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Review Article: Effects of Neural Mobilization Techniques on Pain and Disability in Patients With Neurodynamic Dysfunction: A Systematic Review of Randomized Controlled Trials

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ABSTRACT

Introduction: Neural mobilization is the most important technique used for the treatment of nervous system dysfunction. This study aimed to systematically review and evaluate the therapeutic efficacy of neural mobilization techniques in nervous system dysfunctions by assessing Randomized Controlled Clinical Trials (RCTs).

Materials and Methods: We used all English papers published in five electronic databases from 2000 to 2020 using the following keywords: "neural mobilization", "nerve mobilization", "physical therapy", "nerve glide exercises", "neural stretching", "neurodynamics", and "neural physiotherapy". The full text of the articles identified was reviewed to select papers specifically discussing neural mobilization as a treatment modality. The PEDro scale was used to assess the quality of these trials. The randomized clinical trials were selected that examined the therapeutic effect of neural mobilization.

Results: Twelve RCTs were identified. Five RCTs used the same median nerve tensioning technique in patients with Carpal Tunnel Syndrome (CTS). In some studies, the methods of neural mobilization were different. Fourteen papers examined different neurodynamic dysfunctions such as lateral epicondylalgia, radicular neck pain, postoperative spinal surgery, radicular low back pain, and chronic tension-type headache. There is moderate evidence (Level 2) to support distal nerve tensioning and tendon gliding techniques in CTS patients. Also, there was limited (Level 3) and insufficient (Level 4) evidence about using cervical lateral gliding away from their involved side and upper limb tension test mobilization and the use of slump stretches and combinations techniques in the treatment of neurodynamic dysfunction, respectively. Besides, all studies reported a positive effect compared to neutral effects.

Conclusion: Although clinicians frequently use neuromobilization techniques for both diagnosis and treatment of nervous system dysfunctions, the quality assessment of 20 RCTs has shown insufficient evidence to support the efficacy of these techniques in the treatment of nervous system dysfunctions.

Keywords: Neural mobilization, Neurodynamics, Randomized controlled trial, Systematic review, Therapeutic efficacy

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1. Introduction

Nervous system dysfunction can result in decreased nerve mobility, increased mechanosensitivity, neural ischemia, and decreased axonal transport. Also, intraneural edema following neural dysfunction can damage nerve function. All of these factors can eventually lead to pain and loss of sensation. Therefore, clinicians use neuromobilization techniques to restore nerve function. It is believed that restoring normal nerve movement can restore lost function and reduce pain [1]. Nerve mobilization techniques play an essential role in the treatment of nervous system dysfunction [2]. The cause of nervous system dysfunction is a limitation in nerve system motion [3, 4]. The nervous system's ability to adapt to mechanical loads is vital and must undergo all mechanical changes such as elongation, compression, gliding, and cross-sectional sliding [5]. In the pathologic condition, these protective mechanism fails, and altered neuro-dynamicity can cause symptoms, such as pain and paresthesia [3, 6]. Although the hypothesized benefits of nerve mobilization techniques are facilitated nerve gliding, reduced nerve adherence, increased neural vascularity, and improved axoplasmic flow, there is no adequate evidence to support these functions [7, 8]. So, the theoretical purpose of nerve mobilization techniques is to restore the relative nerve movement against surrounding tissues, reduce intraneural pressure, and improve neural tissues' physiologic function [9]. However, these mechanisms still need further investigation to justify the observed clinical effects of neuromobilization [7, 10]. The clinical outcomes observed with neuromobilization techniques are based on subjective criteria [2, 7]. Previous studies have also reported different results about these techniques' impact on patients with various symptoms and nerve dysfunctions [11-14].

Therefore, this study aimed to systematically review and evaluate the therapeutic efficacy of neural mobilization technics to treat nervous system dysfunction through the assessment of Randomized Controlled Trials (RCTs) that have been conducted on this topic.

