SECOND PRIZE

ADVERSE REACTIONS TO CHIROPRACTIC TREATMENT AND THEIR EFFECTS ON SATISFACTION AND CLINICAL OUTCOMES AMONG PATIENTS ENROLLED IN THE UCLA NECK PAIN STUDY

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ABSTRACT

Background: Minor side effects associated with chiropractic are common. However, little is known about their predictors or the effects of reactions on satisfaction and clinical outcomes.

Objective: The objectives of this study are to compare the relative effects of cervical spine manipulation and mobilization on adverse reactions and to estimate the effects of adverse reactions on satisfaction and clinical outcomes among patients with neck pain.

Methods: Neck pain patients were randomized to receive cervical spine manipulation or mobilization. At 2 weeks, subjects were queried about possible treatment-related adverse reactions and followed for 6 months with assessments for pain and disability at 2, 6, 13, and 26 weeks. Numerical rating scales and the Neck Disability Index were used to measure pain and disability. Perceived improvement and satisfaction with care were assessed at 4 weeks.

Results: Of 960 eligible patients, 336 enrolled and 280 responded to the adverse event questionnaire. Thirty percent of respondents reported at least 1 adverse symptom, most commonly increased pain and headache. Patients randomized to manipulation were more likely than those randomized to mobilization to report an adverse reaction (adjusted odds ratio = 1.44, 95% confidence interval = 0.85, 2.43). Subjects reporting adverse reactions were less satisfied with care and less likely to have clinically meaningful improvements in pain and disability.

Conclusions: Adverse reactions are more likely to be reported following cervical spine manipulation than mobilization. Chiropractors may reduce iatrogenesis and increase satisfaction and perhaps clinical outcomes by mobilizing rather than manipulating their neck pain patients. (J Manipulative Physiol Ther 2004;27:16-25)

Key Indexing Terms: *Chiropractic; Spinal Manipulation; Neck Pain; Adverse Reactions; Side Effects; Iatrogenesis; Patient Satisfaction*

INTRODUCTION

Although major complications resulting from chiropractic care are very rare,[1-3] transient discomfort and other minor side effects of chiropractic care are common. Recent prospective studies have shown 30% to 55% of patients receiving spinal manipulation experience minor side effects, such as local discomfort[4-6] or additional pain[7] shortly after treatment. Much less common are radiating pain or discomfort,[4,5,7] stiffness,[7] headache, and tiredness or fatigue.[4-7] Nausea and dizziness each comprise 5% or less of reported symptoms.[4-7] The majority of reactions have been reported to begin within 24 hours of the treatment visit and to resolve in less than 24 hours. However, little is known about (1) the frequency of adverse reactions specifically following chiropractic treatment of the cervical spine, (2) the effect of type of manual therapy on the incidence of adverse reactions, and (3) the effects of adverse reactions on patient satisfaction and clinical outcomes.

The objectives of this study are to compare the relative effects of cervical spine manipulation and mobilization on

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adverse reactions and to estimate the effects of adverse reactions on satisfaction and clinical outcomes among patients with neck pain.

Methods

Study Design and Source Population

Neck pain patients were randomized in a balanced 2 × 2 × 2 factorial design to manipulation with and without heat and with and without electrical muscle stimulation (EMS) and mobilization with and without heat and with and without EMS. Subjects were followed for 6 months with assessments for pain and disability at 2 and 6 weeks and 3 and 6 months. The source population was approximately 90,000 to 110,000 members of a southern California health care network, which had chiropractors on staff at 4 of its clinics.

Subject Selection

Inclusion and exclusion criteria. Patients were eligible for the study if they (1) were health maintenance organization (HMO) members with the medical group chosen as their health care provider; (2) sought care at 1 of the 4 study sites from February 9, 1998 through June 30, 2000; (3) presented with a complaint of neck pain (defined as pain in the region from the upper thoracic spine to the occiput and the surrounding musculature); (4) had not received neck pain treatment in the past 1 month; and (5) were 18 to 70 years old.

Potential subjects were excluded if they (1) had neck pain due to fracture, tumor, infection, severe spondyloarthropathy, or other nonmechanical cause; (2) had progressive neurological deficit, myelopathy, herniated nucleus pulposus, or severe incapacitating pain; (3) had severe coexisting disease; (4) were being treated by electrical devices; (5) had a blood coagulation disorder or were using corticosteroids or anticoagulant medications; (6) had a history of stroke or transient ischemic attacks; (7) had plans to relocate; (8) were not easily accessible by telephone; (9) lacked the ability to read English; or (10) had pain involving third-party liability or Workers' Compensation.

Patient screening protocol. All patients presenting with neck pain were met by the field coordinator who conducted the screening interview to determine potential eligibility. Patients received an information sheet that described the study's purpose, protocols, and requirements of participation, and explained that subjects would be assigned at random to different treatment plans. A history and physical examination were conducted on each patient who initially agreed to participate. Radiology and laboratory tests were ordered if necessary.

