC MECHANICAL NECK PAIN IN ADULTS TREATED BY MANUAL THERAPY: A SYSTEMATIC REVIEW OF CHANGE SCORES IN RANDOMIZED CLINICAL TRIALS

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ABSTRACT

Objective: This study provides a systematic analysis of group change scores in randomized clinical trials of chronic neck pain not due to whiplash and not including headache or arm pain treated with manual therapy.

Methods: A comprehensive literature search of clinical trials of chronic neck pain treated with manual therapies up to December 2005. Only clinical trials scoring above 11.5 (Amsterdam-Maastricht Scale) were included in the analysis.

Results: From 1980 citations, 19 publications were selected. Of the 16 trials analyzed (3 were rejected for poor quality), 9 involved spinal manipulation (12 groups), 5 trials (5 groups) were for spinal mobilization or nonmanipulative manual therapy (1 trial overlapped), and 2 trials (2 groups) involved massage therapy. No trials included trigger point therapy or manual traction of the neck. For manipulation studies, the mean effect size (ES) at 6 weeks for 7 trials (10 groups) was 1.63 (95% confidence interval [CI], 1.13-2.13); 1.56 (95% CI, 0.73-2.39) at 12 weeks for 4 trials (5 groups); 1.22 (95% CI, 0.38-2.06) from 52 to 104 weeks for 2 trials (2 groups). For mobilization studies, 1 trial reported an ES of 2.5 at 6 weeks, 2 trials reported full recovery in 63.8% to 71.7% of subjects at 7 to 52 weeks, and 1 trial reported greater than 2/10 point pain score reduction in 78.3% of subjects at 4 weeks. For massage studies, 1 reported an ES of 0.03 at 6 weeks, whereas the other reported mean change scores of 7.89/100 and 14.4/100 at 1 and 12 weeks of, respectively.

Conclusions: There is moderate- to high-quality evidence that subjects with chronic neck pain not due to whiplash and without arm pain and headaches show clinically important improvements from a course of spinal manipulation or mobilization at 6, 12, and up to 104 weeks posttreatment. The current evidence does not support a similar level of benefit from massage. (J Manipulative Physiol Ther 2007;30:215-227)

Key Indexing Terms: *Review Literature; Chronic; Neck pain; Musculoskeletal Manipulations; Clinical Trials*

Neck pain is a very common problem, second only to low back pain in its frequency in the general population[1-4] and in musculoskeletal practice.[5] Estimates of the prevalence of chronic neck pain vary. In a Swedish population,[6] 18.5% of females and 13.2% of males had neck pain for longer than 6 months; however, when continuous chronicity was rated, these figures were reduced to 10% and 7%, respectively. A Finnish study[7] reported chronic neck pain in 13.5% of females and 9.5% of males. A Norwegian study[8] reported an overall rate of 13.8% for neck pain greater than 6 months duration; however, for subgroups with age greater than 43, the rate rose above 20%. It would appear that approximately 15% of females and 10% of men have chronic neck pain at any one time. Chronic neck pain produces a high level of morbidity by affecting occupational and avocational activities of daily living and by affecting quality of life.[9-12]

Manual therapy is a generic therapeutic category that is composed of a variety of procedures directed at the musculoskeletal structures in the treatment of mechanical pain.[13-45] Two major subcategories exist that divide these therapies into those which produce joint motion and those which do not. The first subcategory includes manipulation, mobilization, and manual traction. The second subcategory involves both generalized soft tissue therapies, such as the

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many types of massage, and focal soft tissue therapy, such as trigger point therapy, shiatsu, and acupressure. For this review, we used the separate therapy categories of manipulation, mobilization, manual traction, massage, and pressure techniques.

There are numerous systematic reviews of the treatment of neck pain by manual therapy.[16-37] With few exceptions, they have included studies of manual therapies for acute, subacute, and chronic neck pain. They have also included studies of subjects with neck pain due to whiplash-type injury as well as those in which whiplash-associated disorder (WAD) was not involved. These reviews have also included studies of subjects with or without concomitant headache and/or arm pain. The works of Gross et al,[16,22,24,25,36,37] Aker et al,[23] and Bronfort et al[18] are particularly noted as having formed the foundation of the evidence basis for manual therapy for neck pain in general, although the issues raised above pertain to their works as well. Particularly, their reviews have included studies of patients with neck pain who also have headaches, arm pain, and/or whiplash-induced neck pain. Finally, these reviews have included studies where manual therapies have been combined with other therapies such as exercises, relaxation therapy, etc (so-called "multimodal therapy"). The most recent reviews by Gross et al,[36,37] Bronfort et al,[18] and the Canadian Chiropractic Association Clinical Practice Guideline[38] have brought the evidence base up to date but are similarly broad in scope.

