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Randomised controlled pilot trial of high-velocity, low-amplitude manipulation on cervical and upper thoracic spine levels in asymptomatic subjects

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ABSTRACT

Background: High-velocity, low-amplitude (HVLA) manipulation techniques are habitually used on the cervical spine but the effects are not completely clear. The aim of this prospective comparative trial was to evaluate effects of an indiscriminate manipulation on the C5 (AMC5) a manipulation treatment based on a previous evaluation (MT) and a sham intervention (ST) on cervical spine range of motion (ROM); cervical flexion isometric peak force; EMG activation of sternocleidomastoid muscle (SCM) during the cranio-cervical flexion test (CCFT); and EMG signals of right and left biceps at rest were analyzed.
Methods/Design: Randomised controlled pilot study and intention-to-treat analysis was performed.
Setting: The study was conducted at an osteopathic clinic.
Methods: The outcomes were measured pre and immediately post intervention.
Participants: A total of 36 asymptomatic subjects (18 male, mean age 30 years) were randomly enrolled into 3 groups: AMC5 ($n = 12$), MT ($n = 12$), and ST ($n = 12$).
Results: Significant changes ($p < 0.1$) were found in the cervical flexion isometric peak force (−13.15%), however, the effect size was considered moderate ($d = 0.52$). The extension (10.44%) and left rotation ROM (12.25%) showed significant improvement in MT group. During CCFT significant changes were not reported.
Conclusions: The current pilot study suggested that a tendency toward a decrease in the isometric strength peak in the cervical flexion of the MT group may appear. In cervical ROM the MT group achieved significant effects in extension and left rotation movement.

1. Introduction

Cervical spine pain is one of the most prevalent complaints and the largest causes of disability in industrialized countries [1]. Spinal manipulative therapy is frequently used by osteopaths, physiotherapists, chiropractors and doctors. One of the used techniques involves high-velocity, low-amplitude (HVLA) manipulations. The HVLA manipulation technique is a traditional approach that has gained popularity during the past 50 years. These techniques are applied to correct somatic dysfunctions [2].

Multiple benefits have been attributed to HVLA manipulations such as, increase in sympathetic efferent activity at the level of the dermatome of the manipulated segment [3], short-term increase in biceps brachial bilaterally EMG at rest [4], increase in the oxytocin, neurotensin and cortisol blood levels [5], significant increases in the left (10.53%) and right (16.82%) handgrip strength [6] and

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significant changes on standing balance and postural sway [7,8]. On the contrary, controversial results after manipulation have been also reported such as, no significant EMG activity baseline changes in subjects with neck pain [9], or the marginal improvement for maximum isometric handgrip strength [10] reported in asymptomatic athletes after a single C5/C6 HVLA manipulation.

In addition, contradictory results have been also reported in studying the relationship between mouth opening and cervical HVLA manipulation. After cervical HVLA, George et al. [11], observed no significant changes on normal mouth opening in asymptomatic subjects between the control and CSM groups [11], whereas Oliveira et al. [12], showed an immediate increase in mouth opening after cervical HVLA manipulation at the C1/C0 joint (1.5 mm) [12].

In regard to the relationship between cervical range of motion (ROM) and manipulation, a study reported immediate effects on cervical ROM after a single HVLA manipulation [13], whereas Passmore et al. [14] reported moderate effect on mobility improvement in asymptomatic subjects. A recent review has also highlighted a small improvement in cervical spine range of motion (ROM) after the application of articular HVLA manipulation [15].

One of the main limitations of the different studies is the absence of previous evaluations to determine which parameters of ROM restriction were present before manipulation; therefore, these studies fail to adequately determine the proper technique to correct the dysfunction [2]. In previous studies, the C5 was manipulated in an arbitrary way without taking into account whether it was actually affected in terms of joint motion reduction or alteration [4,9]. The C5 vertebral segment is not the only vertebral segment involved in possible cervical spine pathologies. Kayser et al. [16] showed the importance of segments C1 to C3 in cervical pathology, while Cleland et al. [17] showed that the upper dorsal spine is another spine level from which unspecific cervical pain can originate. Therefore, it has been hypothesized that a previous evaluation correctly attached to a protocol will improve the effects of the manipulations on the cervical spine to a greater extent than will an indiscriminate manipulation of a segment without a previous dysfunction assessment. For these reasons, it is necessary to clarify which type of spinal manipulative therapy, is more effective to improve strength, ROM and EMG activation of muscle in asymptomatic subjects.

