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The Efficacy of Neck and Temporomandibular Joint (TMJ) Manual Therapy in Comparison With a Multimodal Approach in the Patients with TMJ Dysfunction: A Blinded Randomized Controlled Trial

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Abstract

Background: Temporomandibular joint disorders (TMJDs) are the main musculoskeletal cause of orofacial pain. This study aimed to assess the efficacy of manual therapy and routine treatment compared with routine treatment on pain, maximum mouth opening (MMO), and cervical range of motion (ROM) in patients with the temporomandibular joint disorder (TMJD).

Methods: This study was performed at the biomechanics laboratory of the physiotherapy department of Iran University of Medical Sciences, Tehran, Iran. A total of 30 patients with TMJD were randomized into 2 groups: an intervention group (manual therapy plus routine treatment) and a control group (conventional treatment). Treatment included 10 sessions. The primary outcome was pain intensity and the secondary outcomes were MMO, and range of cervical flexion and extension. The outcomes were measured at the baseline, at the end of the treatment, and after a 4-week follow-up period. The repeated measures analysis of variance was used to assess group × time interaction, and the Bonferroni adjustment was used for between-group comparisons. The effects size of Cohen's d was used to determine the magnitude of between-group differences.

Results: The results showed that there were significant group × time interactions for pain, MMO, and the cervical flexion ROM ($P<0.001$). In comparion with the baseline, the intervention group showed significant improvements in jaw pain, MMO, and cervical flexion ROM ($P<0.001$), while in the control group, compared with the baseline, only pain and MMO significantly improved ($P<0.05$). Results of between-group comparisons revealed that there were significant and clinical differences between the 2 groups after treatment, and the intervention group had lower jaw pain, more MMO, and cervical flexion than the control group ($P<0.001$). In addition, the efficacy of manual therapy based on the Cohen's d was large for the outcomes of pain, MMO, and cervical flexion.

Conclusion: The findings showed that adding manual therapy of the upper cervical spine and TMJ to the routine treatment could be an effective intervention for patients with TMD.

Keywords: Temporomandibular Joint, Temporomandibular Disorder, Manual Therapy

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Introduction

Temporomandibular joint disorders (TMJDs) are the most common disorders developing pain, and dysfunction

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↑What is "already known" in this topic:
Because of the biomechanical and neuroanatomical relationship between the cervical region and TMJ, in the literature, these regions are considered as a functional unit that any pain or disorder in one region could affect another region.

→What this article adds:
The results showed that manual therapy of the upper cervical spine combined with TMJ could be an effective intervention in relieving pain and increasing month opening and cervical flexion in patients with TMD. In addition, in comparison with routine treatment, improvement of outcomes in the manual therapy group was clinically significant.

in the orofacial region (1-3), and are related to the symptoms in the regions such as the head, ears, and the cervical spine region. They are classified into 3 categories, including myogenous, arthrogenous, and mixed (4). It is estimated that about 25% of the total population suffer from signs and symptoms related to TMJDs (5). TMJDs are generally characterized by pain, clicking sounds, and altered mandibular movements (6, 7).

The etiology of TMJDs is still unclear because they are complex disorders that interact with many factors. Several studies have suggested risk factors that are associated with TMJDs, including physical factors (trauma, muscles spasms, chronic malocclusion, and bruxism), biochemical factors (vitamin deficiency), and psychological factors (stress, anxiety, and depression) (8-11). In addition, it has been suggested that TMJDs are associated with cervical dysfunctions (11, 12). In studies, the cervical spine and TMJ have been considered as a complex interrelated system, and a functional relationship and a sensory-motor interaction have been explained between the 2 regions via the trigeminocervical complex (13, 14), which allows to transfer nociceptive information between TMJ and cervical spine (15).

Different treatments for TMJDs have been reported in the literature and performed in clinical settings. They include physical therapy, such as physical modalities, therapeutic exercise, dry needling, and manual therapy, medication, oral splints, acupuncture, cognitive-behavioral therapy, and surgery (1, 16-18).

Manual therapy is one of the most important interventions that are commonly used for treating musculoskeletal disorders. Manual therapy techniques include mobilization, soft tissue release, and manipulation (1, 19). Generally, the goals of manual therapy are pain reduction, decreasing tissue guarding, and muscle relaxation, circulation improvement, and increasing range of motion (ROM) (19). Several studies have investigated the efficacy of manual therapy alone or in combination with other interventions in patients with TMD (6, 16, 20-22). Herrera-Valencia et al (16) found a significant improvement in pain intensity and a significant increase for maximum mouth opening (MMO) after manual therapy compared with the other treatments in patients with TMDJs. They reported that manual therapy had a medium-term efficacy on pain intensity and a short-term effect on MMO. Furthermore, with regard to the mentioned relationship between TMD and cervical dysfunction, there has been an increasing interest in using the combination of the manual therapy of both regions for treating TMDs. The results of a systematic review (1) showed that compared with the home exercises and the cervical spine treatment alone, a combination of the manual therapy of orofacial and cervical regions has more effectiveness in pain reduction in the patients with TMD. However, they concluded that the included studies had low methodological quality (1).

There is evidence about the effectiveness of manual therapy of cervical region and orofacial in isolation and combination in the patients with TMDs (11, 15, 16, 21-23), however, because of the inconsistencies in the methods, reaching a definitive conclusion is difficult. One of the reasons or these inconsistencies could be attributed to using different manual therapy techniques in studies.

Thus, the purpose of the present study was to investigate and compare the effectiveness of the routine conservative treatment plus the manual therapy of the TMJ and upper cervical spine, including soft tissue release technique and mobilization, compared with the routine conservative treatment alone on the jaw pain intensity, MMO, and range of cervical flexion and extension in patients with TMJDs. Also, this study aimed to determine whether adding a manual therapy intervention of the cervical spine and temporomandibular joint to a conventional treatment affects the outcomes of patients with TMJDs.