Informed consent and randomization. Those patients agreeing to participate and meeting all eligibility criteria were asked to read and sign an informed consent form, which was administered by the field coordinator and witnessed by a third party. The field coordinator was available to answer any study-related questions during the informed consent process. The study protocol and informed consent form were approved by the institutional review boards from the Southern California University of Health Sciences; University of California, Los Angeles (UCLA); and the health care network.

A computer program written by our statistician generated blocks of 16 site-stratified randomized assignments that were placed in site-specific, sequentially numbered, and sealed security envelopes. For each consenting patient, the field coordinator opened the site-specific envelope in sequence and documented the patient for whom the assignment was made. Subjects completed the baseline questionnaire and received their initial chiropractic treatment on the same day. Study subjects received $20 for their time and to offset their copayments, which ranged from $5 to $20 depending on the patient's specific health plan.

Treatment Protocols

All participants received information about posture and body mechanics and 1 or more of the following, as appropriate: stretching, flexibility, or strengthening exercises, and advice about ergonomics and workplace modifications. Subjects assigned to one of the spinal manipulation groups received at least 1 controlled dynamic thrust, applied with high-velocity and low- amplitude force with minimal extension and rotation directed at 1 or more restricted upper thoracic and/or cervical spine joint segments within patient tolerance. Subjects assigned to one of the spinal mobilization groups received 1 or more movements of low velocity and variable amplitude directed to 1 or more restricted upper thoracic and/or cervical spine joint segments. These types of manipulation and mobilization are the most common types of care delivered by chiropractors in the US,[8,9] and our definitions are consistent with those developed by the Mercy Center Consensus Conference for the establishment of guidelines for chiropractic quality assurance and practice parameters.[10]

Subjects assigned to one of the heat groups received a 10-minute application of moist heat prior to the manipulation or mobilization. Subjects assigned to one of the EMS groups received a 10-minute application of this modality prior to manipulation or mobilization. Subjects assigned to receive both heat and EMS received the heat treatment and EMS simultaneously, followed by manipulation or mobilization.

Data Collection and Variables

Sources of data were the baseline history, physical examination, and questionnaire; 2-week and 6-week and 3-month and 6-month mailed follow-up questionnaires; and a telephone interview at 4 weeks.

Baseline data. Eleven-point (0-10) numerical rating scales were used to assess most severe and average pain intensity in the past week. Disability due to neck pain was assessed

with the 10-item Neck Disability Index (NDI),[11,12] which is a modified version of the Oswestry Low Back Pain Disability Index[13] with a scoring range from 0 to 50. The NDI has been shown to have high internal consistency and high test-retest reliability, to be responsive to change, and to correlate well with the McGill Pain Questionnaire.[12]

Health status was assessed with the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36).[14] Five of 8 subscales of this previously validated instrument were used: (1) limitations in physical activities because of physical or emotional problems; (2) limitations in usual role activities because of physical health problems; (3) limitations in usual role activities because of emotional health problems; (4) general health perceptions; and (5) general mental health.[15] In addition, a numerical rating scale for expectation of treatment success was used, where 0 indicates "not confident" and 10 indicates "confident" that treatment will be successful.

Adverse reaction data. At 2 weeks, subjects were queried by mailed questionnaire about possible adverse reactions: "Did you experience any discomfort or unpleasant reaction from chiropractic care during the past 2 weeks?" For each reported symptom, subjects were asked to rate the amount of discomfort on a 0 to 10 numerical rating scale (0 = no discomfort, 10 = unbearable discomfort); how long after the treatment the discomfort began (<30 minutes after treatment, 30 minutes to 4 hours, 4 hours to 24 hours, or >24 hours after treatment); how long the discomfort lasted (<10 minutes, 10 minutes to 1 hour, 1 hour to 24 hours, or >24 hours); and how much the discomfort affected their normal daily activities at home and/or work ("not at all," "a little," or "a lot").

Patient satisfaction. Participants were interviewed at 4 weeks postrandomization about their satisfaction with chiropractic care and perceived change in neck pain symptoms. Data on patient satisfaction were obtained with a 0 to 10 numerical rating scale, where 0 indicates "extremely dissatisfied" and 10 indicates "extremely satisfied" with care, and with an adaptation of a previously validated 10-item (40-point) patient satisfaction instrument.[16] Neck pain status and limitations in daily activities were assessed with 5-point scales of global improvement ("a lot worse" to "a lot better"). Subjects were also asked whether or not they would seek similar care for future neck pain.