The reviews cited above have focused on a systematic analyses of the differential benefit that might result from comparisons between manual therapies (as the "experimental" or "index" therapy) and other interventions (including no-treatment or "usual treatment" controls) within each clinical trial, which answers the question, "What is the difference between the effect of the investigated manual therapy *as compared to other interventions?*" The typical approach taken in systematic reviews is to calculate, summarize, and, when appropriate, pool the effect sizes of the differences between the trial groups in these studies.

In these reports, none of the randomized clinical trials (RCTs) of manual therapies for chronic neck pain not due to whiplash and not including headaches or arm pain has included a no-treatment control group; specifically, there are no placebo-group comparisons. If such studies did exist, and if the results of manual therapies in the subgroup of patients in these trials were found to be not superior to no-treatment conditions, especially placebo-controlled conditions, then no further review would be necessary. In other words, there would be evidence that manual therapies were not superior to no-treatment or placebo. However, this is not the case. What is currently known is that the differential benefit of manual therapies compared with other non-manual therapies has been shown, at present, to not be consistently substantial, and that the inclusion of manual therapies among other therapies appears to produce the optimal outcomes.[36,37]

What have not been systematically reviewed are the intragroup changes in those subjects with chronic neck pain who are randomized to receive manual therapies.[39] Such a review would help to answer the question, "What is the clinical effect (measured as magnitude of change scores) of (various types of) manual therapy obtained in trial subjects with chronic neck pain not due to whiplash and without headache and arm pain who are randomized to receive this therapy?" If the studies included in such an analysis were of sufficiently high quality and if they included subjects that were sufficiently representative of general practice, clinicians could use this analysis to answer the question, "What is the evidence of the benefit (magnitude of change) that can be expected to occur in this type of patient by applying any 1 of the manual therapies investigated these clinical trials?" Our review will, therefore, focus on the change scores within groups randomized to receive manual therapies.

Systematic retrieval and evaluation procedures were used in this review to identify the evidence base of clinical trials of manual therapy for chronic mechanical neck pain in adults not due to whiplash injury and without headache or arm pain. Specifically, the intragroup differences were calculated and, where possible, summarized. Given that this is a secondary analysis, the emphasis will be descriptive as opposed to analytical.

METHODS

A comprehensive literature search was performed in MEDLINE, CINHAHL, AMED, MANTIS, Index to Chiropractic Literature, Alt HealthWatch, the Cochrane Database of Systematic Reviews, the Cochrane Controlled Trials Registry, and several EBSCO Information Services databases (Biomedical Reference Collection, Nursing and Allied Health Collection, Psychological and Behavioral Sciences Collection) using the strategy delineated in Figure 1 (up to December 2005).

Targeted searches were also conducted for "neck pain" and manipulation, mobilization, physiotherapy and massage. Citation searches were also conducted manually. Searches were conducted to mid-2005.

Selections from the initial search were made by 2 investigators according to the following criteria. (1) RCT—the study design had to be an RCT in which at least 1 treatment group of adults with ages 18 to 50 was provided with a course of 1 of the manual therapies (as defined above) for chronic mechanical neck pain. (2) Chronicity—chronic neck pain has been variously defined as to its duration. Some authors require at least 3 months of continuous symptoms, whereas, for others; chronicity can develop after only 1 month of symptoms.[40] We have defined chronic neck pain as being of a minimum of 8 weeks duration. (3) Neck pain—this review included only studies with subjects with neck pain without arm pain, headache, and not due to whiplash injury. The exclusion of whiplash

1	randomized controlled trial.pt.
2	Controlled clinical trial.pt.
3	randomized controlled trials.sh.
4	random allocation.sh.
5	double blind method.sh.
6	single blind method.sh.
7	1 or 2 or 3 or 4 or 5 or 6
8	clinical trial.pt.
9	exp clinical trials/
10	(clin$ adj trial$).ti,ab.
11	((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).ti,ab.
12	Placebos.sh.
13	placebo$.ti,ab.
14	random$.ti,ab.
15	research design.sh.
16	or/8-15
17	comparative study.sh.
18	exp evaluation studies/
19	follow up studies.sh.
20	prospective studies.sh.
21	(control$ or prospective$ or volunteer$).ti,ab.
22	or/17-21
23	7 or 16 or 22
24	neck pain.mp. or exp Neck Pain/
25	exp CERVICAL VERTEBRAE/
26	24 or 25
27	exp alternative medicine/
28	exp plants, medicinal/
29	exp plant oils/
30	exp plant extracts/
31	exp formularies, homeopathic/
32	((complementary or unconventional or folk or alternative) adj (med$ or ther$ or treat$ or care)).ti,ab.
33	exp holistic health/
34	exp Physical Therapy Techniques/
35	(physical ther$ or physiother$).ti,ab.
36	exp osteopathy/ or exp osteopathic medicine/
37	(chiropract$ or naturopath$ or osteopath$ or homeopath$ or acupunct$).ti,ab.
38	or/27-37
39	23 and 26 and 38
40	limit 39 to English language