We performed this pilot study was to compare the immediate effects of an indiscriminate manipulation on the C5 (AMC5) and a manipulation treatment based on a previous evaluation (MT) on cervical spine ROM; cervical flexion isometric peak force; surface cervical flexors EMG activation during cranio-cervical flexion tests; and an EMG signal on the right and left biceps. Also the effects of these two groups were researched using a sham group (ST).

2. Methods

2.1. Study design

This study was a prospective, randomised controlled pilot study. One research spinal physical therapist registered in Spain conducted patient recruitment and screening at an osteopathic clinic. The study was performed in accordance with the Declaration of Helsinki (2000) and was approved by the local office for Medical Research Ethics Committee of The Public University of Navarra. Participants were required to sign a written, informed consent form. No formal sample size calculation was performed.

2.2. Participants

Social network and word of mouth were used to recruit 36 asymptomatic voluntary subjects. The participants were enrolled between February and June 2015. Participants were randomly allocated to either the AMC5 ($n = 12$), MT ($n = 12$), and ST group ($n = 12$), (Fig. 1).

The inclusion criteria were being between 18 and 40 years old and asymptomatic at the time of the study. Exclusion criteria were any type of cranio-cervical trauma during the last two years, including whiplash; pain radiation to the limbs; neurological alterations in the upper limbs; neurological alterations of the central nervous system; diagnosed vertebral disc injury; degenerative, rheumatologic and/or inflammatory pathologies; pregnancy; previous cervical spine surgery; psychiatric pathologies; spine fractures; dislocation; or vertebral artery positive test [18]. Risks was minimised by ruling out contraindications to the testing protocols via a health history and a thorough physical examination prior to the manipulation session.

2.3. Procedure

The randomisation into the three study arms was performed by the osteopathic clinic, using a computer generated randomization (www.randomizer.org) and registered in an index card. The randomization sequence was not concealed from the investigator who was responsible for assigning participants to groups. The likelihood of bias introduced by unconcealed randomization was reduced by enrollment of consecutive participants. All participants and study personnel (including investigators, physical therapy, and statisticians) were blinded to treatment allocation throughout the trial protocol. Further, the investigators who performed the statistical analyses were not masked from group assignment. Once 12 individuals had been assigned to one group, the envelopes that contained said group was automatically retired. A baseline absence of significant differences among groups was established.

2.4. Data collection and outcome measures

The physical therapist that had five years of experience in osteopathic medicine and ten in manual therapies performed the measurement protocol. Every group followed the same measurement protocol.

2.4.1. Cervical spine ROM

All participants' cervical spine mobility was evaluated using a goniometer CROM (Performance Attainment Associates, St. Paul, MN, USA). This device has been validated in several studies and offers a moderate intra-examiner Intraclass Correlation Coefficient (ICC 0.69) and a good inter-examiner ICC (0.75) [19,20]. The CROM goniometer had three inclinometers, with a sensitive range of two degrees. These inclinometers are attached to a frame similar to glasses. The CROM device was mounted over the subjects nose bridge and ears and secured to the head by a strap. The frontal and lateral gravity dependent inclinometers measured the side bending and flexion/extension respectively; the third magnetic dependent inclinometer required a magnetic necklace to measure rotation. In the starting position, the participants were seated relaxed with their feet flat on the floor, their knees and ankles at 90° of flexion, and their hands supported on their thighs. The researcher instructed each subject to move the head correctly before the test. The measurement protocol included, active cervical ROM flexion, extension, right side bending, left side bending, right rotation and left rotation. Three consecutive measurements were obtained and the mean of these 3 trials was used for data analysis.