2. Materials and Methods

Search strategy

Three electronic databases of Scopus, Medline (PubMed), and ProQuest were searched for papers with titles and or abstracts containing one or more of our keywords and published from January 1, 2000, to October 30, 2020. The keywords were "neural mobilization", "intervention", "nerve mobilization", "physical therapy", "pain", "paresthesia", "nerve glide exercises", "neural stretching", "neurodynamics", and "neural physiotherapy". The titles and or abstracts were used to identify the RCT studies using specifically nerve mobilization as a treatment modality. Duplicate papers were checked and removed. Data extraction was performed by one researcher (H.Sh) and the quality of the RCTs by another researcher (K.Kh), who was not involved in the literature search.

Study selection

The method of selection studies followed the proposed guidelines for conducting systematic reviews [15]. Full texts of English papers were included if they were Randomized Controlled Trials (RCTs). The inclusion criteria were based on the following items. The study participants were male and female over 20 with a diagnosis of nervous system dysfunction (pain and or paresthesia are two important symptoms of neurodynamic dysfunction). The intervention was nerve mobilization techniques (sliding, stretching). Finally, the outcomes were pain assessed by Visual Analog Scale (VAS), Range of Motion (ROM) during neural tension test, and disability based on any reliable questionnaire such as Oswestry Disability Index (ODI) (the studies had at least one of them).

Screening and data extraction

The relevant publications were reviewed independently by two authors using EndNote X8 software. Discrepancies between authors were resolved by consensus, or if they did not reach an agreement, an expert provided the final result. Then, the qualified studies were obtained for full-text screening. After the final evaluation, the following information was extracted from the articles: the name of the first author, year of publication, patients' characteristics (sample size, gender, and age of the participants), characteristics of the intervention Group and control Group, primary and secondary outcomes, and results of studies.

Quality assessment of studies

The quality of included studies was assessed using the PEDro scale, developed by the Centre of Evidence-Based Physiotherapy (CEBP). It consists of 11 items; it is a reliable tool used to critique RCTs and grade their methodological quality [16-18].

Two independent reviewers determined the Quality Score (QS) for each paper. The quality score was calculated for 10 of the 11 items. The first criterion of the PEDro scale was not used to determine QS [16]. The agreed QS for each paper is included, too.

The various items of the PEDro score deal with different aspects of RCT analysis, including internal validity, external validity, and statistics. The Internal Validity Score (IVS) was used to determine internal validity and thereby giving an evaluation of methodological quality. The summated score of items 2, 3, and 5 through 9 in the PEDro score were identified to determine IVS.

Based on IVS, the papers were divided into three categories: 1) high methodological quality studies (IVS of 6–7), 2) moderate quality (IVS of 4–5), 3) limited quality (IVS of 0–3) [7, 16].

Analysis of therapeutic efficacy

Because RCTs were heterogeneous (different pathology or interventions), quantitative meta-analysis methods could not be used. In such cases, the qualitative approach is used to assess the quality of the studies [19]. In this study, we used a qualitative assessment based on each type of intervention:

A: Strong evidence: Multiple high-quality RCTs are consistent in their findings.

B: Moderate evidence: One high-quality RCT is compatible with one or more low-quality RCTs.

C: Limited evidence: One moderate-quality RCT is consistent with one or more low-quality RCTs.

D: Insufficient evidence: One or more limited quality RCTs are consistent with each other.

Clinical benefit

To determine neural mobilization clinical benefit, we used a ranking system [15]. If at least one of the outcomes was statistically significant compared to the control Group, a positive effect was considered. A negative effect was regarded if the intervention was less effective than the control. Also, a neutral effect was considered if there was no statistically significant difference between the intervention and control Group for any outcome [7].

3. Results

Study selection

Twenty RCTs were included in the present study based on the inclusion criteria (Figure 1). Table 1 presents more details about the studies.

Methodological quality

IVS was used to evaluate each article's methodological quality, which is detailed in Table 1. Sixteen (out of 20 articles) got IVS scores of 4 or 5. Therefore, they were papers with moderate methodological quality. Four had an IVS of 3 and were considered limited methodological quality studies (Table 1).