Fig 1. *Search strategy used in performing the literature search.*

injury is justified in that whiplash-type injury typically involves rapid flexion-extension or side-to-side forces to the head and neck, such as those resulting from a motor vehicle collision.[41] The most significant feature distinguishing pain arising from whiplash compared with the pain dealt with herein is that whiplash causes WAD—a disorder usually including headache and numerous other symptoms (dizziness, tinnitus, sleep disturbance, mood disturbance, pain in areas outside of the neck).[8] These symptoms are outside our case definition. Furthermore, patients with WAD are very often involved in some form of compensation or litigation exercise, which further complicates the syndrome from the point of view of additional psychosocial issues. The Quebec Task Force excluded any studies not involving whiplash-injured subjects from its WAD review.[41] It is therefore appropriate to separate WAD studies from studies of chronic mechanical neck pain.

Studies were rejected for the following reasons: they included an inseparable mix of patients with acute neck pain and patients with chronic neck pain but did not analyze or report the outcomes data separately for these 2 subgroups; they included patients with both neck and back pain, or multiple areas of pain, or pain that was described as "myofascial" and therefore multisited, but did not analyse and report the data on subjects with chronic neck pain separately; they reported on only 1 treatment.

The method of each initially selected study was scored using the Amsterdam-Maastricht Consensus List,[42] from which we generated a score out of 19. This instrument is currently used by the Cochrane Collaboration Back Review Group for Spinal Disorders. Two assessors scored studies separately, and disagreements were resolved by consensus. A cutoff score of 11.5 (60%) was used for selecting trials for analysis.[42] Evidence tables were compiled from extracted data by the primary author and a research assistant. Data were obtained only from the published works and not from follow-up with authors.

The primary outcome for this review was pain level or level of pain-related improvement. Outcome instruments were typically pain scales in the style of a visual analogue scale (VAS) or numerical rating scale. Data on measures of function or self-rated disability were not analyzed in this review.

When continuous data were reported, as means (SD) for baseline and outcome intervals, absolute and relative changes were calculated. Intragroup effect sizes were calculated according to the method of Cohen.[43,44] Where median scores were reported, the confidence intervals (CIs) were used to calculate proxy standard deviations, and the median was treated as the mean. Where only change scores were reported, the effect size was not calculated. Given that this is a secondary analysis, no further analysis such as pooling of effects was undertaken.

Results

The search generated 1980 citations. Nineteen publications[45-63] were retrieved according to the inclusion/exclusion criteria described above. These reports included 18 separate trials. For spinal manipulative therapy, there were 12 publications of 11 trials. For spinal mobilization or non-manipulative manual therapy, there were 5 reports of 6 trials. One of these trials overlapped with a manipulation trial, as they had groups receiving each of these 2 therapies.[55] There were 2 trials of massage therapy. One trial of a course of manual trigger point therapy was identified.[59] No trials of manual traction of the neck were found.

The quality scores ranged from 9.5 to 17 of 19 on the Maastricht Scale. Sixteen trials scored greater than 11.5 and