Clinical outcomes. The primary clinical outcome variables are changes in neck pain intensity and related disability. Pain and disability were measured by 0 to 10 scales and NDIs at each follow-up assessment. Each outcome is treated as a continuous and as a dichotomous variable. Cut points of 2+ points (vs. less than 2 points) on the 0 to 10 scales and 5+ points (vs. less than 5 points) on the NDI were used as dichotomous outcomes. These cut points were chosen because they were most strongly associated with patients' global assessment of their improvement ("better" or "a lot better" vs. no improvement). Differences between groups of 2+ points on the 0 to 10 scales and 5+ points on the NDI were considered clinically meaningful.

Statistical Methods

Descriptive statistics were used to summarize patient sociodemographic and health characteristics measured at baseline for each treatment group. Means, standard deviations, and medians were computed by treatment group for continuous variables, and frequency distributions were generated for categorical variables.

Logistic regression was used to (1) estimate the effects of manipulation versus mobilization on reports of any adverse symptoms and on specific treatment-related adverse symptoms reported in the first 2 weeks; (2) estimate the effects of reporting any adverse symptoms on patient satisfaction (9+ vs. <9/10) and on perception of improvement (a lot better vs. not a lot better and better/a lot better vs. same/worse) at 4 weeks; and (3) estimate the effects of adverse symptom reporting in the first 2 weeks on 2-point and 5-point reductions in pain and disability, respectively, from 2 weeks to each subsequent follow-up assessment. Sex, age, duration of neck pain episode at baseline, baseline neck pain intensity and disability, and treatment group assignment were included as covariates in the models under (1) and (2); the baseline value of the outcome variable was included in addition to these covariates in the (3) models. The logistic model results were used to estimate odds ratios (ORs) and 95% confidence limits (CIs).

Ordinary least squares (OLS) regression models were used to (1) estimate the effects of reporting any adverse symptoms on patient satisfaction (0 to 10 numerical rating and 0 to 40 point scales) at 4 weeks and (2) estimate differences in mean change on each continuous clinical outcome from 2 weeks to each subsequent follow-up assessment. The OLS models included the same covariates as the logistic models.

Given that symptoms reported to have occurred shortly after treatment and with a degree of severity may have been relatively more likely to be associated with treatment, in a subset of models we considered adverse symptoms only if they were reported to have started within 24 hours of treatment and with a severity of at least 2 on the 0 to 10 numerical rating scale. SAS version 8 (SAS Institute, Cary, NC) was used for all analyses.

Results

Screening, Enrollment, and Follow-Up

We screened a total of 1848 patients. Eight hundred eighty-eight (48%) patients were excluded for the following nonmedical reasons (frequency): pain not primarily in the neck (283), over 70 years old (169), third-party liability or workers' compensation (112), fee-for-service or non-HMO insurance (104), treatment in the past 1 month (100), less than 18 years old (24), inability to read English (24), plans

to relocate (14), and not easily accessible by telephone (4). Patients were excluded for the following medical reasons (frequency): severe coexisting disease (21); fracture, tumor, infection, or spondyloarthropathy (13); blood coagulation disorder or use of anticoagulant or corticosteroid medications (9); history of stroke or transient ischemic attacks (6); progressive neurological deficit, myelopathy, herniated nucleus pulposus, or severe incapacitating pain (3); and treatment with electrical device (2).

Of the 960 eligible patients, 624 (65%) refused to participate and 336 were enrolled. Participation was declined because of lack of interest (460), inconvenience (103), and specific treatment preferences (60). One patient was not enrolled because of cognitive impairment.

Two-week and 6-week follow-up questionnaires were returned by 316 (94%) and 301 (89.6%) participants, respectively. Three-month and 6-month questionnaires were returned by 292 (89.6%) and 269 (80.1%) subjects, respectively. Three hundred three subjects (90.2%) were successfully interviewed at 4 weeks; 280 (83%) responded to the adverse symptom query at 2 weeks.

Baseline Characteristics

Tables 1 and 2 show baseline distributions of selected characteristics by type of manual therapy. The participants were predominantly middle-aged, female, white, college educated, married, and employed. The majority of participants had subacute or chronic pain; two thirds had headaches; and many reported having arm pain, numbness, or tingling in the past week. The majority of the NDI scores were consistent with mild to moderate disability. The treatment groups did not appreciably differ with respect to demographic or clinical factors.

Treatment-Related Adverse Symptoms

Thirty percent of respondents reported at least 1 adverse symptom from chiropractic care in the first 2 weeks. Patients had an average of 2.5 visits; visit frequency did not differ by type of treatment. Eight-five patients reported a total of 212 adverse symptoms (120 symptoms in 48 manipulation group patients and 92 symptoms in 37 mobilization group patients). Increased pain and headache were the most common symptoms, followed by tiredness, radiating pain, and dizziness. Table 3 shows the frequency, severity, and onset of adverse symptoms reported by subjects during the first 2 weeks of care by type of manual therapy. Eighty percent of the symptoms began within 24 hours of treatment. The majority of symptoms disappeared within 24 hours of onset and did not appreciably affect daily activities. No known serious complications requiring institutional review board notification were reported.