2.4.2. Cervical flexion isometric peak force

Maximum voluntary isometric force was measured using a

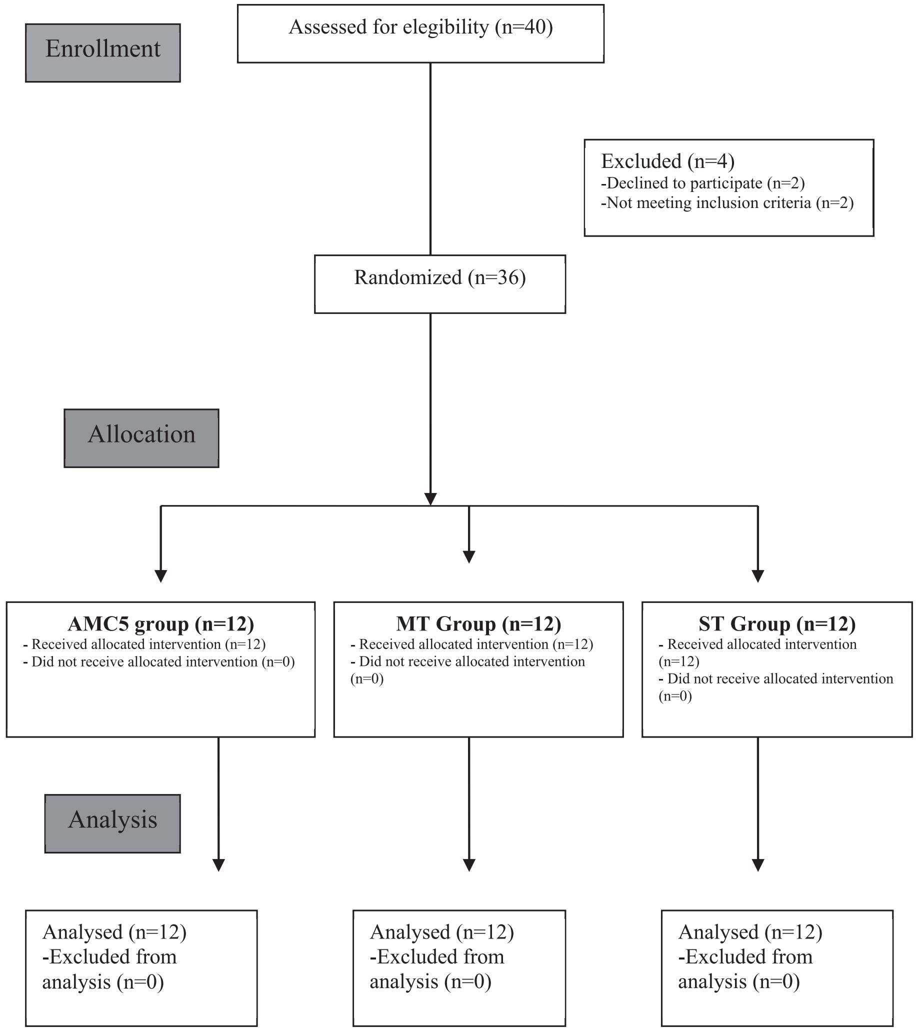

Fig. 1. Flow of participants through the study.

hand-held dynamometer Micro Fet 3 (Hoogan Health Industries, West Jordan UT). Hand-held dynamometers have excellent inter-examiner ICC s (0.94) [21] and excellent intra-examiner ICC (0.80) [22]. The dynamometer is a good option if there is no access to more sophisticated and expensive equipment, such as an isokinetic machine [23]. The subject was situated in supine position with straight legs; first of all, the participant was instructed to perform the correct movement. The test was performed with the head supported and the dynamometer's load cell placed at the frontal bone, the participant was asked to lift his or her head off the table as much as possible, while the researcher maintained the device still obtaining an isometric contraction. Three consecutive measurements were obtained at intervals of 60 s; the mean of these 3 trials was used for data analysis.

2.4.3. Measurement of surface EMG

The surface electromyography (sEMG) activity of both sternocleidomastoid muscles (SCMs) during the cranio-cervical flexion test were measured. In addition, the sEMG activity from these two muscles, the cervical erector spinae muscles, and the biceps brachial muscles were measured during rest. An EMG-USB Multichannel Bioelectrical Amplifier (Bioelecttronica, Torino, Italy) device was used. It displayed the information in real time and stored it on the disk of a personal computer. Surface EMG was recorded with 24 mm diameter round adhesive bipolar connector electrodes (Spes Medica, Battipaglia, Italy). The skin was cleaned with water before electrode placement. The sEMG signals were recorded at a sample rate of 2048 Hz and were post-processed offline using MATLAB (Mathworks, Inc). The sEMG signals were band -pass filtered between 10 Hz and 500 Hz, and the amplitude RMS value was obtained for each muscle.

2.4.4. Measurement of the efficiency of cervical deep flexor muscles

To measure of the efficiency of cervical deep flexor muscles, SCM activity was assessed by performing the cranio-cervical flexion test [24,25]. Both studies tested the relationship between neck pain, the inhibition of cervical deep flexor muscles (longus capitis and longus colli muscles), and increased EMG activity of the SCM. With the patient in the supine position, a pressure sensor was inflated to 20 mmHg and placed below the neck. The operator instructed the patient to perform five contractions of 10 s each. In the first contraction, the patient produced enough pressure to raise the pressure device to 22 mmHg; in the second, the device rose to 24 mmHg; in the third to 26 mmHg; in the fourth to 28 mmHg fourth; and in the fifth contraction the patient achieved maximum force. Between contractions, the patient rested for 30 s. During the test, the operator placed the electrodes in the sternal portion of the SCM [26] to assess its activity. To obtain the activation value of the

SCM during the cranio-cervical flexion test, an average between the maximum and four sub-maximum values was determined.