Table 1. *Relevant data from the accepted studies*

Study/Year	Manual therapy (sample size)	Comparative treatments (sample size)	Outcome intervals (baseline = T1)	Results: pain	Adverse reactions	Quality score (/19)
Manipulation trials Rogers, 1997[45]	1. Manipulation (n = 10) 6 tx over 3-4 wk	2. Stretching exercises (n = 10) twice daily at home	T2. 4 wk	Pain (0-100) 1. SMT: T1: 36 (27) T2: 20 (29)* ES = .40 *$P < .05$ 2. EXER: T1: 40 (17) T2: 37 (27)	None reported	11.5
Parkin-Smith and Penter, 1998[46]	1. Manipulation: cervical only (n = 13) 6 tx over 3 wk 2. Manipulation: cervical and upper thoracic (n = 17) 6 tx over 3 wk		T2. 3 wk	Pain (0-100) 1. SMT 1: T1: 33.89 (12.47) T2: 17.17 (18.41)* ES = 1.06 2. SMT 2: T1: 33.0 (13.99) T2: 13.18 (10.56)* ES = 1.54 *pre-post $P < .05$ NS between groups	None reported	12
Jordan et al, 1998[48]	1. Spinal manipulation (SMT) (n = 40) 2 tx per wk for 6 wk	2. Intensive training (n = 40) 2 tx per wk for 6 wk 3. Physiotherapy (n = 39) 2 tx per wk for 6 wk	T2 = 6 wk T3 = 16 wk T4 = 52 wk	Pain (0-30) 1. SMT*: T1: 13 (10-15) T2: 6 (4-7) ES = 1.96 T3: 6 (5-8) T4: 6 (6-8) *Scores are median (90% CI)	None reported	15
Giles and Muller, 1999[50] van Schalwyk and Parkin-Smith, 2000[51]	1. Spinal manipulation (n = 23) 6 tx over 3-4 wk 1. Spinal manipulation (supine rotary break) (n = 15) 10 tx over 4 wk 2. Spinal manipulation (supine lateral break) (n = 15) 10 tx over 4 wk	2. NSAIDs (n = 12) 3. Acupuncture (n = 15) 6 tx over 3-4 wk	T2. 4 wk T2. 4 wk T3. 8 wk (1 mo follow-up)	Pain: change scores (0-10) 1. SMT*: T2: −1.5 [−3;0], $P = .002$ *Scores are median [95% CI] Pain (0-100) 1. SMT (1): T1: 38.28 (12.47) T2: 9.4 (5.47)* ES = 3.2 T3: 11.83** (11.8) ES = 2.23 2. SMT (2): T1: 33.25 (9.56) T2: 17.54 (12.47) NS	None reported	13 12

				ES = 1.43 T3: 18.52*** (14) ES = 1.10 *P = .0003 (baseline to 4 wk) **P = .003 ***P = .009 (from baseline to 8 wk) No significant differences between groups at either outcome point		
Wood et al, 2001[52]	1. Manual manipulation (n = 15) 8 tx over 4 wk 2. Manually assisted instrumented manipulation (n = 15) 8 tx over 4 wk		T2. 4 wk	Pain (0-100) 1. SMT (man): T1: 42.5 (18.7) T2: 18.7 (14.1)* ES = 1.9 2. SMT (inst): T1: 50.0 (12.6) T2: 23.5 (18.2)** ES = 1.8 * P = .0003 **P = .0019 NS between groups	None reported	12.5
Bronfort et al, 2001[53]	1. Spinal manipulation with sham microcurrent therapy (n = 64)	2. Spinal manipulation with low-tech exercises (n = 64) 1 and 2: 20 1-h sessions over 11 wk 3. Hi-tech strength and high-level aerobic exercises (n = 63) 20 1-h sessions over 11 wk	T2. wk 5 T3. wk 11 (primary outcome) T4. mo 3 T5. mo 6 T6. mo 12 (see text and Evans et al for discussion of 3-, 6-, and 12-mo follow-up data)	Pain (0-100) 1. SMT: T1: 56.6 (12.8) T3: 31.3 (21.8)* ES = 1.4 *P < .05 NS between groups	None reported	15
Evans et al, 2002[54]	1. Spinal manipulation with sham microcurrent therapy (n = 64)	2. Spinal manipulation with low-tech exercises (n = 64) 1 and 2: 20 1-h sessions over 11 wk 3. Hi-tech strength and hi-level aerobic exercises (n = 63) 20 1-h sessions over 11 wk	T5. 6 mo T6. 12 mo T7. 24 mo	Pain (0-10) (T1: see Bronfort et al) 1. SMT: T5: 3.5 (2.5) ES = .78 T6: 3.5 (2.3) ES = .78 T7: 3.9 (2.3) ES = .63	see Bronfort et al)	see Bronfort et al
Hurwitz et al, 2002[55]	1. Manipulation (with or without heat; with or without EMS) (n = 171) No data on treatment dose	2. mobilization (with or without heat; with or without EMS) (n = 165) No data on treatment dose	(a) 2 wk (b) 6 wk (c) 13 wk (d) 24 wk	Outcomes were reported for: (i) Most severe pain (ii) Average pain (iii) Neck Disability Index	No major side effects in either group. For minor side effects in the first 4 wk:	15.5

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Table 1 (*continued*)