Study characteristics

Five RCTs used the same median nerve tensioning technique in patients with Carpal Tunnel Syndrome (CTS). In some studies, the methods of neural mobilization were different (e.g. cervical lateral glide, leg movement, cervical traction, peripheral nerve sliders, etc.). Other studies combined these techniques with home-based neural mobilization exercises. Fourteen (out of 20) papers also examined various neurodynamic dysfunctions such as lateral epicondylalgia, radicular neck pain, postoperative spinal surgery, radicular low back pain, and chronic tension-type headache. So, these RCTs were clinically heterogeneous, preventing a quantitative meta-analysis, and results were analyzed qualitatively. The details of study characteristics are presented in Table 1.

Therapeutic efficacy

According to the qualitative rating system, there is moderate evidence (Level 2) to support the use of distal nerve tensioning and tendon gliding techniques in CTS patients. Also, there was limited evidence (Level 3) about the use of cervical lateral gliding away from their involved side and upper limb tension test mobilization in treating neurodynamic dysfunction. Also, there was insufficient evidence (Level 4) about using slump stretches and combination techniques to treat neurodynamic dysfunction (Table 1).

Clinical benefit

Table 1 shows the details of 20 studies. More studies reported a positive effect than neutral effects. No study reported adverse effects.

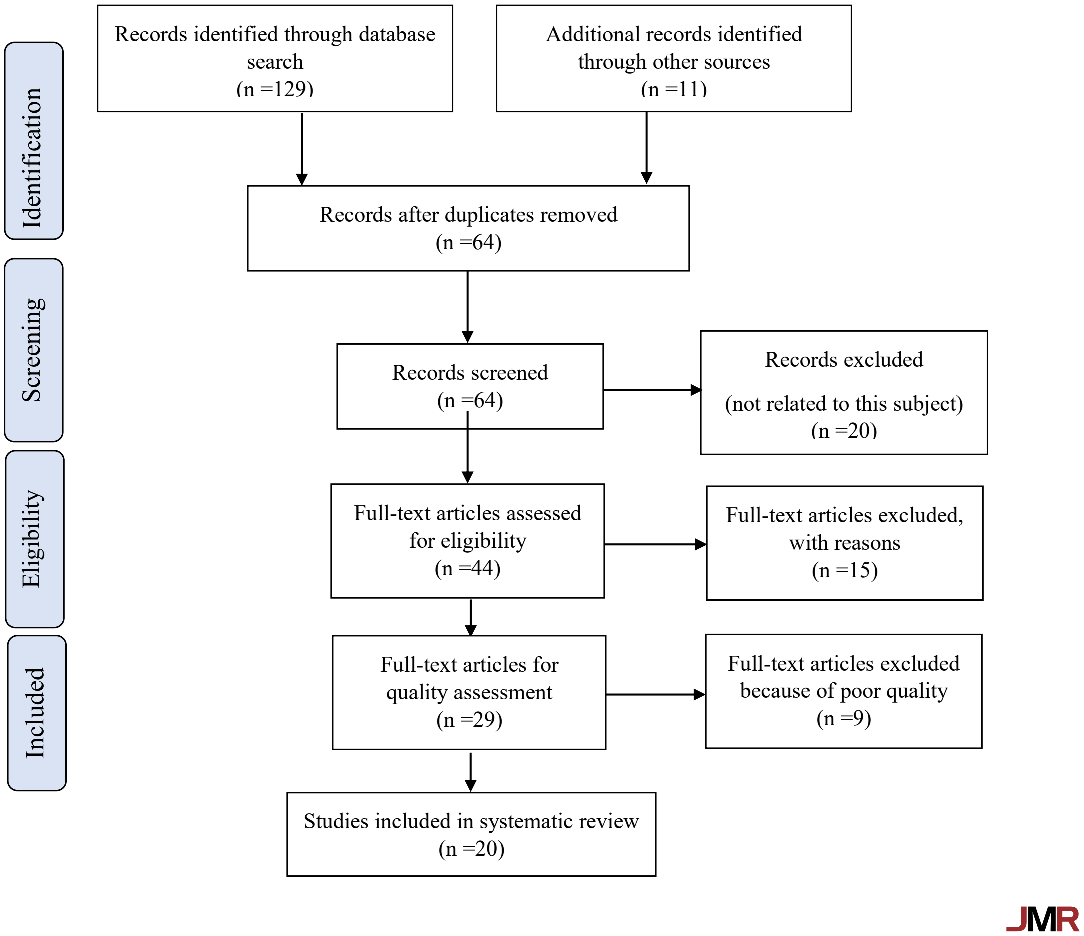

Figure 1. Flow diagram of the study selection process

4. Discussion

This study aimed to review RCTs conducted from 2000 to 2020 related to the effects of neuromobilization techniques on nervous system dysfunctions and evaluated the level of studies based on the PEDro scale. A total of 20 RCTs were assessed to evaluate the impact of neuromobilization techniques on