

Effectiveness of Percutaneous Electrical Nerve Stimulation on Range of Motion, Pain Pressure Threshold in the Management of Myofascial Trigger Point: A Systemic Review

Dr. Maithili Deshpande¹, Dr. Deepali Patil²

- ¹ Assistant Professor, Musculoskeletal Physiotherapy, Ravi Nair Physiotherapy College, Datta Meghe Institute of Higher Education and Research, Wardha. Email: deshpandemaithili5@gmail.com
- ² Associate Professor, Musculoskeletal Physiotherapy, Ravi Nair Physiotherapy College, Datta Meghe Institute of Higher Education and Research, Wardha. Email: dvjphysio@gmail.com

KEYWORDS

Percutaneous Electrical Nerve Stimulation, Quality of Life, Sleep quality, Disability, Range of Motion, Pain

ABSTRACT

This review of randomized controlled trials sought to evaluate the efficacy of Percutaneous Electrical Nerve Stimulation (PENS) on range of motion, pain, and pain pressure threshold, as well as to investigate the specific factors influencing its effectiveness. The search for relevant studies published between 2017 and 2024 was conducted in PubMed, Scopus, The Cochrane Library, and the Physiotherapy Evidence Database. Fifteen studies met the inclusion criteria, with primary outcomes focusing on pain, range of motion, and quality of life. The findings indicate that percutaneous Electrical Nerve Stimulation (PENS) is effective in providing short-term pain relief, improving range of motion, and enhancing quality of life when compared to no intervention, sham, or placebo treatments. However, there is insufficient evidence regarding its impact on disability, analgesic medication intake, and sleep quality. In conclusion, while some evidence supports the short-term benefits of Percutaneous Electrical Nerve Stimulation (PENS), further high-quality randomized clinical trials with standardized procedures are necessary.

1. Introduction and Background

Myofascial pain occurs due to discomfort resulting from inflammation or irritation of the muscle fascia which cause localized or referred pain in various patterns. It is a known condition, affects nearly 85% of the normal subjects at some point in their lives. "These hyperirritable spots are classified into active myofascial trigger points (MTrPs), which cause spontaneous pain and replicate the patient's pain when palpated, and latent Myofascial Trigger Points, which do not cause sudden pain but are more painful upon palpation. Trigger Point in Myofascia are frequently observed in individuals with musculoskeletal pain. In the 1950s, Dr. Janet Travell introduced the concept of myofascial pain syndrome, describing it as a muscle pain disease caused by a hypersensitive point in a taut band of muscles which referred pain to region either distant from the tenderness. Myofascial pain disorder is a known source of discomfort as well as disability, causing dull, aching, deep pain that can be continuous or intermittent. This pain can limit the range of motion, lead to muscle weakness, and result in sustained muscle fibre shortening, complicating daily activities. (1)

Common treatment methods include phonophoresis, myofascial release techniques, release of soft tissue, TENS, moist heat application, progressive exercise programs active movement, slow passive stretching, relaxation therapy with ergonomic assistance, acupuncture, strain-counter strain and superficial or subcutaneous dry needling. Therapy for Trigger point involves soft tissue manipulation aimed at dissolve myofascial trigger points, enhancing blood circulation, and reducing pain (2).

Percutaneous Electrical Nerve Stimulation also known by the other name as Percutaneous Neuromodulation therapy. It is a technique used for neuromodulation to reduce pain that become more popular in recent years. Another form of Myofascial Trigger Point treatment is PENS, which is the combine effect of systematically placed acupuncture needles with the delivery of electrical current at the site of Trigger Point⁽³⁾. In contrast relation to traditional Chinese acupuncture, the theory behind this is underpinnings of PENS lie in neuroanatomy as well as with neurophysiology. With the help of this technique, the needles are placed superficially along dermatomes, myotomes, as well as sclerotomes to activate peripheral nerves, and electrical stimulation with different frequencies which is used to stimulate the release of endogenous opioids.

The delivery of electricity rather than the precise placement of needles at acupuncture points is to be PENS' key



therapeutic element. PENS has undergone primary investigation for a variety of conditions, including migraine headaches, sciatica, peripheral neuropathy, and with pain associated along with metastatic bone disease⁽⁴⁾.

Percutaneous electrical nerve stimulation (PENS) is known as a novel analgesic treatment which combines the advantages of both Transcutaneous Electrical Nerve Stimulation with electroacupuncture by utilizing acupuncture- like needle probes positioned in the soft tissues and/or muscles to stimulate peripheral sensory nerves at the dermatomal levels corresponding to the local pathology (5). In a recently published sham-controlled study involving PENS therapy (Ghoname et al., 1999a), it was found to be preferable to Transcutaneous Electrical Nerve Stimulation and exercise therapy in the treatment of chronic low back pain. (6)