Study/Year	Manual therapy (sample size)	Comparative treatments (sample size)	Outcome intervals (baseline = T1)	Results: pain	Adverse reactions	Quality score (/19)
Hurwitz et al, 2002[55]				No pre-post data were reported.Comparative estimated effects of treatment contrasts were reported: No significant differences were reported for manipulation vs mobilization at any outcome point.	Manip: 16% Mob = 8.7% P = .051	
Giles and Muller, 2003[56]	1. Spinal manipulation (n = 18) 2 tx per wk up to 9 wk	2. Medication (n = 13) 3. Acupuncture (n = 19) 2 tx per wk up to 9 wk	T2. 2 wk T3. 5 wk T4. 9 wk (main end-point = T4)	Pain: (0-10) 1. SMT: T1: 6 (3-7) T4: 3 (1-6) P = 0.14 ES = 0.81	None reported	15
Mobilization trials						
Brodin, 1985[57]	1. Manual mobilization (n = 23) (9 tx over 3 wk) + aspirin + 3 h neck school	2. Daily aspirin for 3 wk (n = 23) 3. Daily aspirin + 3 h neck school + 'mock therapy' (9 tx over 3 wk) (n = 17)	T2. 4 wk (1 wk post-tx)	Pain improvement (% with >2-point reduction on 0-10 scale) T2: 78.3% (48% pain-free) 1 > 2 and 3 (P < .05)	None reported for manual therapy 16% reported mild discomfort with the aspirin	11.5
David et al, 1998[58]	1. Mobilization: 6 tx over 6 wk (n = 35)	2. Acupuncture: 6 tx over 6 wk (n = 35)		Pain 0-100 1. MOB T1: 51 (10) T2: 21 (7) ES = 2.5	None reported	15.5
Hurwitz et al, 2002[55]	1. Mobilization (with or without heat; with or without EMS) (n = 165) No data on treatment dose	2. Manipulation (with or without heat; with or without EMS) (n = 171) No data on treatment dose	T2. 6 wk T3. 6 mo (a) 2 wk (b) 6 wk (c) 13 wk (d) 24 wk	Outcomes were reported for: (i) Most severe pain (ii) Average pain2 (iii) Neck Disability Index No pre-post data were reported. Comparative estimated effects of treatment contrasts were reported: No significant differences were reported for manipulation vs mobilization at any outcome point.	No major side effects in either group. For minor side effects in the first 4 wk: Manip = 16% Mob = 8.7% P = .051	15.5
Hoving et al, 2002[60]	1. MT:spinal mobilization (n = 60) 1 session per wk for 6 wk	2. Physical therapy: mostly exercises (n = 59)	T2. 3 wk post-randomization T3. 7 wk	Improvement rates: (full recovery) MT T3: 68.3%*	Minor benign short-term adverse reactions were reported more	17

		1 session per wk for 6 wk 3. Medical care (MD) (n = 64)		T3: 1 > 2 and 3, *P > .05 Pain difference scores on 0-10 scale MT T3: 3.5 (2.3)* T3: 1 > 2 and 3, *P > .05 T3: 1 > 2 and 3, *P > .05 Pain difference scores on 0-10 scale MT T3: 3.5 (2.3)* T3: 1 > 2 and 3, *P > .05	often for groups 1 and 2: 1. Neck pain for > days: MT: 11%(18.3) PT: 4% (6.8) MT:3% (4.7) 2. Headache: MT: 17% (28.3) PT: 19% (32.3) MD: 11% (17.2) 3. Pain and tingling in the extremities: MT: 8% (13.3) PT: 9% (15.3) MD: 4% (6.3) 4. Dizziness: MT: 6% (10) PT:7% (11.9) MD: 4% (6.3)	
Korthals-de Bos, et al, 2003[61]	1. MT: spinal mobilization (n = 60) 1 session per wk for 6 wk	2. Physical therapy: mostly exercises (n = 59) 1 session per wk for 6 wk 3. General practitioner care (MD) (n = 64)	T4. 13 wk T5. 52 wk	Improvement rates: (full recovery) MT T3: 68%* T5: 71.7 (43) T3: 1 > 2 and 3, *P > .05 T5: NS between groups Pain Difference scores on 0-10 scale MT T5: 4.2 (2.4) 1 > 2, P > .05	Minor benign short-term adverse reactions were reported more often for groups 1 and 2: 1. Neck pain for > days: MT: 11% (18.3) PT: 4% (6.8) MT: 3% (4.7) 2. Headache: MT: 17% (28.3) PT: 19% (32.3) MD: 11% (17.2) 3. Pain and tingling in the extremities: MT: 8% (13.3) PT: 9% (15.3) MD: 4% (6.3) 4. Dizziness: MT: 6% (10) PT: 7% (11.9) MD: 4% (6.3)	16