2.4.5. Bilateral biceps brachial EMG signal at rest

The patient was seated relaxed with their feet flat on the floor, their knees and ankles at 90° of flexion, the arm was resting on the table with 90° elbow flexion and supination, the wrist in neutral position and the fingers relaxed. The skin was cleaned with water swabs. The operator placed the 24 mm diameter round adhesive bipolar connector electrodes (Spes Medica, Battipaglia, Italy), on the belly of the long head of biceps in an imaginary line from the acromion to the biceps tendon [26]. Prior to any data collection, subject was instructed not to move any part of the body and relax as much as possible. After the instruction training the test was performed and the operator monitored the biceps for 5 s during the rest period. The procedure was repeated with the other biceps brachial.

3. Interventions

3.1. AMC5 group

The overall goal for the AMC5 group was to perform HVLA manipulation technique on the C5 after completing the measurement protocol. With the patient in the supine position, the operator stood at the head of the table and made contact with the right C5 transverse process with his right hand's distal interphalangeal joint while cradling the participant's head with his left hand. During the manipulation, the participant maintained global flexion and analytical extension, right side bending, and left rotation until the C5-C6 segment reached the barrier, at which time the operator performed an HVLA left rotation movement, taking the glabella point as the direction of the thrust [2,27,28]. The operator then returned the patient to a neutral position in a passive and slow way. After 30 s, the measurement protocol was performed again.

3.2. MT group

In the MT group, after the measurement protocol assessment, joint dysfunction was evaluated. The method chosen for the evaluation was exclusively manual, based on a study by G. Jull 1998 that showed high reliability in assessing dysfunctions using manual methods [29]. In our study, we used passive mobility tests and tests of anterior-posterior and lateral pressure. These tests have been validated by radiographic studies of the cervical spine and have shown high inter- and intra-examiner reliability, as well as a good relationship between manual diagnosis and hypomobility [30,31]. For the upper thoracic spine, operators used anterior-posterior pressure tests and passive mobility tests [27]. The patient was evaluated in the neutral, flexion and extension positions. Also tenderness, tissue texture changes and asymmetry were assessed [2]. After the diagnosis of dysfunctions, the operator proceeded to perform the HVLA manipulation [2,27,28]. After manipulation, the operator repeated the measurement protocol.

3.3. ST group

The ST group followed the same protocol as AMC5 group, but with a modified sham technique (in the absence of drop) in place of the C5 technique [32]. To perform the technique, the patient was placed in the supine position with the operator at the head of the table. The operator used the thumb of his right hand to make contact with the right C5 transverse process while his left hand cradled the participant's head. In this position, the operator performed right side bending and left rotation of the C5-C6 segment without reaching the barrier and performed three rotation movements in the direction of the glabella.

Additional outcomes of this study were participant adverse events (such as: pain, headache, dizziness or other symptoms) occurring in the week following the study.

4. Statistical analysis

In order to retain data of all randomly allocated participants, an intention-to-treat analysis was performed. The statistical analysis was performed by a statistician blinded to the randomization, measuring and intervention protocol. An alpha level of 0.1 was used for all statistical analyses. Statistical analyses were conducted using SPSS Statistics 20 for Windows (SPSS, Inc., Chicago, Illinois). Numerical variables were summarized as means ± SD, whereas categorical variables were given as frequencies and percentages. Prior to the planned statistical analyses, preliminary analysis was conducted (Levene test) to confirm data distribution normality. The Levene statistic showed a normal distribution ($P > 0.05$) in flexion, extension; right rotation; left and right side bending mobility increment; in cervical flexion isometric peak force increment; increment in the amplitude of the EMG rest signal of the left brachial biceps and an increment on both sides of the SCM muscle during the cranio-cervical flexion test. On the contrary, the Levene statistic showed no normal distribution (heterogeneous) in left rotation mobility increment and in the EMG rest signal amplitude increment of the right brachial. When this normality assumption failed, non-parametric statistics were applied for means comparisons. For outcomes analysis, we used linear mixed-effects modeling for repeated measures over time using continuous outcome variables as the dependent variable and effects for time, group (AMC5, MT, and ST group), and time by group interaction. Within the mixed model, we calculated 95% CIs and P values for 3 pre-specified intergroup contrasts and for change in all variables within each group over time. Finally, to calculate the effect size the Cohen's d was used, a small effect was defined as Cohen's d scores around 0.2. A moderate effect was defined as Cohen's d scores around 0.5 and finally scores around 0.8 was considered as a large effect.