Effects of Manipulation Versus Mobilization on Adverse Reactions

Table 4 shows crude and adjusted odds ratios of manipulation versus mobilization on reporting adverse symptoms during the first 2 weeks of care by type of symptom and onset/severity status. Patients randomized to manipulation were more likely than those randomized to mobilization to report an adverse symptom (adjusted OR = 1.44, 95% CI = 0.85, 2.43).

Effects of Adverse Reactions on Patient Satisfaction and Perceived Improvement

Table 5 shows crude and adjusted odds ratios of reporting at least 1 treatment-related adverse symptom during the first 2 weeks of care on satisfaction with care, predilection to choose assigned treatment in the future, and perceived improvement in neck symptoms at 4 weeks by outcome variable. Subjects reporting any adverse symptoms in the first 2 weeks were less likely at 4 weeks to be highly satisfied with care (OR = 0.69, 95% CI = 0.40, 1.20) and to perceive their pain as being "a lot better" (OR = 0.50, 95% CI = 0.28, 0.91). Linear regression modeling revealed that, on average, subjects reporting any adverse symptoms were less satisfied with care according to the 0 to 10 numerical rating scale (adjusted mean difference = −0.48, 95% CI = −0.99, 0.025) and to the 10-item satisfaction instrument (adjusted mean difference = −0.55, 95% CI = −1.41, 0.32). Models that included variables representing changes in pain and disability from baseline to 2 weeks resulted in similar estimates (data not shown).

Effects of Adverse Reactions on Clinical Outcomes

Table 6 shows adjusted odds ratios of reporting any treatment-related adverse symptoms during the first 2 weeks of care on 2+ point improvements in most severe and average pain in the past week and on 5+ point improvements in disability during subsequent follow-up. Subjects reporting adverse reactions were less likely to have clinically meaningful improvements in pain and disability. Compared with subjects who reported at least 1 treatment-related adverse symptom during the first 2 weeks of care, subjects who did not report any adverse symptoms had somewhat greater mean improvements in pain and disability (Table 7). Given the relatively small estimates and wide confidence intervals, these estimates are also consistent with no effect of adverse reactions on clinical outcomes, however.

Discussion

The results from this study of neck pain patients randomized to receive chiropractic manipulation or mobilization suggest that cervical spine manipulation is associated with relatively more adverse reactions than cervical spine mobilization and that experiencing an adverse reaction during the first 2 weeks of care results in relatively less satisfaction and perceived improvement 2 weeks later and less reductions in pain and disability after 6, 13, and 26 weeks of follow-up. Although these latter findings are suggestive of an effect of adverse reactions on clinical outcomes, the estimates are

Table 1. *Frequency distributions (numbers and percents) and/or means (standard deviations) and medians of selected sociodemographic and health status variables by type of manual therapy*

		Treatment Group					
		Manipulation (n = 171)		Mobilization (n = 165)		Total	
Variable	Category	Number	Percent	Number	Percent	Number	Percent
Age (y)	<30	18	10.5	17	10.3	35	10.4
	30-39	31	18.1	34	20.6	65	19.4
	40-49	58	33.9	51	30.9	109	32.4
	50-59	46	26.9	38	23.0	84	25.0
	≥60	18	10.5	25	15.2	43	12.8
	Mean (SD)	45.7 (11.8)		45.7 (12.2)		45.7 (12.0)	
	Median	46		46		46	
Sex	Male	55	32.2	50	30.3	105	31.3
	Female	116	67.8	115	69.7	231	68.8
Race/ethnicity	White/Non-Hispanic	102	59.7	106	64.2	208	61.9
	Latino/Hispanic	43	25.2	45	27.3	88	26.2
	Asian/Pacific Islander	13	7.6	7	4.2	20	6.0
	African American/Black	6	3.5	3	1.8	9	2.7
	Other	7	4.1	4	2.4	11	3.3
Education	Some high school or less	1	0.6	4	2.4	5	1.5
	High school graduate	33	19.3	43	26.1	76	22.6
	Some college	76	44.4	62	37.6	138	41.1
	College degree	45	26.3	33	20.0	78	23.2
	Professional or graduate degree	16	9.4	23	13.9	39	11.6
Household income	Less than $20,000	7	4.1	10	6.1	17	5.1
	$20,000 to $39,999	30	17.7	36	22.0	66	19.8
	$40,000 to $59,999	48	28.2	47	28.7	95	28.4
	$60,000 to $79,999	38	22.4	32	19.5	70	21.0
	$80,000 or more	47	27.7	39	23.8	86	25.8
Marital status	Married	118	69.0	102	62.2	220	65.7
	Widowed	4	2.3	7	4.3	11	3.3
	Divorced/separated	22	12.9	26	15.9	48	14.3
	Not married, in relationship	4	2.3	4	2.4	8	2.4
	Never married	23	13.5	25	15.2	48	14.3
Employment status	Employed full time	124	72.5	115	69.7	239	71.1
	Employed part time	16	9.4	18	10.9	34	10.1
	Employed, but on leave	3	1.8	2	1.2	5	1.5
	Unemployed	12	7.0	14	8.5	26	7.7
	Retired	16	9.4	16	9.7	32	9.5
General health status	Poor	0	0.0	2	1.2	2	0.6
	Fair	16	9.4	14	8.5	30	8.9
	Good	69	40.4	73	44.2	142	42.3
	Very good	68	39.8	60	36.4	128	38.1
	Excellent	18	10.5	16	9.7	34	10.1