(*continued on next page*)

Table 1 (*continued*)

Study/Year	Manual therapy (sample size)	Comparative treatments (sample size)	Outcome intervals (baseline = T1)	Results: pain	Adverse reactions	Quality score (/19)
Massage trials						
Gam et al, 1998[62]	1. Sham ultrasound, massage and exercises (n = 18)	2. Ultrasound, massage and exercise (n = 20) 2 tx per wk for 4 wk 3. Control (n = 18)	T2-6. weekly for 6 wk	Pain at rest: 0-10 VAS No significant differences at any time Pain during function: 0-10 VAS No significant differences at any time ES for Group 1 for "pain on function" = .03 at 6 wk	None reported	15
Irnich et al, 2001[63]	1. Massage (n = 60)	2. Acupuncture (n = 56) 3. Sham laser acupuncture (n = 61) 1, 2 and 3: 5 treatments over 3 wk	T2. 1 wk T3. 12 wk (posttreatment)	Pain related to motion: change scores on 0-100 VAS (mean; 95% CI) 1. MASS: T2: 7.89 (.6,15.2) T3: 14.4 (31.9) T2: 2 > 1, $P = .005$ 1 = 3, NS T3: NS between groups	Mild, brief discomfort in 7% with massage No serious side effects	17
Excluded trials						
Cilliers and Penter, 1998[47]	1. Manipulation: 1 segment (n = 15) 2. Manipulation: 2 segments (n = 15) 8 tx over 4 wk		T2. 4 wk	Pain (percent reduction: 0-100) 1. SMT (1): T2: 28% reduction* 2. SMT (2): T2: 38% reduction* *pre-post $P < .05$ NS between groups	None reported	9
Moodley and Brantingham, 1999[49]	1. Manipulation (n = 15) 8 tx over 4 wk	2. Ultrasound (n = 15) 8 tx over 4 wk	T2. 4 wk T3. 8 wk	Pain 0-100 Both groups reported reductions in pain at 4 and 8 wk. ($P < .05$) NS between groups	None reported	10
Hanten et al, 2000[59]	1. Self-administered trigger point pressure + stretching (n = 20) Twice daily at home for 5 d	2. Stretching (n = 20) Twice daily at home for 5 d	T2. 1 wk	Pain (0-100) 1. TRIGGER T1: 25.7 (15.3) T2: 13.2 (16.0) ES = .56 1 > 2, $P = .04$	None reported	10.5

SMT, Spinal manipulative therapy; *EXER*, exercise; *ES*, effect size; *MOB*, mobilization; *MT*, manual therapy; *MASS*, massage; *Manip*, manipulation; *Mob*, mobilization; *tx*, treatment; *EMS*, electrical muscle stimulation; *PT*, physiotherapy.

Table 2. *Change scores and effect sizes for studies of manipulation: 0 to 6 weeks, 7 to 12 weeks, and more than 12 weeks*

Outcome interval (no. of studies)	Millimeter change	% change	Effect size
0-6 wk (n = 7)	20.6 (5.8)	58.2 (11.7)	1.63 (1.13-2.13)
7-12 wk (n = 4)	22 (7)	56 (12)	1.56 (0.73-2.39)
>12 wk (n = 2)	22	50	1.22 (0.38-2.06)

were included in the analysis. The average score (SD) of these trials was 13.8 (1.7). Of the 3 trials that were excluded after quality scoring, 2 involved spinal manipulation,[47,49] and 1 involved trigger point therapy.[59] This yielded 12 groups for analysis of spinal manipulation, 5 for mobilization, and 2 for massage.

The average baseline pain score in the manipulation groups was 42.7 (3.1)/100. Only 1 mobilization trial reported baseline pain data[58] with a value of 51 (10).

Table 1 displays the relevant data from the accepted studies. Table 2 lists the effect sizes for 8 trial reports of a course of manipulation at 3 combined outcome intervals: up to 6 weeks, 7 to 12 weeks, and more than 12 weeks. For mobilization and massage/soft tissue therapy, there were too few trials from which effect sizes could be calculated to summarize these in a similar fashion. Table 3 summarizes the reported results, at varying outcome intervals, of the mobilization trials of a course of therapy. In addition, a follow-up report of Hoving et al[64] has presented longer-term results of the original 2002 trial. The 2 massage therapy studies will be summarized below in the text.