5. Results

5.1. Subjects

Fig. 1 shows the flowchart of this randomised clinical trial. A total of 40 potential subjects were assessed for eligibility, of which 4 persons were excluded for not meeting inclusion criteria. Thirty-six participants were enrolled and randomly assigned into 3 groups: AMC5 ($n = 12$), group MT ($n = 12$), and group ST ($n = 12$). The comparative test indicated no statistically significant differences ($p > 0.05$) in baseline characteristics between groups. (Table 1).

5.2. Cervical flexion isometric peak force data

The changes in the isometric peak force of the cervical flexion in the MT group were significantly greater (−13.15%; $P = 0.09$) than those observed in the C5 articular manipulation and sham technique groups (−7.8% and −1.7%, respectively), but the effect size was considered moderate ($d = 0.52$) (Table 2).

5.3. Biceps brachial at rest EMG data

No significant differences were observed in the changes in SCM in the left biceps brachial at rest among the three intervention groups. However, the changes in the RMS of the right biceps brachial at rest showed a tendency ($P = 0.14$) to increase in the

Table 1
Baseline characteristics of the subjects included in the study.

	AMC5 Group	MT Group	ST Group	P value
Sex (% males)	50% (6/12)	41.66% (5/12)	58.33% (7/12)	AMC5-MT: 0.696 AMC5-ST: 0.696 MT-ST: 0.436
Age (years) (mean ± SD)	30.50 ± 3.11	30.75 ± 3.98	31.16 ± 2.24	AMC5-MT: 0.849 AMC5-ST: 0.613 MT-ST: 0.751
Weight (kg) (mean ± SD)	66.22 ± 14.36	62.18 ± 7.89	67.66 ± 7.19	AMC5-MT: 0.385 AMC5-ST: 0.766 MT-ST: 0.241
Height (cm) (Mean ± SD)	170 ± 7.52	168 ± 8.04	172 ± 3.65	AMC5-MT: 0.376 AMC5-ST: 0.584 MT-ST: 0.159
BMI (Mean ± SD)	22.56 ± 4.01	21.93 ± 1.56	22.26 ± 2.14	AMC5-MT: 0.610 AMC5-ST: 0.817 MT-ST: 0.788

Table 2
Cervical Flexion Isometric Peak Force results.

	n	Mean (SD)		From baseline to post intervention, Mean (95% CI)	
		Baseline	Post intervention	Within-Group Change	Between-Group Difference in Change
Cervical flexion isometric peak force					
AMC5 Group	12	24.87 (7.54)	22.90 (7.48)	−7.81 (−15.05 to −0.55)	NA
MT Group	12	24.53 (11.47)	19.80 (6.08)	−13.15 (−25.73 to −0.57)	NA
ST Group	12	23.43 (10.22)	21.93 (7.08)	−1.74 (−11.58 to 8.10)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.41
ST Group vs MT Group	NA	NA	NA	NA	0.09
AMC5 Group vs ST Group	NA	NA	NA	NA	0.36

Pre and post values are expressed as mean (Newtons) (SD) in three groups and all variables.

AMC5 group compared with the ST and MT groups, the effect size was considered large (d = 0.91) (Table 3).

5.4. Cervical range of motion data

Immediately after all manipulations, no significance differences were observed in flexion, right rotation, or left and right side bending range changes in the three intervention groups. However, the changes in extension range in the MT and AMC5 groups were significantly greater (10.4% and 6.9%, respectively; p = 0.01) than those observed in the ST group (−3.37%), furthermore the effect size for the MT group was considered large (d = 0.88). In the left rotation range, the MT group effect side was considered large (1.07). The changes in the MT group were significantly greater (12.2%; p = 0.01) than those observed in the AMC5 and ST groups (4.03% and 5.8%, respectively) (Table 4).

5.5. Cranio-cervical flexion test

After all manipulations, no significant differences were observed in the RMS of the both sides of SCM during the cranio-cervical flexion test changes in the three intervention groups. Large effect sizes were not found in any group (Range from d = 0.16 to d = 0.54) (Table 5).

Finally, no adverse events were reported over the course of this investigation.