N = 336.

also compatible with no such effect. Our findings are consistent with other recent studies showing that minor side effects of chiropractic treatment are common[4-7]; however, we are the first, to our knowledge, to show that manipulation is associated with a greater risk of adverse events than mobilization and that this risk has possible implications for patient satisfaction and subsequent clinical outcomes.

In the Senstad et al[4] pilot study, 10 Norwegian chiropractors collected data on reactions that were reported by 10 consecutive patients per chiropractor. Side effects were reported in about one third of the 368 treatments among 95 patients. Ninety percent of the reactions were rated as moderate or slight, and 83% had disappeared within 24 hours. Similar findings were reported in their follow-up study of 1058 patients (4712 visits) treated by 102 chiropractors.[5] Local discomfort was the most common symptom (53%), far ahead of headache (12%), tiredness (11%), and radiating discomfort (10%). Leboeuf-Yde et al[6] tracked 625 patients of 66 chiropractors (1858 visits) who recorded self-reported unpleasant reactions following spinal manipulation. Two thirds of the reactions involved local discomfort in the treatment area; headache, fatigue, and pain in other areas

Table 2. *Frequency distributions (number and percent) and/or means (standard deviations) and medians of baseline neck pain variables by type of manual therapy*

		Treatment Group					
		Manipulation (n = 171)		Mobilization (n = 165)		Total	
Variable	Category	Number	Percent	Number	Percent	Number	Percent
Duration of episode	<3 weeks	40	23.4	47	28.5	87	25.9
	3 weeks-3 months	37	21.6	31	18.8	68	20.2
	3 months-1 year	34	19.9	18	10.9	52	15.5
	>1 year	60	35.1	69	41.8	129	38.4
Neck Disability Index (0-50 scale)	≤5	17	10.1	12	7.3	29	8.7
	6-10	51	30.2	46	28.1	97	29.1
	11-15	47	27.8	53	32.3	100	30.0
	16-20	33	19.5	31	18.9	64	19.2
	>20	21	12.4	22	13.4	43	12.9
	Mean (SD)	13.1 (6.2)		13.3 (6.3)		13.2 (6.2)	
	Median	12		12		12	
Most severe neck pain (past week, 0-10 scale)	Mean (SD)	6.4 (2.1)		6.6 (2.1)		6.5 (2.1)	
	Median	7		7		7	
Average neck pain (past week, 0-10 scale)	Mean (SD)	4.7 (1.9)		4.8 (1.9)		4.8 (1.9)	
	Median	5		5		5	
Cut-down days due to neck pain (past month)	Mean (SD)	4.3 (5.9)		4.8 (6.8)		4.6 (6.4)	
	Median	2		3		2	
Over-the-counter pain medication (past week)	Yes	147	86.0	148	89.7	295	87.8
	No	24	14.0	17	10.3	41	12.2
Prescription pain medication (past 6 months)	Yes	43	25.2	37	22.4	80	23.8
	No	128	74.8	128	77.6	258	76.2
Headache (past week)	Yes	108	63.2	114	69.1	222	66.1
	No	63	36.8	51	30.9	114	33.9
Arm pain (past week)	Yes	81	47.4	70	42.4	151	44.9
	No	90	52.6	95	57.6	185	55.1
Arm numbness or tingling (past week)	Yes	70	40.9	66	40.0	136	40.5
	No	101	59.1	99	60.0	200	59.5
History of previous neck pain episodes	Yes	125	73.1	118	71.5	243	72.3
	No	46	26.9	47	28.5	93	27.7
History of traumatic neck injury	Yes	46	36.8	39	33.3	85	35.1
	No	79	63.2	78	66.7	157	64.9
History of previous neck pain treatment	Yes	144	84.2	131	79.4	275	81.9
	No	27	15.8	34	20.6	61	18.2

N = 336.

each comprised about 10% of the reactions; and most symptoms disappeared within 24 hours. Barrett and Breen[7] collected data from 68 chiropractic patients, 53% of whom experienced an adverse symptom, most commonly additional or radiating pain. Dizziness and nausea were the least commonly reported symptoms in all studies, each comprising 5% or less of the reported reactions.