Methods

Participants

This study was a superiority parallel single-blinded randomized controlled trial that was performed from November 2019 to February 2021 at the biomechanics laboratory of the physiotherapy department of Iran University of Medical Sciences. The study was written based on the Consolidated Standards of Reporting Trials (CONSORT) statement and included the CONSORT checklist (24). A total of 30 patients with TMJDs were recruited to participate in this study. The eligible patients were selected from the patients with TMJDs who attended the orofacial pain clinic at the school of dentistry of Tehran University of Medical Sciences, and at the clinic of the maxillofacial surgery of Shariati hospital. This study was approved by the Ethics Committee of Iran University of Medical Sciences and was registered in the Iranian Registry of Clinical Trials Center.

A standardized examination based on the Diagnostic Criteria for TMJD (DC/TMD) (25) was conducted to diagnosis TMJD before a decision was made to include eligible patients. The standard TMJD examination including assessment of the joint pain and masticatory muscles, presence of the crepitation, and asymmetric motions between the right and left TMJ.

The patients were included in this study if they had unilateral or bilateral TMJDs according to the DC/TMD, and maximum pain intensity based on the visual analog scale (VAS) more than 3 for at least 3 months before the study.

Exclusion criteria were as follows: age>50 years; a traumatic injury causing the symptoms in the TMJ and the orofacial region during the last 3 months; a history of the orofacial surgery during the last 6 months; and any neurological and systemic diseases, such as rheumatoid arthritis, Parkinson, Multiple Sclerosis, positional vertigo, pregnancy, and severe deformity in the jaw or face region.

In addition to the mentioned criteria, before starting the manual therapy of cervical spine, the special tests of cervical ligaments, including the sharp-purser test and the lateral-flexion and rotation stress test, were performed by the examiner.

For the sharp-purser test (26), the patients were asked to hold the neck in a semi-flexion posture while sitting. The examiner placed one hand's palm on the patient's forehead and the other hand's index finger on the axis' spinous process. A slipping motion of the head posteriorly in relation

to the axis indicates atlantoaxial instability when the head is pushed backward.

For the lateral-flexion and rotation stress test (27), the patients were asked to lay in the supine position. Then, the head and atlas were side bent around the atlantoaxial joint's coronal axis. For inhibiting ipsilateral rotation of the axis, the therapist gripped and stabilized the spinous process of the axis. After that the end feel and the amount of motion were assessed. If the alar ligament was intact, little to no side-bending could have occurred and the end feel would be capsular. This test was repeated with rotation of the head and atlas on the axis and the end feel was assessed again.

The patients were excluded from the study if they had a positive sign for any one of the above tests.

One TMJ of each participant was included in this study. If one TMJ of a participant met the inclusion criteria, that side was assessed and treated. If there was a bilateral involvement of TMJ in a participant, both sides were treated but the side with more disability at the baseline was considered for further analyses.

Written consent was obtained from each participant after they were informed about the study procedure.

Randomization and Blinding

Those patients who met the study inclusion criteria were allocated randomly into 2 groups: the control group (routine conservative treatment group; n = 15) and the intervention group (routine conservative treatment plus the manual therapy of the TMJ and upper cervical spine; n = 15). A block balanced randomization (1:1) with a block size of 4 was used for random allocation. A random allocation was performed using the website of www.randomization.com. To conceal the sequence of the random allocation, numbered closed envelopes containing A or B groups were used and the envelopes were given to the clinic secretary. Group A received the routine conservative treatment plus the manual therapy of the TMJ and cervical spine, and group B received the routine conservative treatment alone.

In the present study, participants and those who assessed the outcomes were blinded while the therapist was not blinded.

Sample Size

The sample size was calculated using the G power software (Version 3.1.9.2) for primary outcome (pain) using the analysis of variance (ANOVA) (repeated measures, between factors), the minimal clinically important difference (MCID) of 2 (28, 29), pain of the control group (mean, 5.8; SD, 2.2), pain of the intervention group (mean, 3.8; SD, 2.4) (6), the effect size of 0.43, with a significant level of .05, the power of 80%, 2 groups, 3 measurements, and a correlation of 0.4 between repeated measurements, a total of 15 patients with TMD were estimated for each group.

Outcome Measures

The primary outcome was pain intensity, and the secondary outcomes included cervical flexion ROM, cervical extension ROM, and range of MMO. The assessments were performed at the baseline, after the end of the treatment, and after a 4-week follow-up period.

Primary Outcome

Pain Intensity. The intensity of the jaw pain was recorded according to the VAS. The participants were asked to determine the jaw pain intensity using the VAS from 0 (no pain) to 10 (the worst level of pain). The validity and reliability of the VAS for grading pain intensity were demonstrated in previous studies (30, 31).

Secondary Outcomes

MMO was measured with a calibrated caliper with 1 mm accuracy. Each participant sat on a comfortable back-supported chair with their heads supported in a neutral position. The patients were then instructed to open their mouths until they felt pain. The gap between the upper and lower central incisor teeth was then measured (23) (Fig. 1A).

The flexion and extension ROM of the cervical spine were measured by a goniometer (32). The fixed arm of the goniometer was established parallel to the horizontal line and its movable arm moved along a card fixed between the participant’s teeth in a clenching position (bite plane).

To measure the cervical flexion, participants were asked to look down and bring their chin to the manubrium of the sternum while the therapist’s index finger was monitoring the spinous process of the first thoracic vertebra (T1) to prevent the movement of the thoracic spine. For the cervical extension, participants were instructed to look at the ceiling until the examiner felt a movement in the first thoracic vertebra (Fig. 1B).

Treatment

Ten sessions of treatment for each group were performed during 8 weeks by a physical therapist (Kh. R., first author). Patients received the first 4 sessions in 2 weeks. During the treatment period, participants were asked not to take any nonsteroidal anti-inflammatory drugs or muscle relaxants.

Routine Conservative Treatment

All patients received the routine conservative treatment, including transcutaneous electrical nerve stimulation (TENS) (Stimulator733X, Novin Co), ultrasound (Ultrasound 215p, Novin Co), and a gentle massage for 25 minutes in each session.

For electrotherapy, the electrodes of the multistimulator apparatus were placed between the TMJ and the coronoid process. The intensity of the TENS was determined based on the patients' sensitivity threshold and the total time of stimulation was 15 minutes (33, 34).