Table 3
Biceps Brachial EMG RMS at rest results.

	n	Mean (SD)		From baseline to post intervention, Mean (95% CI)	
		Baseline	Post intervention	Within-Group Change	Between-Group Difference in Change
Right Biceps Brachial					
AMC5 Group	12	91.95 (43.57)	146.96 (73.56)	54.08 (9.34–98.82)	NA
MT Group	12	115.40 (74.10)	135.34 (100.37)	23.45(−10.49 to 57.39)	NA
ST Group	12	108.13 ± 95.73	126.24 (128.13)	11.21(−3.12 to 25.55)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.21*
ST Group vs MT Group	NA	NA	NA	NA	0.95*
AMC5 Group vs ST Group	NA	NA	NA	NA	0.14*
Left Biceps Brachial					
AMC5 Group	12	115.40 (93.79)	131.82 (56.66)	23.99 (−7.69 to 55.69)	NA
MT Group	12	136.33 (85.27)	148.99 (96.87)	5.67 (−16.37 to 27.72	NA
ST Group	12	11.92 (64.01)	150.02 (135.20)	23.02 (−0.74 to 46.79)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.27
ST Group vs MT Group	NA	NA	NA	NA	0.30
AMC5 Group vs ST Group	NA	NA	NA	NA	0.95

Pre and post values are expressed as mean (mV) (SD) three groups and all variables. Significant group interaction (P < 0.01). * p-values were drawn from nonparametrical tests.

Table 4
Summary cervical range of motion results.

	n	Mean (SD)		From baseline to post intervention, Mean (95% CI)	
		Baseline	Post intervention	Within-Group Change	Between-Group Difference in Change
Flexion					
AMC5 Group	12	60.75 (11.96)	63.50 (10.02)	3.40 (−2.56 to 9.36)	NA
MT Group	12	61.66 (11.11)	64.50 (11.18)	5.16 (−1.19 to 11.52)	NA
ST Group	12	60.66 (11.79)	61.00 (11.29)	1.59 (−6.74 to 9.91)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.70
ST Group vs MT Group	NA	NA	NA	NA	0.43
AMC5 Group vs ST Group	NA	NA	NA	NA	0.69
Extension					
AMC5 Group	12	73.83 (14.95)	78.33 (13.15)	6.98 (1.35–12.60)	NA
MT Group	12	68.83 (6.52)	75.83 (9.24)	10.44 (3.11–17.77)	NA
ST Group	12	70.80 (7.55)	68.00 (8.79)	−3.37 (−13.14 to 6.39)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.46
ST Group vs MT Group	NA	NA	NA	NA	0.08
AMC5 Group vs ST Group	NA	NA	NA	NA	0.04
Right Side Bending					
AMC5 Group	12	45.41 (12.10)	47.50 (8.82)	3.62 (−3.30 to 10.54)	NA
MT Group	12	43.16 (6.11)	46.50 (7.48)	7.65 (3.14–12.15)	NA
ST Group	12	45.00 (7.74)	48.00 (11.56)	5.98 (−1.67 to 13.62)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.34
ST Group vs MT Group	NA	NA	NA	NA	0.68
AMC5 Group vs ST Group	NA	NA	NA	NA	0.57
Left Side Bending					
AMC5 Group	12	44.16 (11.70)	46.50 (9.42)	6.90 (1.55–12.25)	NA
MT Group	12	44.16 (7.83)	48.33 (7.66)	10.05 (4.66–15.44)	NA
ST Group	12	45.83 (6.68)	50.00 (10.23)	5.85 (−0.56 to 12.27)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.39
ST Group vs MT Group	NA	NA	NA	NA	0.26
AMC5 Group vs ST Group	NA	NA	NA	NA	0.78
Right Rotation					
AMC5 Group	12	68.67 (13.62)	77.50 (10.48)	8.70 (3.60–13.78)	NA
MT Group	12	71.16 (10.17)	77.16 (6.05)	7.66 (1.40–13.92)	NA
ST Group	12	71.83 (7.30)	76.66 (7.30)	7.09 (1.42–12.74)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.78
ST Group vs MT Group	NA	NA	NA	NA	0.87
AMC5 Group vs ST Group	NA	NA	NA	NA	0.66
Left Rotation					
AMC5 Group	12	72.33 (12.38)	76.50 (12.56)	4.03 (1.91–6.14)	NA
MT Group	12	68.00 (8.35)	75.83 (6.17)	12.25 (6.51–17.98)	NA
ST Group	12	70.16 (6.17)	74.33 (10.12)	5.81 (−0.67 to 12.28)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.009*
ST Group vs MT Group	NA	NA	NA	NA	0.10*
AMC5 Group vs ST Group	NA	NA	NA	NA	0.32*

Pre and post values are expressed as the mean (degrees) (SD) of the three groups and all variables. Significant group interaction ($P < 0.01$). * p-values were drawn from non-parametrical tests.