A recent randomized trial comparing manual therapy (primarily mobilization and specifically excluding manipulation), physical therapy (primarily active exercise therapy), and continued care by a general practitioner for patients with neck pain found a greater frequency of increased neck pain lasting more than 2 days among patients in the manual therapy group than in the other groups and relatively more headache, upper extremity pain or paresthesia, and dizziness in the manual and physical therapy groups than the medical group.[17] No serious complications from spinal manipulation or other chiropractic or manual treatment have been reported from any of the published clinical trials involving manipulation or mobilization for neck pain.[1,18]

Although there have been a few attempts to identify predictors of adverse events related to chiropractic care or spinal manipulation,[19-23] only 1 published study has focused on the identification of potential predictors of minor adverse reactions resulting from chiropractic care,[24] and none has dealt exclusively with patients presenting with neck pain. Senstad et al[24] found no association between type of treatment (eg, spinal manipulation, soft-tissue therapy) and reported side effects, though they did find women (65% vs. 44% in men) and those aged 27 to 46 years (60% vs. 49% in 47 to 64 year olds) to be somewhat more likely to experience side effects during the course of care. Sex and

Table 3. *Frequency, percent, mean (standard deviation) severity on 0 to 10 numerical rating scale, and time of onset of adverse symptoms reported by subjects during the first two weeks of care by type of manual therapy*

	Manipulation (n = 141)					Mobilization (n = 139)				
Symptom	No.	%	Severity mean (SD)	Onset No.	≥24 hours %	No.	%	Severity mean (SD)	Onset No.	≥24 hours %
Neck pain, stiffness/soreness	39	27.7	5.0 (2.2)	31	79.5	31	22.3	5.1 (2.4)	26	83.9
Radiating pain/discomfort	9	6.4	5.2 (3.5)	7	77.8	8	5.8	4.6 (3.1)	5	62.5
Tiredness/fatigue	17	12.1	4.7 (2.3)	16	94.1	11	7.9	5.2 (2.8)	8	72.7
Headache	22	15.6	5.6 (2.5)	21	95.5	22	15.8	4.6 (2.9)	16	72.7
Dizziness/imbalance	6	4.3	5.2 (2.4)	6	100	3	2.2	7.0 (1.7)	2	66.7
Fainting	0	0	—	—	—	0	0	—	—	—
Nausea/vomiting	3	2.1	3.7 (2.9)	2	66.7	2	1.4	6.0 (2.8)	2	100
Blurred or impaired vision	4	2.8	4.0 (2.9)	3	75.0	0	0	—	—	—
Ringing in the ears	5	3.5	4.0 (2.2)	4	80.0	1	0.7	1.0	0	0
Arm or leg weakness	4	2.8	5.5 (3.9)	3	75.0	3	2.2	4.7 (2.9)	2	66.7
Confusion or disorientation	2	1.4	1.0 (0.0)	1	50.0	2	1.4	2.5 (2.1)	1	50.0
Depression or anxiety	3	2.1	6.0 (1.7)	2	66.7	3	2.2	3.0 (2.7)	2	66.74

N = 280.

Table 4. *Crude and adjusted effect estimates (odds ratios and 95% confidence intervals) of manipulation versus mobilization on reporting adverse symptoms during the first two weeks of care by type of symptom and onset/severity status*

		Crude estimate		Adjusted estimate*	
Symptom	Onset/severity	OR	95% CI	OR	95% CI
Neck pain, stiffness/soreness	Any	1.36	(0.79, 2.34)	1.38	(0.79, 2.40)
	Onset within 24 hours and severity 2+/10	1.31	(0.72, 2.38)	1.29	(0.70, 2.37)
Radiating pain/discomfort	Any	1.12	(0.42, 3.01)	1.39	(0.49, 3.89)
	Onset within 24 hours and severity 2+/10	1.49	(0.41, 5.41)	1.64	(0.43, 6.26)
Tiredness/fatigue	Any	1.61	(0.72, 3.58)	1.69	(0.74, 3.84)
	Onset within 24 hours and severity 2+/10	2.23	(0.88, 5.67)	2.25	(0.87, 5.83)
Headache	Any	0.99	(0.52, 1.89)	1.00	(0.52, 1.92)
	Onset within 24 hours and severity 2+/10	1.61	(0.77, 3.39)	1.63	(0.77, 3.46)
Other†	Any	1.19	(0.47, 3.02)	1.19	(0.45, 3.16)
	Onset within 24 hours and severity 2+/10	2.02	(0.67, 6.15)	1.94	(0.61, 6.18)
Any adverse symptom	Any	1.46	(0.86, 2.42)	1.44	(0.85, 2.43)
	Onset within 24 hours and severity 2+/10	1.44	(0.84, 2.47)	1.44	(0.83, 2.49)

Results from logistic regression analyses (N = 280).
OR, odds ratios; *CI*, confidence intervals.
*Effects adjusted for sex, age, duration of neck pain episode at baseline, baseline neck pain intensity and disability, and treatment group assignment.
†Other symptoms are dizziness/imbalance, nausea/vomiting, blurred or impaired vision, ringing in the ears, arm or leg weakness, confusion or disorientation, and depression or anxiety.

age were not associated with adverse reactions in the current study.