Sensitivity Analysis for 7 Manipulation Trials

The effect sizes of the 7 manipulation trials in Table 1 with quality scores from 13 to 16[48,50,53-56] were compared to those with scores of 11.5 or 12.[45,46,51,52] At the 6-week outcome point 2 higher-quality study groups were compared with 7 lower-quality study groups. At the 12-week outcome interval, the comparison was between 3 and 2 groups. No significant differences were found between the effect sizes in each of these subgroups.

Discussion

Currently, the Cochrane Review by Gross et al[36,37] and the work of Bronfort et al[18] form the standard for evaluating the evidence for the treatment of neck pain by manipulation or mobilization. Our review differed from these works in several ways. With respect to the studies included, our review included not only studies of manipulation and mobilization but also of massage and other manual therapies as well. Our review included several studies that Gross et al and Bronfort et al had excluded because they were not studies comparing manipulation or mobilization to another form of therapy. Rather, these studies compared one form of these therapies

Table 3. *Mobilization trials: change scores*

Study	Outcome point (wk)	Result
Brodin[57]	4	78.3% with >2 point reduction
David et al[58]	6	Effect size = 2.5
Hurwitz et al[55]	2, 6, 13, 24	NS difference between mobilization and manipulation
Hoving et al[60]	7	Full recovery = 63.8% of subjects
Korthals-de Bos et al[61]	13 52	Full recovery = 68% of subjects Full recovery = 71.7% of subjects

NS, not significant.

with another form. In our review, each of these study groups was appropriate because they included selected, randomized subjects receiving one of the therapies of interest.

With respect to exclusions, we did not include studies involving subjects with acute neck pain, neck and arm pain, neck pain due to whiplash injury, or those with headache, whether clearly cervicogenic in nature or not. Thus, our review has remained within the boundaries of studies of chronic neck pain treated with one or more forms of manual therapy.

Our review did not include several studies that reported on subjects with neck pain that had been included in larger spine pain groups but did not clearly separate the results of the subjects with neck pain nor did they provide separate results for those with chronic neck pain.[65-69]

The primary difference between these reviews and our review lies in the analysis of change scores within groups so as to identify levels of improvement as opposed to determining whether differences between groups occurred as a measure of the "effectiveness" of the experimental (in this case, manual therapy) treatment. Interestingly, Bronfort et al[18] specifically endorse this line of inquiry (p 351); however, they do not pursue it in their review. In fact, they reported only the percentage differences between groups in their review of studies of manipulation and mobilization for spinal pain (including chronic neck pain). They do not even provide the outcome data for the study groups (as was done here) so that the reader might make these intragroup determinations (as a form of subgroup analysis within the larger review).

The recent Clinical Practice Guideline published by the Canadian Chiropractic Association[38] also explicitly distinguishes between the improvement obtained within groups and the effect of a treatment versus other comparative treatments (between-group effects) and focuses on the former in its evidence synthesis.

Gross et al[36,37] did provide the mean values pre- and postintervention for all their study groups. However, they did not provide intragroup variability measures, and they did not analyze the degree of intragroup change at all. In other words, no summary of the change scores either as percentage difference, absolute difference, or effect size was provided. The sole thrust of their analysis, as sophisticated as it was, was the intergroup comparisons. In this, they

provided intergroup differences as mean values and CIs that, when appropriate, were pooled to provide a summary measure of these differences. Additional analyses, such as "number needed to treat" were performed with the same intergroup theme in mind. Their conclusions were that, "The evidence did not favor manipulation and/or mobilization done alone or in combination with various other physical medicine agents; when compared to one another, neither was superior" (36, p 1).

As noted above, they did find supportive evidence ("for short-term and long-term maintained benefits") for a multimodal approach of manipulation and/or mobilization combined with exercises for subacute/chronic mechanical neck disorders (as defined above).

With respect to our approach to subgroup analysis, it could be asked if it is appropriate to conduct intragroup analyses from a set of published RCTs. In none of the manipulation or mobilization trials included in this review was there a comparison between a form of manual therapy and a placebo control procedure. These trials are more properly seen as randomized comparative trials in which none of the subjects in these trials were blinded as to the form of treatment they received. Interestingly, both trials of massage are placebo-controlled clinical trials.

We maintain that once the intergroup outcomes are analyzed in standard systematic reviews, it then becomes appropriate to assess the magnitudes of change within each treatment group randomized to receive the therapy of interest and, if possible, summarize these results among studies. In fact, several studies in this review only report change scores. After hypothesis testing has been conducted, it is only sensible to assess these scores on their own for their clinical relevance. Our subgroup analysis only extends this exercise to the collective body of trials in this area.