Table 5
Summary cranio-cervical flexion test results.

Cranio-cervical Flexion Test	n	Mean (SD)		From baseline to post intervention, Mean (95% CI)	
		Baseline	Post intervention	Within-Group Change	Between-Group Difference in Change
Right SCM					
AMC5 Group	12	38.57 (19.11)	34.34 (21.79)	−7.30 (−33.64 to 19.04)	NA
MT Group	12	51.51 (23.92)	40.08 (20.88)	−19.20 (−48.99 to 10.59)	NA
ST Group	12	41.27 (25.88)	45.73 (30.93)	8.23 (−26.53 to 42.99)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.53
ST Group vs MT Group	NA	NA	NA	NA	0.17
AMC5 Group vs ST Group	NA	NA	NA	NA	0.41
Left SCM					
AMC5 Group	12	51.51 (23.50)	39.46 (21.50)	−16.90 (−44.04 to 10.23)	NA
MT Group	12	49.18 (19.98)	39.60 (26.05)	−12.75 (−54.37 to 28.86)	NA
ST Group	12	39.50 (26.52)	31.80 (22.66)	−3.70 (−43.44 to 36.04)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.85
ST Group vs MT Group	NA	NA	NA	NA	0.69
AMC5 Group vs ST Group	NA	NA	NA	NA	0.55

Pre and post values are expressed as the mean (mV) (SD) of the three groups and all variables.

6. Discussion

The findings of the present study suggest that MT manipulation immediately induces a decrease in the isometric strength peak in the cervical flexion as well as a meaningful increase of cervical spine extension and left rotation range of motion. These results suggests the importance of prior evaluation of vertebral dysfunction and suggests that a manipulation treatment based on a previous evaluation enhances the effects of an articular manipulation on the C5 compared to a sham technique. There are few studies comparing the effects of a treatment based on a previous standardized diagnostic screening to both an isolated manipulation of the C5 and a control group that used a previously studied sham technique [32,33].

Maximal voluntary isometric strength performance during cervical flexion provides information on the activity of the superficial flexor SCM and scalene muscles [34]. In the present study, the manipulation group results suggest more inhibition than the other groups. Although this result might at first seem questionable, it could be related to an activation of the deep flexor muscles and therefore, to a manipulation-induced decrease in the surface flexors' activation [24,25].

Immediate effects on extension and left rotation range of motion in the manipulation group were noticeably greater than those observed in the C5 and placebo groups. The extension ROM showed significant changes, and improvements in the C5 group were also significant compared to the placebo group. These results are within our expectations because the correction technique of C5 is focused on improving extension. However, the effect size of MT group in extension was considered large ($d = 1.07$), while the AMC5 group was considered moderate ($d = 0.32$).

There were movements that did not improve with the manipulation group, including right and left side bending, right rotation and flexion. Regarding both side bendings, the non-improvement may be due to the measures in the pre-treatment intervention, which showed 44.52° right side bending and 44.72° left side bending. These measurements are already similar to normal [35], and therefore, any gain would be minimal and insignificant. If symptomatic subjects had been studied, the results may have been similar to those of Martinez - Segura et al. [13]. These authors found mobility improvement after middle cervical spine manipulation in symptomatic patients, who showed significant improvements in flexion, extension, and both side bending ranges of movement but not in rotation. This last result could be explained by the absence of limitation in rotation movement of the subjects or by not having included the manipulation of the C1, C2, C7 and upper thoracic segments in the examination protocol.

In terms of right rotation and flexion, we suggest that the results of our study can be explained by the absence of treatment of the temporomandibular joint (TMJ). Von Piekartz et al. [36] emphasized the relationship between TMJ dysfunction and upper cervical spine dysfunctions in terms of decreased flexion and particularly rotation movements. On the other hand, Kayser et al. [16], showed the importance of segment C0, which we did not take into account, and this may have caused the mobility correction to be incomplete. However, we did take into account upper thoracic dysfunction because this area is considered to be the seat of dysfunction affecting cervical mobility [27,37].

In a study of symptomatic patients suffering from headaches, Whittingham et al. [38] reported improvements in both rotation and side bending. In that study, the authors did not consider flexion or extension because they related those to the weight of the head.