various neurodynamic dysfunctions. All studies showed the positive effect of neural mobilization techniques on various neurodynamic dysfunctions. Seven papers got a neutral benefit indicating that neural mobilization was no more effective than conventional treatment or placebo. Sixteen studies demonstrated moderate methodological quality, and three studies had limited methodological quality.

Because of the heterogeneity of reviewed studies (different types of techniques in various neural dysfunctions were examined, the use of quantitative meta-analysis for analysis was not proper, and the papers were assessed qualitatively [7]. Also, it is imperative to choose the appropriate technique and the right patient in evaluating the efficacy of these techniques. Studies in this field have used different neuromobilization techniques, making it more challenging to assess their effectiveness in heterogeneous studies. Shacklock also believed that a large sample size is needed to evaluate the effectiveness of neuromobilization techniques on neural dysfunction [8]. Studies in this field had a small sample size, which makes the evaluation more difficult.

Besides, studies have shown weaknesses in random allocation and blinding; thus, investigating the efficacy of neuromobilization techniques on nervous system dysfunction was difficult. In this review, 13 studies had blinded the raters. Methodological weakness can result in unrealistic findings. Although blinding in manual therapy studies is difficult, it can significantly eliminate bias and is essential in clinical trial studies [37].

One of the methods used to determine the therapeutic effect in clinical studies is the Minimal Clinically Important Different (MCID) score. For example, MCID determines whether an outcome measure has become

Table 1. Randomized controlled trials of neural mobilization as a treatment modality