Patients also received the ultrasound (1 MHz, 0.8 to 1.5 W/cm2 continuous outputs) for 5 minutes on the painful TMJ (33, 34).

Fig. 1. A) Position of patient for measuring maximal mouth opening. B) Position of patient for measuring flexion and extension ROM of the cervical spine

A gentle massage began using the second and third fingers in a circular direction over the masseter muscles for 5 minutes in each session (35).

Manual Therapy of the TMJ and Cervical Spine

The manual therapy techniques were performed by the same physical therapist who had 2 years of experience in this field (Kh. R., first author). After checking cervical spine ligaments, manual therapy of TMJ and cervical spine was performed.

For manual therapy of the TMJ (36), patients were positioned in side-lying and partially opened their mouth. In the current study, TMJ mobilization was performed in both medial and anterior-posterior directions. Before the manual therapy, patients were asked to open and close the mouth 10 times. The palm of the therapist's hand was placed over the thumb digit of another hand and the mandibular condyle was mobilized medially. Another mobilization direction was anterior-posterior and applied through the auditory canal. The frequency of mobilization was 1 oscillation per 2 sec. Mobilization in each direction was applied in 3 series of 2 min, with 30 sec of rest in between, resulting in a total of 7 min.

The cervical spine manual therapy included the cervical soft tissue release technique and cervical mobilization (1, 19).

For cervical soft tissue release (37), participants were positioned supine with their knees stretched and the therapist sat on a stool and placed his supinated forearms and extended elbows on the table. The participants were instructed to raise their heads from the treatment table. The tips of the first 3 digits of the therapist were inserted into the soft tissue under the arc of the atlas. The fingers were stabilized in a flexed position around 45° at the metatarsal phalangeal joints and proximal interphalangeal joints, the therapist was firmly pressed his finger pads against the inferior aspect of the atlas. This technique was repeated 3 times in each session and lasted around 3 minutes.

For upper cervical mobilization (14), patients were placed in the supine position with the cervical spine in a neutral position. The therapist stabilized the occipital region and with the other hand applied a posteriorly directed force on the frontal region of the patient (anterior to posterior force). Mobilization was performed at a slow rate of

approximately 1 oscillation every 2 s, which was monitored by the physical therapist. Mobilization was performed in 3 sets of 2 min, with 30 sec rest in between, for a total of 7 min. The intensity of the technique was chosen by the therapist according to tissue resistance.

Statistical Analysis

SPSS software (Statistical Package for Social Sciences software, Version 19) was used to perform the statistical analyses. The distribution of data was evaluated using the Shapiro-Wilk test, skewness, kurtosis, and probability-probability plot (PP plot). Based on these tests, the primary and secondary outcomes during repeated measurements had a normal distribution.

A repeated measures analysis of variance (3 × 2) for each outcome measure, with the group as the independent factor (2 levels) and the time of measurements as the dependent variable (3 levels: at baseline, after 8 weeks of intervention, and after the follow-up period) was separately used to compare the 2 groups in repeated measurements and then post hoc comparisons of between groups with Bonferroni adjustments were performed.

Within-group analysis with a Bonferroni post hoc comparison test for each outcome measure was performed using the repeated measures ANOVA. The effects size of Cohen's d with 95% confidence interval (CI) was calculated for all between-group comparisons. The regions of the effect size of Cohen's d were interpreted as follows: the trivial region (inconsiderable efficacy) from 0 to 0.19, the region with small efficacy from 0.2 to 0.49, the region with medium efficacy from 0.5 to 0.79, and the region with large efficacy ≥0.8 (38). The level of significance was set at .05.

Results

A total of 135 patients were screened for eligibility criteria. After screening, 90 patients were excluded: 59 were excluded because they did not meet the inclusion criteria, and 31 declined to participate because of fear of COVID-19, lack of time, and other reasons. Finally, 45 patients with TMJD were randomly allocated into 2 groups. In the intervention group, 8 patients did not complete the treatment period and in the control group, 7 patients discontinued the treatment. The overall flow of the participants' enrollment for the 2 groups is shown in Figure 2.

The demographic characteristics of both groups are presented in Table 1. Table 2 provides an overview of demographic characteristics of the patients who discontinued the treatment. There were no significant differences in jaw pain at the baseline (p=0.175), sex (p= 0.750), and affected side (p=0.890) between those patients completing the study and those who did not complete the study.

27% of the intervention group and 33% of the control group had bilateral involvement of TMJ (Table 1). The results of the independent sample t-test showed a similarity between the 2 groups at baseline variables (24).

Mean (SD) of the outcomes during repeated measurements are shown in Table 3. The trend of changes of the primary and secondary outcomes in both groups during repeated measurements is presented in Figure 3.

The results, as shown in Table 4, indicate that there were significant group × time interactions for the jaw pain intensity (p<0.001), MMO (p<0.001), and the cervical flexion ROM (p<0.001), while the interaction of group ×