Results from All Trials

From the baseline pain scores, it is evident that this body of trials involves patients with chronic neck pain, with mild to moderately severe neck pain. Most studies included outcome assessments up to 6 to 10 weeks. Several studies provided long-term outcomes up to 52 weeks, with one[54] providing outcomes to 104 weeks. There was considerable variance in the format of reporting the outcomes in these trials. Most studies reported pre- to posttreatment changes in primary outcomes. Some trials, reported only change scores,[60,61,63] whereas others only reported the percentage of subjects achieving a criterion level of outcome.[57,60,61]

Manipulation Trials

The largest number of trial reports is available for manipulation (n = 9). All groups showed positive changes. Effect sizes could be calculated from 7 of 9 trials of a course of manipulation. Table 2 shows these effect sizes ranging from 0.56 to 3.2, most of which would be characterized as "large."[43,44] These effect sizes are maintained up to 12 weeks posttreatment. For long-term outcome, the data from 2 trials are less conclusive but still shows large effect sizes for up to 104 weeks.

The other 2 trials of a course of manipulative therapy[50,56] reported change scores differently. In the first trial of Giles and Muller,[50] 4-week mean reductions of scores on a 10-point VAS were reported as statistically significant for only the manipulation group (mean reduction, 1.5 [3.0] out of 10) as compared with the groups receiving non-steroidal anti-inflammatory drugs or acupuncture. Hurwitz et al[55] did not report change scores per se and only indicated that none of their contrasts between manipulation and mobilization achieved statistical significance at any outcome point. In all, 8 of 9 trials of a course of spinal manipulation reported statistically significant or clinically important changes in the group receiving manipulation. No trial group was reported to remain unchanged, and no trial group was reported to have worsened. In none of these trials were any major adverse reactions reported.

Mobilization Trials

Five studies are available to determine the outcome of a course of mobilization therapy, one of which did not provide pre- and posttreatment pain scores.[55] All groups showed positive changes. Two studies[59,60] provide data up to the 6- to 7-week outcome point. Only one of these[59] permits the calculation of an effect size, which was found to be large and at the upper end of the range found in the manipulation studies for the same period. Two studies provided data on the percentage of subjects achieving a clinically important improvement[57] or full recovery.[60,61] From these, it appears that approximately 70% of patients achieve this level of improvement at the 6- to 7-week point. Only 1 study provided long-term data,[61] showing full recovery in approximately 70% of subjects at 13 and 52 weeks.

Massage Trials

Only 2 trials of massage for chronic neck pain were retrieved. An effect size was calculated from Gam et al[62] for a group receiving massage and exercises of 0.03 at the 6-week outcome point. Irnich et al[63] reported the change scores in 100 mm VAS points at 1 week (7.89) and at 12 weeks (14.4), neither of which exceeds the 20 mm (2 of 10 points) level established by Brodin[57] and others[70,71] as a clinically important difference in chronic pain patients.

There are several ways to assess the clinical relevance of change scores. They can be compared with what is known as the "minimum clinically important change."[39] However, this value is properly derived from an analysis of patients' minimum expectations of change on a specific instrument as compared with a global or objective standard of change. To our knowledge, this has not specifically been done for pain scores for chronic neck pain patients.

More generally, Farrar et al[70] have reviewed the change scores on the 11-point pain scale in 10 clinical trials for a variety of chronic pain complaints (2724 subjects) and have determined that a 2-point or 20 of 100 mm change is clinically relevant for patients with chronic pain.

It could be argued that these change scores represent the natural history of chronic neck pain or the placebo effect within a trial and therefore do not reflect the influence of the treatments provided. We have investigated the average change scores* in a separate group of controlled clinical trials of conservative treatments for chronic neck pain[71] and found that these are not generally greater than 15 mm on a 100 mm VAS (around 25% improvement). In several of these studies, there was no change at all in the control groups over up to 10 weeks posttreatment. Given these findings, the changes obtained in this review would appear to exceed what could be ascribed to either the natural history or the placebo affect.

Notwithstanding these comparisons with published benchmarks for clinical change, there is an urgent need for placebo- or sham-controlled clinical trials of manual therapies for chronic neck pain. Until such trials are performed, it will not be possible to accurately determine the attributable effect of these therapies over and above the nonspecific effects that are generally present in all clinical trials but even more strongly present during manual therapies in particular.

Conclusion

There is moderate- to high-quality evidence that subjects with chronic neck pain not due to whiplash and without arm pain and headaches who are randomized to receive a course of spinal manipulation or mobilization show clinically important improvements at 6, 12, and up to 104 weeks posttreatment. The current evidence does not support a similar level of benefit from massage therapy. There is a need for controlled studies of these therapies for chronic neck pain.

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