Author(s)	Patients' Demographics	Intervention	Comparison	Outcomes	Result	QS	IVS
Tal-Akabi et al. (2000) [20]	N=21 Age range (29-85 y) All patients were waiting for surgery	Group 1: Seven subjects with CTS intervention by ULTT 2a Group 2: Seven subjects with CTS intervention by carpal bone mobilization and flexor retinaculum stretch	Group 3: Seven subjects in the control Group No intervention	Pain (VAS) Functional Box Scale (FBS) Pain-Relief Scale (PRS) Range of Motion (ROM) wrist flexion-extension Surgery	A Positive effect of neural mobilization and mobilization on pain and ROM compared with no treatment. It was not superior to the effect neural mobilization compared with carpal bone mobilization and flexor retinaculum stretch	8	5
Allison et al. (2002) [21]	N=30 Twenty females Ten males Age range (18-75 y)	Group 1: Passive mobilization of neural tissue for 8 weeks Group 2: Gleno-humeral joint mobilization thoracic mobilization, for 8 weeks	Group 3: Control Group with no intervention for 8 weeks	Measurements taken pretreatment- 4 weeks into treatment-post-treatment McGill pain questioner Pain (VAS) Northwick park questionnaire	Manual therapy included both nerve mobilization, and joint mobilization was effective in improving pain intensity and functional disability. However, a Group difference was observed for the 8 weeks, with the nerve mobilization Group having a significantly lower score	7	4
Akalin et al. (2002) [22]	N=36 Thirty-four females Two males Age range (38-64 y)	Group 1: 18 patients with CTS: Tendon glide exercise in 5 positions, Nerve mobilization of the median nerve in 6 positions for 4 weeks	Group 2: 18 patients with CTS Wrist splint should be worn all night and during the day for 4 weeks	Measure pre-treatment and 8 weeks post-treatment. Symptom Tinel's sign, Grip strength, Pinch strength, Functional status score Phalen's sign	Both Group interventions had slightly greater scores, but the difference between Groups was not significant except for pinch strength	6	3
Coppieters et al. (2003) [23]	N=20 Patients with cervicobrachial neurogenic pain	Group1: Received a cervical lateral gliding away from their involved side after 2 trials, 3 repetitions	Group 2: Received ultrasound 5 minutes at the most painful region (dose, 0.5 W/cm^2; sonation time, 20 size of treatment head, 5 cm2; frequency, 1 MHz)	Range of elbow extension Symptom distribution, Pain intensity during the neural tissue provocation test for the median nerve	Increase in elbow extension from 137.3° to 156.7° A 43.4% decrease in the area of symptom distribution Decreased pain intensity from 7.3 to 5.8 was significant (P=0.003) For the ultrasound Group, there were no significant improvements.	6	4
Cleland et al. (2007) [24]	N=30 Twenty-one females Nine males Age range (18-60 y) Patients with low back pain	16 low back pain patients Same as control plus: Slumped stretching exercise/ Home exercise slump stretches for 3 weeks 2 times for a week	14 low back pain patients posterior/ anterior lumbar mobilization exercise program (squats, pelvic tilts, bridging) for 3 weeks 2 times for a week	Pain Rating Scale (PRS), Modified Oswestry Disability Index (ODI)	The intervention Group demonstrated significantly greater improvements in pain and disability (P=0.001)	8	5

Author(s)	Patients' Demographics	Intervention	Comparison	Outcomes	Result	QS	IVS
Bialosky et al. (2009) [25]	N=40 Female Age range (18-70 y) Patient with CTS	Group 1: Intervention with the splint and median nerve mobilization for 3 weeks	Group 2: Intervention with the only splint for 3 weeks (control Group)	Patient-Centered Outcome Questionnaire (PCOQ); 101-point) Numeric Rating Scales (NRSs)	Within-session decreases in clinical pain intensity and pressure pain sensitivity were observed independent of Group assignment. Reduction of temporal summation was observed only in participants receiving nerve mobilization. Significant improvements in clinical pain intensity and upper extremity disability were observed at 3 weeks, independent of Group assignment.	6	4
Bardak et al. (2009) [26]	N=111 Age range (22-74 y) Patient with CTS	Group 1: Standard treatment distal nerve tensioning /tendon gliding (n=35) Group 2: Only exercise for 6 weeks (n=35)	Group 3: Standard treatment wrist orthosis and betamethasone injection (n=41)	Functional performance (FSS) Pain (VAS) Physical examination: 1-Tinel's test 2-Phalen's test 3-Reverse Phalen's test 4-Compressionstest	Functional performance score in Group 1 compared with Group 2, significantly improved (P<0.001). There was no significant difference between Groups 2 and 3. Pain: not reported. Physical examination: not reported	7	4
Atya et al. (2011) [27]	N=30 Female Age range (30-45 y) Patient with CTS	Nerve tensioning and tendon gliding for 2 months (n=15)	Low-level laser (n=15)	Pain (VAS)	Intervention Group demonstrated significantly greater improvements in pain (P<0.05)	7	4
Čolaković et al. (2013) [28]	N=60 Patients with radicular low back pain	Group 1: Neural mobilization and lumbar stabilization, for 4 weeks (n=30)	Group 2: Active range of motion (ROM) and lumbar stabilization exercises for 4 weeks (n=30)	pain (VAS) ROM (SLR)	After treatment, there was statistically significant improvement between Groups in favor of Group 1	7	4
Oskouei et al. (2014) [29]	N=20 Patients with carpal tunnel syndrome (totally 32 hands) Age range (18-65 y)	Group 1: Treatment Group Routine physiotherapy combined with neuromobilization maneuver 3 days a week for 4 weeks (n=16 hands)	Group 2: Control Group Routine physiotherapy (rest splint, TENS, and therapeutic ultrasound). 3 days a week for 4 weeks (n=16 hands)	Pain (VAS) Symptoms severity scale, functional status scale, Phalen's sign	In all variables, significant differences were reported between Groups in favor of Group 1 (P<0.001)	7	4