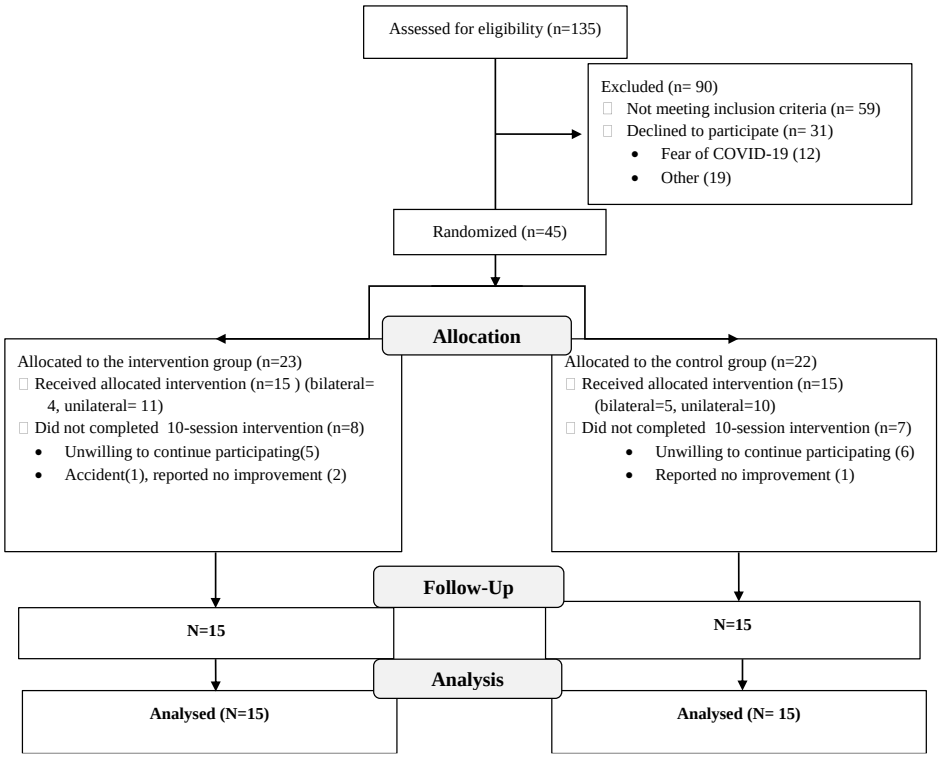

Fig. 2. Flow diagram of the recruitment of the patients throughout the course of the study

Table 1. The demographic characteristics of both groups

Baseline variables		Control group (n=15)	Intervention group (n=15)
		Mean (SD) / number (%)	Mean(SD) / number (%)
Age(years)		28.33 (5.43)	27.65(4.04)
Height (cm)		165.53 (6.54)	164.62 (4.32)
Weight (kg)		68.20 (12.02)	66.70 (11.90)
Sex	Male	6 (40%)	7 (46.7%)
	Female	9 (60%)	8 (53.3%)
Affected side	Unilateral	10 (67%)	11 (73%)
	Bilateral	5 (33%)	4 (27%)

Control group received routine conservative treatment group, Intervention group received routine conservative treatment group plus manual therapy

Table 2. Lost to follow-up

Variables		Control group (n=7)	Intervention group (n=8)	Total(n=15)
		Mean (SD) /number (%)	Mean(SD) / number (%)	Mean(SD) / number (%)
Jaw pain		6.14 (1.06)	5.75 (1)	5.93 (1.03)
Sex	Male	3 (42.9%)	3 (37.5%)	6 (40%)
	Female	4 (57.1%)	5 (62.5%)	9 (60%)
Affected side	Unilateral	5 (71.4%)	7 (87.5%)	12 (80%)
	Bilateral	2 (28.6%)	1 (12.5%)	3 (20%)

Control group received routine conservative treatment group, Intervention group received routine conservative treatment group plus manual therapy

Table 3. Mean (SD) of the primary and secondary outcomes

Outcome measures	Control group (n=15) Mean (SD)			Intervention group (n=15) Mean (SD)		
	Baseline	After treatment	After follow-up	Baseline	After treatment	After follow-up
Jaw pain intensity (VAS)	5.40 (1.06)	4.20 (0.78)	4.13 (0.91)	5.60 (0.91)	1.67 (0.62)	2.40 (0.74)
MMO (mm)	47.33 (5.63)	48.27 (3.19)	42.53 (2.53)	46.27 (3.81)	53.20 (2.96)	53.33 (2.41)
Cervical flexion (degree)	40.27 (5.32)	44.07 (3.55)	41.93 (3.49)	38.73 (4.17)	49.07 (2.49)	50.13 (2.07)
Cervical extension (degree)	76.80 (2.70)	77.40 (2.20)	76.93 (1.83)	75.47 (2.75)	76.20 (2.76)	75.73 (2.22)

Control group received routine conservative treatment group, Intervention group received routine conservative treatment group plus manual therapy
mm= millimeter, SD= standard deviation, VAS=visual analog scale

time for the cervical extension ROM was not significant (p=0.970).

The between-group comparisons showed that in comparison with the control group, the patients in the intervention group exprienced a significant pain reduction and a significant increase in MMO and cervical flexion ROM after the end of the treatment and after the follow-up period (p<0.001) (Table 4).

In addition to the statistical significance, from the data in Table 4, it is apparent according to the effect size of Cohen's d that there was a high efficacy for the manual therapy group in the primary outcome (effect size > 0.8). The effect sizes of jaw pain intensity with 95% CI after the end of the treatment and after the follow-up period were between -4.8 to -2.42 and between -2.7 to 1.17, respectively. Also, a high efficacy was observed for the secondary outcomes, including MMO and cervical flexion ROM after the treatment and after the follow-up period (effect size >0.8).

while no significant difference was observed between the 2 groups in the cervical extension ROM after the treatment and after the follow-up period (p>0.050**)**, adding the manual therapy intervention of the cervical spine and TMJ to rutine conservative treatment showed an efficacy from small to medium for cervical extension ROM (Table 4).

The results obtained from the within-group analyses of primary and secondary outcomes are summarized in Table 5.

Within-control group analysis results showed that compared with the baseline, after the end of the treatment and after the follow-up, there was a significant reduction for jaw pain intensity, in addition, the difference between the baseline and after the follow-up period for MMO showed a statistical significance (p=0.022) (Table 5).

Results of within-group analysis for the intervention group showed that after the end of the treatment and after the follow-up period, there were significant differences in pain intensity, MMO, and cervical flexion compared with baseline measurements (p<0.001**)**, the jaw pain intensity significantly decreased, and MMO and cervical flexion significantly increased. No significant increase in cervical extension ROM was detected between the repeated measurements in the intervention group.

Discussion

This study aimed to investigate the effectiveness of manual therapy of TMJ and upper cervical spine on jaw pain intensity, MMO, and cervical ROMs in patients with TMJDs.

In our study, a multimodal approach, including routine conservative treatment for the control group and a combination of manual therapy and routine treatment for the intervention group was used.