In the EMG at rest of the studied muscles, there was not significant change in any of the groups before and after the interventions and only an increase in the signal in the right brachial biceps after manipulation of the C5, this increase was not significant but had a large effect size (0.91). These data could be related to those reflected in a study by Dunning and Rushton that studied the effects of a manipulation technique at the C5-C6 level. The authors demonstrate an increased signal of RMS at rest in both biceps after applying an HVLA manipulation in asymptomatic patients [4]. These results can be explained because after spine manipulation, the alpha motor neuron can facilitate increased muscle activity at rest or decrease inhibition [39]. In addition, in that study, the C5 was manipulated to the right and the defect was in the ipsilateral biceps. This result was in agreement with Symons et al., who analyzed the response after mechanical manipulation using an activator device and found responses only at the ipsilateral level, in this case C2-C3, and they analyzed the splenius capitis and the upper trapezius in asymptomatic male subjects [40]. This is important because patients with chronic neck pain usually show an inhibition of the brachial biceps, and manipulation techniques on the C5 may minimize the inhibition, as noted by Suter et al. [41].

On the other hand, there were not significant changes in the SCM EMG signal during the cranio-cervical flexion test in three groups. This test is very important for its clinical application because the efficiency of cervical deep flexor muscles is related to cervical spine pathology [24,25]. Sterling et al. [42] referred to a significant effect after the application of an HVLA technique at the C5-C6 level, this phenomenon could explained by the reflex facilitation of the deep flexor of the neck which can prevent surface musculature from contracting during the test. However, we not achieved any significant results, this difference may be related to the fact that Sterling et al. used symptomatic subjects and our study used asymptomatic ones. Maybe it is possible that the manipulation of the segments in dysfunction improved the cervical proprioception more than an isolated manipulation would have, particularly because the origins of cervical deep muscles do not focus only on the C5-C6 level but further investigation is needed in symptomatic subjects.

More studies comparing the immediate effects of an isolated manipulation and a manipulation treatment based on a previous evaluation (MT) are needed, especially on symptomatic subjects. Also more research is needed to investigate the immediate effects of cervical HVLA manipulations.

However, our findings from the present study are limited but support the feasibility for a future definitive trial. The study was performed on asymptomatic subjects, and this type of subject will be less influenced by possible limitations in mobility or strength. The results may not be as significant as expected. Given the high cut-off we chose for our significance level ($p < 0.1$) and the number of statistical tests that were done, we cannot exclude that some of our results are solely due to random error. This study is exploratory and therefore will need replication before conclusions can be drawn about the true effects of manipulation.

The relatively small sample size of the present study is a further limitation which increases the risk of statistical type 2 errors, i.e. we may have failed to detect true changes that would have been statistically significant with a larger sample size. Having many different outcomes measures (about 10 in the present study) increases the risk of statistical type 1 errors, i.e. significant findings due to chance. However, adjusting for multiple outcomes – e.g. by Bonferroni correction – causes overly conservative P-values [43]. Thus, the results of the present study should be interpreted with limitations in mind and can therefore be considered exploratory in nature. Future large scale studies should confirm the present findings before solid recommendations can be provided. A future well-designed, adequately powered trial will require a larger sample size and long-term follow-up periods to confirm the effect of HVLA manipulations.

We cannot say with certainty that results observed after manipulation at the C5-C6 level are unique to this segment, and there are studies that suggest a low specificity of the technique in question [44]. In addition, the strength and speed of the impulse during the procedure is not reproducible, and these variations may alter the effects [39].

Fine wire EMG and transcranial magnetic stimulation (TMS) might make it easier to detect subtle changes in motor function within deeper muscles. TMS would make it possible to provide a controlled impulse from the motor region and the muscular response read by the fine wire would be more specific.

In summary, our results may lead us to suggest that there maybe a tendency toward a decrease in the isometric strength peak in the cervical flexion of the MT group compared to the sham group. Additionally, a slight tendency toward an increase in the EMG signal can be observed while the right brachial biceps is at rest in the AMC5 group compared to the sham group. Regarding mobility, we may suggest that the MT group achieved better effects compared to the sham group and AMC5 group in extension movement. In terms of left rotation movement, the MT group also improved more than the sham and C5 groups, whereas the changes in SCM signal during the cranio-cervical flexion test was not significance in all three groups. This preliminary and exploratory research may suggest that the efficacy of a manipulation treatment based on a previous evaluation enhances the effects of an articular manipulation on the C5 compared to a sham technique.

Conflict of interest

None declared.

Ethical statement

The trial protocol was reviewed by the Independent Ethics Committee of the medical faculty of the Public University of Navarra and approved on February 2015 (approval number 2/2015). The privacy rights of human subjects were observed.

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