Our finding suggesting that cervical spine manipulation confers greater risk than mobilization for minor adverse events could have implications on predicting the risk of more serious events, such as vertebrobasilar accidents. Although the numbers are small and should be interpreted cautiously, symptoms consistent with vertebrobasilar artery compromise, including dizziness, nausea or vomiting, and blurred or impaired vision, were more common among patients randomized to receive cervical spine manipulation. These symptoms are among the most frequent presenting symptoms in cerebrovascular accident patients after manual therapy involving the cervical spine, with almost 90% occurring less than 24 hours following treatment.[22] In our study, these symptoms were more likely to occur within 24 hours in manipulated than mobilized patients. The authors of a recent systematic literature review of vertebral artery

Table 5. *Crude and adjusted effect estimates (odds ratios and 95% confidence intervals) of reporting at least one treatment-related adverse symptom during the first two weeks of care on satisfaction with care (0-10 scale), predilection to choose assigned treatment in the future, and perceived improvement in neck symptoms at four weeks by outcome variable and onset/severity of adverse symptom*

Outcome variable contrast	Onset/severity	Crude estimate		Adjusted estimate*	
		OR	95% CI	OR	95% CI
Satisfaction with care	Any onset, severity	0.73	(0.43, 1.24)	0.69	(0.40, 1.20)
9+ versus <9/10	Onset ≤24 hours, 2+/10	0.71	(0.40, 1.25)	0.65	(0.36, 1.17)
Choose assigned treatment in future	Any onset, severity	0.33	(0.19, 0.57)	0.24	(0.13, 0.44)
Yes versus no/maybe	Onset ≤24 hours, 2+/10	0.32	(0.18, 0.57)	0.24	(0.13, 0.45)
Perceived improvement	Any onset, severity	0.59	(0.34, 1.01)	0.50	(0.28, 0.91)
A lot better versus not a lot better	Onset ≤24 hours, 2+/10	0.79	(0.45, 1.38)	0.68	(0.37, 1.25)
Better/a lot better versus same/worse	Any onset, severity	0.70	(0.39, 1.25)	0.63	(0.34, 1.15)
	Onset ≤24 hours, 2+/10	0.81	(0.44, 1.49)	0.73	(0.39, 1.39)

Results from logistic regression analyses.
OR, odds ratios, *CI,* confidence intervals.
*Effects adjusted for sex, age, duration of neck pain episode at baseline, baseline neck pain intensity and disability, and treatment group assignment.

Table 6. *Adjusted* effect estimates (odds ratios and 95% confidence intervals) of reporting any treatment-related adverse symptoms during the first two weeks of care on 2+ point improvements in most severe and average pain in the past week (0-10 numerical rating scales) and on 5+ point improvements in disability (0-50 point Neck Disability Index), by outcome variable, onset/severity of adverse symptom, and follow-up interval. Results from logistic regression analyses.*

Follow-up interval	Onset/severity	Most severe pain		Average pain		Neck disability	
		OR	95% CI	OR	95% CI	OR	95% CI
2-6 weeks	Any onset, severity	0.68	(0.34, 1.37)	0.50	(0.24, 1.03)	0.66	(0.33, 1.31)
	Onset ≤24 hours, 2+/10	0.57	(0.28, 1.16)	0.54	(0.25, 1.17)	0.56	(0.28, 1.13)
2-13 weeks	Any onset, severity	1.07	(0.57, 1.98)	0.58	(0.31, 1.09)	0.69	(0.37, 1.29)
	Onset ≤24 hours, 2+/10	0.96	(0.50, 1.82)	0.55	(0.29, 1.07)	0.70	(0.37, 1.34)
2-26 weeks	Any onset, severity	0.87	(0.47, 1.61)	0.88	(0.45, 1.69)	0.76	(0.41, 1.41)
	Onset ≤24 hours, 2+/10	0.74	(0.39, 1.38)	0.78	(0.39, 1.56)	0.69	(0.36, 1.31)

*Effects adjusted for sex, age, duration of neck pain episode at baseline, treatment group assignment, and baseline value of the outcome variable.
OR, odds ratios; *CI,* confidence intervals.

dissections following cervical manipulation and minor and major trauma, as well as those reported as spontaneous, concluded that there is inadequate evidence that allows for the identification of the patient at risk or the type of neck movement likely to cause a dissection of the vertebral artery.[21] These authors have also shown that cerebrovascular accidents and strokes occur in patients shortly after even nonforce and neutral position procedures.[22,23] However, no study to date has been designed to provide a valid estimate of the relative risk of serious complications resulting from cervical spine manipulation versus mobilization.