The results showed that after 10 sessions of treatment and after the follow-up period, the difference of pain and MMO between the 2 groups was significant, and the manual therapy group experienced more improvement in pain and MMO than the control group. In addition, based on the effect size of Cohen's d, after the intervention and after the follow-up period, there was a large efficacy (d > 0.8) for pain and MMO favoring the manual therapy.

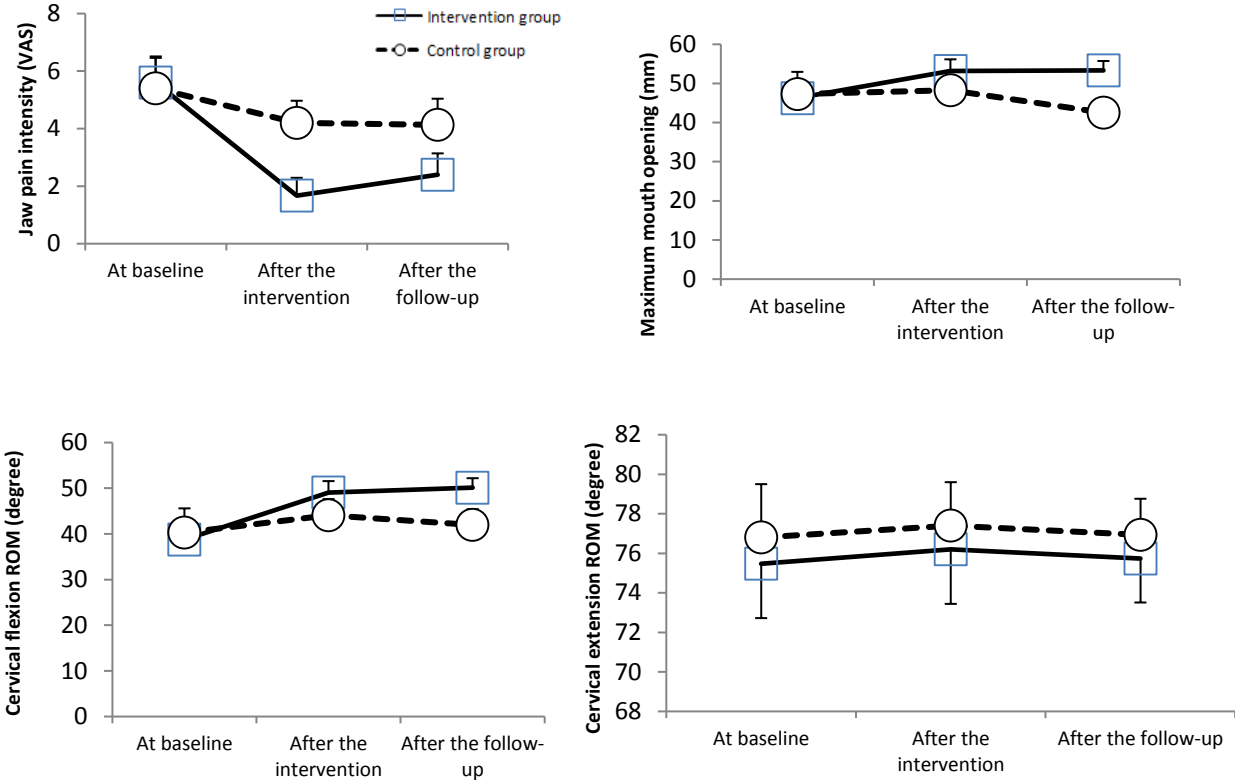

Fig. 3. The changes of the primary and secondary outcomes in both treatment groups during repeated measurements, mm= millimeter, VAS=Visual analog scale

Table 4. The results of the two-way analysis of variance, pairwise comparisons with Bonferroni correction, effect sizes of mean difference, and Cohen's d with 95% CI

Outcome measures	Interaction time × group		Between-group comparisons pvalue *			Mean difference (95%CI) (Intervention group – Control group)			Cohen's d (95%CI)		
	pvalue	F	T1	T2	T3	T1	T2	T3	T1	T2	T3
Jaw pain intensity (VAS)	<0.001	21	0.583	<0.001	<0.001	0.2 (-0.54 to 0.94)	-2.53 (-3.06-2)	-1.73 (-2.35 to -1.11)	0.2 (-0.52 to 0.92)	-3.63 (-4.8 to -2.42)	-2.08 (-2.97 to -1.17)
MMO (mm)	<0.001	27	0.548	<0.001	<0.001	-1.07 (-4.67 to 2.53)	4.93 (2.63-7.23)	10.8 (8.95 to 12.64)	-0.22 (-0.94 to 0.5)	1.60 (0.76 to 2.42)	4.37(3.01 to 5.70)
Cervical flexion (degree)	<0.001	17	0.387	<0.001	<0.001	-1.53 (-5.10 to 2.04)	5 (2.70 to 7.3)	8.2 (6.05 to 10.35)	-0.32 (-1.04 to 0.40)	1.62 (0.78 to 2.65)	2.86 (1.81 to 3.88)
Cervical extension (degree)	0.970	0.03	0.191	0.198	0.117	1.33 (-0.70 to 3.37)	1.2 (-0.67 to 3.06)	-1.2 (- 0.32 to 2.72)	0.49 (-0.24 to 1.21)	0. 48 (-0.24 to 1.20)	0.58(-0.15 to 1.32)

Control group received routine conservative treatment group, Intervention group received routine conservative treatment group plus manual therapy
CI= confidence interval, mm=millimeter, VAS=visual analog scale, T1=at baseline, T2= end of the treatment, T3=after the follow-up period
* Adjustment for multiple comparisons was performed using the Bonferroni test

These results are in agreement with previous studies indicating that manual therapy of the cervical region can be an effective intervention in TMJD patients. La touché et al (15) in a single-group before-after study found that mobilization and exercises directed at the cervical spine had a considerable effect on pain improvement and increasing pressure pain threshold, and MMO in patients with TMDJ. In the study of Espí-López et al (11) it was reported that the best results in improving outcomes in patients with TMDJ were obtained with the combination of splint therapy and manual therapy, which included TMJ and upper cervical mobilization, and myofascial release techniques on masseter, temporal, and sternocleidomastoid muscles. Garrigós-Pedrón et al (39) showed the superiority of manual therapy of the cervical and orofacial region in comparison with cervical manual therapy in pain reduction and increasing MMO of patients with TMJD.