Author(s)	Patients' Demographics	Intervention	Comparison	Outcomes	Result	QS	IVS
Anwar et al. (2015) [30]	N=30 for 6 weeks	Group 1: Treatment Group, Routine physiotherapy combined with neuromobilization maneuver	Group 2: Control Group, Routine physiotherapy (intermittent cervical traction, cervical muscles stretching, hot pack)	Pain (VAS) neck disability index (NDI)	In all variables, significant differences were reported between Groups in favor of Group 1 (P<0.001)	6	3
Ferragut-Garcías et al. (2017) [31]	N=97 Seventy-eight females Nineteen males Patients with chronic tension-type headache Age range (35-56 y)	Group (B): Soft tissue techniques Group (C): Neural mobilization techniques Group (D): Combination of soft tissue and neural mobilization techniques	Group (A): Placebo superficial massage	Pressure pain threshold (PPT) Frequency and maximal intensity of pain the outcomes were assessed before, after, and 15 and 30 days after the intervention	PPT/frequency and maximal intensity of pain in Groups (B, C, D) significantly improved compared to Group A (in all measurements time) (P<0.001) After the intervention, the highest values of PPT and the lowest frequency was related to the Group (D)	8	5
Das et al. (2018) [32]	N=90 Patients with lumbar radiculopathy	Group 1: Neural mobilization with conventional physiotherapy Group 2: Spinal mobilization with leg movement along with neuromobilization and conventional physiotherapy	Control Group: Back extension exercises and hot pack	Pain based on Numerical Pain Rating Scale (NPRS) ROM Straight Leg Raise (SLR)	All Groups showed significant differences after interventions (P<0.001)	6	4
Calvo-Lobo et al. (2018) [33]	N=62 Patients with cervicobrachial pain	Group 1: Neural mobilization for 6 weeks (n=31)	Group 2: Oral ibuprofen, for 6 weeks (n=31)	Pain (NPRS), Cervical ROM (CROM)	Both interventions were effective, but there was a statistically significant improvement in pain between Groups in favor of Group 2 (P<0.05)	7	4
Wolny et al. (2019) [4]	N=103 Fifty-two females Fifty-one males Mean age: 53 y, Patients with carpal tunnel syndrome	Group 1: Neurodynamic techniques (Twice weekly for 5 weeks) (n=58)	Group 2: Control Group (n=45)	Nerve Conduction Study (NCS), Pain (NPRS), Symptom Severity (FSS) strength of grips	In variables of NCS, NPRS, and FSS, significant differences were reported after intervention (P<0.001) There were no significant differences in strength of grip (P>0.05)	8	5
Elsayyad et al. (2021) [34]	N=60 Patients with lumbar spine fusion	Group 1: Neural mobilization plus stabilization exercises Group 2: Myofascial release and stabilization exercises (3 times a week for 4 weeks)	Group 3: Stabilization exercises only (3 times a week for 4 weeks)	Disability: Oswestry Disability Index (ODI) Pain: (VAS) Back Range of Motion (BROM)	All Groups showed significant differences after interventions (P<0.05)	6	3
Savva et al. (2021) [11]	N=66 Patients with cervical radiculopathy (3 times per week for 4 weeks)	Group 1: Cervical traction combined with neural mobilization (n=22)	Group 2: Cervical traction combined with sham neural mobilization (n=22) Group 3: Wait-list control (n=22)	Disability: Neck Disability Index (NDI) Pain: (NPRS)	After 4 weeks follow up, in both variables, there were significant differences between Groups 1 and 2 in favor of Group 1 (P<0.05) There were no significant differences were reported between Groups 2 and 3 (P>0.05)	8	5