Major limitations of the study are potential bias due to misclassification and confounding, lack of generalizability, and the imprecision of some of the effect estimates. Despite prospective data collection, low loss to follow-up, and multivariable modeling, our effect estimates may be biased. Because patients were asked at 2 weeks to report symptoms associated with all chiropractic visits that occurred during the first 2 weeks, there may have been inaccuracies in recall for some patients. The misclassification would likely be nondifferential with respect to treatment status, resulting in treatment effect estimates biased toward the null. Misclassification could have also biased estimated associations of adverse symptoms with satisfaction and clinical outcomes. Again, the bias would likely be nondifferential, since adverse symptoms were reported at 2 weeks and outcomes were measured at 4 weeks and beyond and we have no evidence that accuracy of recall would be dependent on subsequent outcomes. Because of randomization, treatment effect estimates are not likely confounded. However, adverse symptom effect estimates may be confounded by predictors of satisfaction and other outcomes. We considered many factors in the multivariable models, though the estimates could remain confounded because of other known and unknown factors.

The findings may not be generalizable to other settings because of differences in patients and providers. For example, a large number of neck pain patients refused to participate, leaving the study population with a group of self-selected volunteers that may not reflect neck pain patients

Table 7. *Estimated* effects (adjusted mean differences in improvement and 95% confidence intervals) of reporting any treatment-related adverse symptoms during the first two weeks of care on most severe pain and average pain intensity in the past week (0-10 numerical rating scales) and in disability (0-50 point Neck Disability Index) from 2 weeks to each subsequent follow-up assessment by outcome variable, onset/severity of adverse symptom, and follow-up interval. Results from ordinary least squares regression analyses.*

		Most severe pain		Average pain		Neck disability	
Follow-up interval	Onset/severity	Mean differences	95% CI	Mean differences	95% CI	Mean differences	95% CI
2-6 weeks	Any onset, severity	0.23	(−0.39, 0.85)	0.31	(−0.22, 0.85)	0.58	(−0.79, 1.96)
	Onset ≤24 hours, 2+/10	0.43	(−0.22, 1.07)	0.23	(−0.33, 0.80)	0.92	(−0.52, 2.37)
2-13 weeks	Any onset, severity	0.20	(−0.52, 0.93)	0.39	(−0.21, 1.00)	0.85	(−0.80, 2.50)
	Onset ≤24 hours, 2+/10	0.36	(−0.40, 1.13)	0.46	(−0.18, 1.09)	1.19	(−0.54, 2.92)
2-26 weeks	Any onset, severity	−0.05	(−0.80, 0.70)	0.18	(−0.47, 0.84)	0.80	(−0.71, 2.32)
	Onset ≤24 hours, 2+/10	0.27	(−0.51, 1.06)	0.37	(−0.31, 1.05)	1.45	(−0.11, 3.02)

*Effects adjusted for sex, age, duration of neck pain episode at baseline, treatment group assignment, and baseline value of the outcome variable. Positive values indicate more improvement in the group that did not report any adverse symptoms during the first 2 weeks.
CI, confidence intervals.

presenting elsewhere. Also, the chiropractors in our study do not necessarily manipulate and mobilize patients in the same way as chiropractors do in other practice settings, though the chiropractors did use the types of spinal manipulation and mobilization techniques that are most commonly used by practicing US chiropractors.[8,9] Because of the relatively small sample size and the low frequency of certain adverse reactions, we did not have the power to detect small but potentially important effects of treatment on neurologic symptoms and other clinical findings that may be related to subsequent risk of serious complications, such as stroke.

Conclusion

Among neck pain patients treated by chiropractors, adverse reactions are more likely to be reported following cervical spine manipulation than cervical spine mobilization. Compared with subjects who did not report any adverse treatment effects, the findings suggest that subjects with adverse symptoms (1) were relatively less satisfied with care, (2) perceived less improvement in neck symptoms, and (3) had more pain and disability during subsequent follow-up. Larger prospective studies should be conducted to obtain more precise estimates of effect and to identify additional predictors and clinical consequences of adverse reactions associated with chiropractic care. If replicated in subsequent investigations, our findings suggest that chiropractors may be able to reduce iatrogenic symptoms and improve patient satisfaction and perhaps clinical outcomes by mobilizing rather than manipulating their neck pain patients.

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