In other studies, it has been suggested that myofascial release techniques on the suboccipital, masseter, and pterygoid muscles produced significant pain reduction and function improvement in patients with TMJD (22, 40, 41).

In our study, although in the routine treatment group, pain intensity decreased after the end of the treatment period and MMO increased after the follow-up period, it was demonstrated that manual therapy of upper cervical combined with TMJ was a more effective treatment

Table 5. The results of Within-group analysis with Bonferroni post hoc test

Outcome measures	Main effect of time Pvalue (F)		control group (n=15) Mean difference (95%CI), pvalue*			Intervention group (n=15) Mean difference (95%CI), pvalue*		
	Group		T1 vs. T2	T1 vs. T3	T2 vs. T3	T1vs. T2	T1 vs. T3	T2 vs. T3
	Control group	Intervention group						
Jaw pain intensity (VAS)	0.001 (8.86)	<0.0001 (124)	1.20 (0.35 to 2.05) 0.005	1.26 (0.13 to 2.40) 0.028	0.7 (-.066 to 0.8) 0.999	3.93 (3.13 to 4.55) <0.0001	3.20 (2.31 to 4.08) <0.0001	-0.73 (-1.35 to-11) 0.019
MMO (mm)	<0.0001 (12.84)	<0.0001 (29.09)	-0.93 (-3.69 to 1.82) 0.999	4.80 (0.63 to 8.9) 0.022	5.73 (2.97 to 8.5) <0.0001	-6.93 (-10.1 to -3.77) <0.0001	-7.07 (-10.45 to -3.69) <0.0001	-0.13 (-1.99 to 1.72) 0.999
Cervical flexion ROM (degree)	0.013 (5.07)	<0.0001 (60)	-3.80 (-7.94 to 0.34) 0.077	-1.67 (-4.67 to 1.34) 0.463	2.13 (-0.22 to 4.5) 0.082	-10.3 (-13.8 to -6.8) <0.0001	-11.40 (-15.13 to -7.67) <0.0001	-1.07 (-2.73 to 0.6) 0.311
Cervical extension ROM (degree)	0.418 (0.89)	0.211 (1.64)	-0.6 (-1.8 to 0.6) 0.566	-0.13 (-1.7 to 1.5) 0.999	0.47 (-0.5 to 1.42) 0.611	-0.73 (-2.14 to 0.68) 0.542	-0.27 (-1.16 to 0.63) 0.999	0.46 (-0.48 to 1.41) 0.611

Control group received routine conservative treatment group, Intervention group received routine conservative treatment group plus manual therapy
CI= confidence interval, mm=millimeter, mm= millimeter, T1=at baseline, T2= end of the treatment, T3=after the follow-up period, VAS=visual analog scale
* Adjustment for multiple comparisons was performed using the Bonferroni test

than routine treatment.

In addition to the large efficacy of manual therapy, based on the minimal clinically important difference threshold, the differences of pain and MMO between the 2 groups were clinically significant. The MCID is characterized as the smallest change in a treatment outcome that shows a clinical significance (42). Generally in chronic pain conditions, an MCID range of 1.5 to 3.2 has been determined for a clinical improvement (29, 43-45), while in the study of Calixtre et al (42), they reported that in patients with TMJD a change of 1.2 on the maximum pain, a change of 0.9 on the minimum pain, and a change of 1.9 on the current pain could be considered as a clinical difference. These values are consistent with the data in our study. According to the MCID range of 1.5 to 3.2 for chronic pain and MCID value of 1.2 for maximum pain, the mean difference (MD) of pain intensity after the end of the treatment period (MD, -2.53), and after the follow-up (MD, -1.73) showed a clinical significance favoring the manual therapy intervention. In addition, considering an MCID range from 3 to 9 (42, 46), after the treatment (MD, 4.3) and after the follow-up period (MD, 10.8), the manual therapy group experienced a clinical improvement for MMO.

There are several possible explanations for our findings. The efficacy of manual therapy techniques in TMJDs can be explained by the fact that these interventions through decreasing pain and increasing circulation can improve the mobility and function of tissue and muscles (1, 21). Furthermore, previous studies have argued that "pain interference theory" may be a possible explanation for inhibiting voluntary muscle function, and when pain sensation is decreased, normal muscle function can be restored (47). In our study, following pain improvement, the MMO of the manual therapy group significantly increased, and based on the "pain interference theory" it may partly be attributed to the relationship between pain reduction and function improvement. In addition, because of the biomechanical and neuroanatomical relationship between the cervical region and TMJ, in the literature, these regions are considered as a functional unit that any pain or disorder in one region could affect another region (3). Thus, consistent with data obtained from previous studies (6, 14, 21, 39), in our study, adding manual therapy of cervical spine to TMJ manual therapy had positive effects in patients with TMD.

Another important finding in the present study was that the cervical flexion significantly increased in the manual therapy group compared with the control group. There were no previous studies that specifically assessed the cervical ROMs in patients with TMJD after treatment.

For cervical flexion ROM, the results of the Cohen's d showed that manual therapy was a highly effective treatment in patients with TMJD. Although MMO is closely related to the upper cervical extension and the compensatory upper cervical extension can increase mouth opening, in the present study, MMO significantly improved in the intervention group, but there was no considerable difference among the 2 groups for cervical extension ROM, and the effect size showed a small efficacy for manual therapy intervention.

There were some limitations for our study. One limitation of the study is that the results cannot be attributed to a special type of TMJDs. Another limitation is the short follow-up period, which is typical due to time constraints. In addition, all findings were based on the per-protocol analysis, and intention to treat analysis (imputation) was not performed.