Author(s)	Patients' Demographics	Intervention	Comparison	Outcomes	Result	QS	IVS
Akhtar et al. (2020) [35]	N=80 Patients with shoulder impingement syndrome for 11 weeks	Group 1: Routine physiotherapy combined with neural mobilization (n=40)	Group 2: Neural mobilization for 11 weeks (n=40)	Pain (VAS) Functional disability (University of California at Los Angeles rating score)	After 11 weeks of treatment, there was statistically significant improvement between Groups in favor of Group 1	8	5
Yilmaz et al. (2020) [36]	N=40 Twenty-six females Fourteen males Mean age: 42.80 y Patients with lateral epicondylitis	Group 1: Treatment Group, Conservative rehabilitation combined with radial nerve mobilization. 7 days a week For 6 weeks	Group 2: Control Group, Conservative rehabilitation without neuromobilization, 7 days a week for 6 weeks	Pain (VAS) grip strength pinch strength	A significant difference was reported in VAS between Groups in favor of Group 1 (P<0.001). There were no significant differences in strength between Groups (P>0.05).	7	4

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VAS: Visual Analog Scale; CTs: Carpal Tunnel Syndrome; ULTT: Upper Limb Tension Test; FSS: Functional Status Score; TENS: Transcutaneous Electrical Nerve Stimulation.

clinically acceptable after treatment. It divides the findings into two types: failure or success [38]. None of the reviewed RCTs have reported this criterion, and because of the heterogeneity of outcome measures, the comprehensive evaluation was more difficult.

Most studies have examined the effect of these techniques on patients with CTS. The studies in these patients are homogeneous compared to other dysfunctions, and the meta-analysis will be proper for them. Because of both homogeneity and moderate evidence of CTS studies, the use of neural mobilization techniques in treating these patients is recommended. There is limited evidence supporting neural mobilization techniques in lateral epicondylitis, shoulder impingement syndrome, cervical and lumbar radiculopathy, chronic tension-type headache, and cervicobrachial pain.

As mentioned in the introduction section, nervous system dysfunction means that this system has limited movement, and neuromobilization techniques improve nerve movement. However, further studies should be conducted and show decreased and increased nerve movement before and after neuromobilization techniques. Measuring nerve movement before and after the intervention through ultrasound seems to be an essential step in neuromobilization research. Future studies should also consider nerve movement along with changes in neurophysiological features such as nerve conduction velocity before and after neurodynamic techniques in people with neural system dysfunctions. Measurement of other physiological features, such as changes in nerve blood flow, should also be considered to justify the association between movement and neural physiology.

Although neuromobilization studies have increased since the last decade, studies in this field are still limited quantitatively and qualitatively. Future studies should examine similar dysfunctions with comparable techniques to determine the effectiveness of these techniques on neurodynamic dysfunctions.

5. Conclusion

Clinicians frequently use neuromobilization techniques for both diagnosis and treatment of nervous system dysfunctions. Their justification for using these techniques is based on some clinical trials. In this review, 20 RCTs were evaluated. Quality evaluation of these studies showed insufficient evidence to support the efficacy of neuromobilization techniques on nervous system dysfunctions. Although the reviewed studies were not of high methodological quality, most showed the positive effect of neural mobilization techniques on neurodynamic dysfunctions. More homogenous studies should be done to evaluate the efficacy of neurodynamic techniques on peripheral nervous system dysfunction.

Ethical Considerations

Compliance with ethical guidelines

All procedures performed in studies involving data extracted from articles were in accordance with the ethical standards of the Shahid Beheshti University of Medical

Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Authors contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no competing interests.

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