Conclusion

The present study concluded that adding manual therapy of the upper cervical spine and TMJ to the routine conservative treatment could be an effective intervention in relieving pain and increasing MMO and cervical flexion in patients with TMJDs. The triad of results based on the per-protocol analysis, including statistical significance, high efficacy according to the Cohen's d effect size, and the existence of clinical significance (MD ≥MCID) confirmed a conclusive finding for the efficacy of manual therapy combined with routine treatment for jaw pain intensity and MMO. In addition, the results showed that manual therapy had an effective role in increasing cervical flexion ROM, while no significant differences were found between the 2 groups for cervical extension ROM.

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Ethical Approval

This randomized controlled trial was approved by the Ethics Committee of Iran University of Medical Sciences (Ethical No. IR.IUMS.REC.1397.1054).

Conflict of Interests

The authors declare that they have no competing interests.

References

1. Armijo-Olivo S, Pitance L, Singh V, Neto F, Thie N, Michelotti A. Effectiveness of manual therapy and therapeutic exercise for temporomandibular disorders: systematic review and meta-analysis. Phys Ther. 2016;96(1):9-25.
2. de Resende CMBM, de Oliveira Medeiros FGL, de Figueiredo Rêgo CR, Bispo AdSL, Barbosa GAS, de Almeida EO. Short-term effectiveness of conservative therapies in pain, quality of life, and sleep in patients with temporomandibular disorders: A randomized clinical trial. CRANIO®. 2019.
3. Kang JH. Effects on migraine, neck pain, and head and neck posture, of temporomandibular disorder treatment: Study of a retrospective cohort. Arch Oral Biol. 2020;114:104718.
4. Al-Moraissi E, Farea R, Qasem K, Al-Wadeai M, Al-Sabahi M, Al-Iryani G. Effectiveness of occlusal splint therapy in the management of temporomandibular disorders: network meta-analysis of randomized controlled trials. Int J Oral Maxillofa Surg. 2020;49(8):1042-56.
5. Perez CV, de Leeuw R, Okeson JP, Carlson CR, Li HF, Bush HM, et al. The incidence and prevalence of temporomandibular disorders and posterior open bite in patients receiving mandibular advancement device therapy for obstructive sleep apnea. Sleep Breath. 2013;17(1):323-32.
6. Calixtre LB, Oliveira AB, de Sena Rosa LR, Armijo-Olivo S, Visscher CM, Alburquerque-Sendín F. Effectiveness of mobilisation of the upper cervical region and craniocervical flexor training on orofacial pain, mandibular function and headache in women with TMD. A randomised, controlled trial. J Oral Rehabil. 2019;46(2):109-19.
7. Paço M, Peleteiro B, Duarte J, Pinho T. The effectiveness of physiotherapy in the management of temporomandibular disorders: a systematic review and meta-analysis. J Oral Facial Pain Headache. 2016;30(3):210-20.
8. Levy BM, Gorlin RJ. The temporomandibular joint in vitamin C deficiency. J Den Res. 1953;32(5):622-5.
9. Dijkgraaf LC, de Bont LG, Boering G, Liem RS. Normal cartilage structure, biochemistry, and metabolism: a review of the literature. J Oral Maxillofa Surg. 1995;53(8):924-9.
10. Chaves TC, Turci AM, Pinheiro CF, Sousa LM, Grossi DB. Static body postural misalignment in individuals with temporomandibular disorders: a systematic review. Braz J Phys Ther. 2014;18(6):481-501.
11. Espí-López GV, Arnal-Gómez A, Cuerda del Pino A, Benavent-Corai J, Serra-Añó P, Inglés M. Effect of manual therapy and splint therapy in people with temporomandibular disorders: a preliminary study. J Clin Med. 2020;9(8):2411.
12. Armijo-Olivo S, Silvestre RA, Fuentes JP, da Costa BR, Major PW, Warren S, et al. Patients with temporomandibular disorders have increased fatigability of the cervical extensor muscles. Clin J Pain. 2012;28(1):55-64.
13. Goadsby PJ, Hoskin KL. The distribution of trigeminovascular afferents in the nonhuman primate brain Macaca nemestrina: a c-fos immunocytochemical study. J Anat. 1997;190(3):367-75.
14. La Touche R, París-Alemany A, Mannheimer JS, Angulo-Díaz-Parreño S, Bishop MD, Lopéz-Valverde-Centeno A, et al. Does mobilization of the upper cervical spine affect pain sensitivity and autonomic nervous system function in patients with cervico-craniofacial pain?: a randomized-controlled trial. Clin J Pain. 2013;29(3):205-15.
15. La Touche R, Fernández-de-Las-Peñas C, Fernández-Carnero J, Escalante K, Angulo-Díaz-Parreño S, Paris-Alemany A, et al. The effects of manual therapy and exercise directed at the cervical spine on pain and pressure pain sensitivity in patients with myofascial temporomandibular disorders. J Oral Rehabil. 2009;36(9):644-52.
16. Herrera-Valencia A, Ruiz-Muñoz M, Martin-Martin J, Cuesta-Vargas A, González-Sánchez M. Efficacy of Manual Therapy in Temporomandibular Joint Disorders and Its Medium-and Long-Term Effects on Pain and Maximum Mouth Opening: A Systematic Review and Meta-Analysis. J Clin Med. 2020;9(11):3404.
17. de Resende C, de Oliveira Medeiros FGL, de Figueiredo Rêgo CR, Bispo ASL, Barbosa GAS, de Almeida EO. Short-term effectiveness of conservative therapies in pain, quality of life, and sleep in patients with temporomandibular disorders: A randomized clinical trial. Cranio. 2019:1-9.
18. Cleland J, Palmer J. Effectiveness of manual physical therapy, therapeutic exercise, and patient education on bilateral disc displacement without reduction- of the temporomandibular joint: a single-case design. J Orthop Sports Phys Ther. 2004;34(9):535-48.
19. Bialosky JE, Bishop MD, Price DD, Robinson ME, George SZ. The mechanisms of manual therapy in the treatment of musculoskeletal pain: a comprehensive model. Man Ther. 2009;14(5):531-8.
20. La Touche R, París-Alemany A, Mannheimer JS, Angulo-Díaz-Parreño S, Bishop MD, Lopéz-Valverde-Centeno A, et al. Does mobilization of the upper cervical spine affect pain sensitivity and autonomic nervous system function in patients with cervico-craniofacial pain?: A randomized-controlled trial. Clin J Pain. 2013;29(3):205-15.
21. Calixtre L, Moreira R, Franchini G, Alburquerque-Sendín F, Oliveira A. Manual therapy for the management of pain and limited range of motion in subjects with signs and symptoms of temporomandibular disorder: a systematic review of randomised controlled trials. J Oral Rehabil. 2015;42(11):847-61.
22. Kalamir A, Graham PL, Vitiello AL, Bonello R, Pollard H. Intra-oral myofascial therapy versus education and self-care in the treatment of chronic, myogenous temporomandibular disorder: a randomised, clinical trial. Chiropr Man Ther. 2013;21(1):1-10.
23. La Touche R, París-Alemany A, von Piekartz H, Mannheimer JS, Fernández-Carnero J, Rocabado M. The influence of cranio-cervical posture on maximal mouth opening and pressure pain threshold in patients with myofascial temporomandibular pain disorders. Clin J Pain. 2011;27(1):48-55.
24. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux P, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. Int J Surg. 2012;10(1):28-55.
25. Schiffman E, Ohrbach R, Truelove E, Look J, Anderson G, Goulet JP, et al. Diagnostic criteria for temporomandibular disorders (DC/TMD) for clinical and research applications: recommendations of the International RDC/TMD Consortium Network and Orofacial Pain Special Interest Group. J Oral Facial Pain Head. 2014;28(1):6.
26. Uitvlugt G, Indenbaum S. Clinical assessment of atlantoaxial instability using the sharp-purser test. Arthritis Rheum. 1988;31(7):918-22.
27. Osmotherly PG, Rivett D, Rowe LJ. Toward understanding normal craniocervical rotation occurring during the rotation stress test for the alar ligaments. Physical therapy. 2013;93(7):986-92.
28. MacDowall A, Skeppholm M, Robinson Y, Olerud C. Validation of the visual analog scale in the cervical spine. J Neurosurg Spine. 2017;28(3):227-35.
29. Farrar JT, Young Jr JP, LaMoreaux L, Werth JL, Poole RM. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. Pain. 2001;94(2):149-58.
30. Revill S, Robinson J, Rosen M, Hogg M. The reliability of a linear analogue for evaluating pain. Anaesthesia. 1976;31(9):1191-8.
31. Boonstra AM, Preuper HRS, Reneman MF, Posthumus JB, Stewart RE. Reliability and validity of the visual analogue scale for disability in patients with chronic musculoskeletal pain. Int J Rehabil Res. 2008;31(2):165-9.
32. Swinkels RA, Swinkels-Meewisse IE. Normal values for cervical range of motion. Spine. 2014;39(5):362-7.
33. Robertson V, Ward A, Low J, Reed A, MCSP D. Electrotherapy explained: principles and practice: Elsevier Health Sciences; 2006.
34. Kirupa K, Divya Mary S, Vaishnavi G, Nisha RN, Mercy JR, Jaiganesh G. A comparative study of ultrasound therapy and transcutaneous electrical nerve stimulation in reducing pain for temporomandibular joint disorder. Drug Invent Today. 2019;12(3):515-7.

35. de Paula Gomes CAF, Politti F, Andrade DV, de Sousa DFM, Herpich CM, Dibai-Filho AV, et al. Effects of massage therapy and occlusal splint therapy on mandibular range of motion in individuals with temporomandibular disorder: a randomized clinical trial. J Manipulative Physiol Therapeut. 2014;37(3):164-9.
36. Edmond SL. Joint mobilization/manipulation: Elsevier; 2006.
37. Ajimsha M, Al-Mudahka NR, Al-Madzhar J. Effectiveness of myofascial release: systematic review of randomized controlled trials. J Bodyw Mov Ther. 2015;19(1):102-12.
38. Cohen J. Statistical power analysis for the behavioral sciences: Academic press; 2013.
39. Garrigós Pedrón M, La Touche Arbizu R, Desentre N, Gracia Naya M, Segura Ortí E. Effects of a physical therapy protocol in patients with chronic migraine and temporomandibular disorders: a randomized, single-blinded, clinical trial. J Oral Facial Pain Head. 2018;32(2).
40. Espejo-Antúnez L, Castro-Valenzuela E, Ribeiro F, Albornoz-Cabello M, Silva A, Rodríguez-Mansilla J. Immediate effects of hamstring stretching alone or combined with ischemic compression of the masseter muscle on hamstrings extensibility, active mouth opening and pain in athletes with temporomandibular dysfunction. J Bodyw Mov The. 2016;20(3):579-87.
41. El Hage Y, Politti F, de Sousa DFM, Herpich CM, dos Santos Gloria IP, de Paula Gomes CAF, et al. Effect of mandibular mobilization on electromyographic signals in muscles of mastication and static balance in individuals with temporomandibular disorder: study protocol for a randomized controlled trial. Trials. 2013;14(1):1-11.
42. Calixtre LB, Oliveira AB, Alburquerque-Sendín F, Armijo-Olivo S. What is the minimal important difference of pain intensity, mandibular function, and headache impact in patients with temporomandibular disorders? clinical significance analysis of a randomized controlled trial. Musculoskelet Sci Pract. 2020;46:102108.
43. Maughan EF, Lewis JS. Outcome measures in chronic low back pain. Eur Spine J. 2010;19(9):1484-94.
44. Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. J Pain. 2008;9(2):105-21.
45. Lee JS, Hobden E, Stiell IG, Wells GA. Clinically important change in the visual analog scale after adequate pain control. Acad Emerg Med. 2003;10(10):1128-30.
46. Kropmans T, Dijkstra P, Stegenga B, Stewart R, De Bont L. Smallest detectable difference of maximal mouth opening in patients with painfully restricted temporomandibular joint function. Eur J Oral Sci. 2000;108(1):9-13.
47. Arab AM, Nourbakhsh MR. The relationship between hip abductor muscle strength and iliotibial band tightness in individuals with low back pain. Chiropr Osteopath. 2010;18(1):1-5.