2. Method

Data sources and searches

According to the search strategy outlined by Dickersin et al. (12), a comprehensive literature search was carried out with no language restrictions. RCTs from January 2017 to January 2024 were sought in EMBASE, PubMed, the Physiotherapy Evidence Database (PEDro), and the Cochrane Library. The search focused on medical subject headings in titles, abstracts, or index word fields such as 'Percutaneous Electrical Nerve Stimulation' and 'Physiotherapy'. Two researchers independently assessed the titles and, where available, the abstracts of the publications identified in the databases. If a publication was considered to potentially meet the inclusion criteria by either researcher, or if there was insufficient information to decide, a full copy of the article was obtained. The second stage of the search involved manually checking the reference lists of all retrieved papers and accessible systematic reviews to identify any unpublished or overlooked studies. Furthermore, websites containing clinical trial data, theses, or dissertations were examined. Citation indexing was utilized to monitor frequently cited influential authors in the field, and local authorities were also consulted for additional information.

Study selection:

The analysis encompassed research studies that focused on trigger point patients undergoing Percutaneous Electrical Nerve Stimulation, without regard to the seriousness of their condition. Gender or specific age group were not criteria for exclusion in the selection of studies.

Types of Interventions:

RCTs were eligible for inclusion if they compared physical therapy interventions with a placebo condition, a control intervention, or standard care. As per the policy statement of the World Confederation for Physical Therapy, experimental physical therapy interventions may encompass aerobic exercises, strength training, balance drills, basic body awareness exercises, and electrotherapeutic modalities. The primary element of a physical therapy intervention is physical therapy itself, which can be utilized independently or in conjunction with other treatments. Interventions that integrated physical therapy as part of a multi-component weight control plan were excluded due to the inability to ascertain the specific impact of physical therapy. Additional therapies could involve pharmacotherapy, psychoeducation, and cognitive-behavioural or motivational techniques associated with exercise behaviour. Standard care was described as the routine care participants would have received if they had not taken part in the study, including hospitalization, outpatient therapy, and at-home exercise programs. To be considered for inclusion, the duration of the experimental and comparison interventions needed to be similar.

Types of outcomes:

The findings were classified based on evaluations of pain pressure threshold, range of motion in the cervical spine, and the patient's numerical pain rating scale following Percutaneous Electrical Nerve Stimulation.

Primary Outcomes:

- Cervical Spine Range of Motion: This measures the flexibility of the cervical spine, indicating potential limitations and overall movement capability.
- Pain Pressure Threshold: This evaluates the patient's responsiveness to pain at the trigger point.
- Neck Disability Index (NDI): A self-reported survey that assesses restrictions in daily activities due to neck pain, with higher scores indicating more significant disability.



Secondary Outcomes:

- Numerical Pain Rating Scale (NPRS): This scale gauges pain intensity on a numerical scale, offering a standardized evaluation of pain severity, with higher scores indicating more intense pain.
- Quality of Life (QoL): This outcome evaluates overall quality of life, encompassing physical, mental, and social well-being, reflecting the broader impact of symptoms on daily functioning.
- Global Rating of Change (GROC): This subjective measure enables individuals to rate their perceived change in symptoms or overall condition, providing a patient-centred perspective on treatment effectiveness.

Data extraction and quality evaluation:

Two assessors conducted independent quality evaluations. Discrepancies were resolved through deliberation, and if consensus was not reached, a third reviewer made the final judgment. The reporting quality, comprehensiveness, and potential bias of each study were assessed using the 5-point Jadad scale, which assesses randomization quality, blinding, and withdrawals. This well-established tool is the sole published instrument developed based on psychometric principles, with scores ranging from 0 to 5. Higher scores reflect better trial reporting or execution standards. A score of 3 or higher signifies robust quality, while a score below 3 indicates methodological weaknesses.

Data synthesis and analysis:

Each study underwent evaluation utilizing the PEDro rating system created by Verhagen et al. This approach, previously utilized in systematic reviews of physical therapy, offers a thorough evaluation of study methodologies. It takes into account factors pertinent to physical therapy practice, such as participant characteristics, sample size, therapy descriptions, and the validity and reliability of outcome measures chosen. Each article was reviewed based on the 11 criteria of the PEDro scale, with the first criterion, eligibility, not receiving a score. The remaining 10 criteria were scored accordingly. Two evaluators independently assessed each study following this rating system. Responses for each criterion were categorized as either yes (met criterion) or no (did not meet criterion). If a publication lacked information on a specific criterion, no response was provided. Quality criteria scores were evaluated separately. Scores falling between 0 to 3 were deemed poor, 4 to 5 as fair, 6 to 8 as good, and 9 to 10 as excellent. Out of the 10 articles analysed in the study, 2 were rated as fair, 7 as good, and 1 as excellent.

Search Strategy:

Our preliminary exploration of electronic databases resulted in pertinent articles. In order to guarantee thoroughness, we conducted manual searches of bibliographies, online searches, and sought advice from specialists, uncovering one more potentially relevant article. Following the elimination of duplicates and meticulous examination of titles, abstracts, and full texts, we ultimately incorporated eight RCTs in this analysis. (Table 1). The selection process for articles is outlined in a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart. (Figure 1)



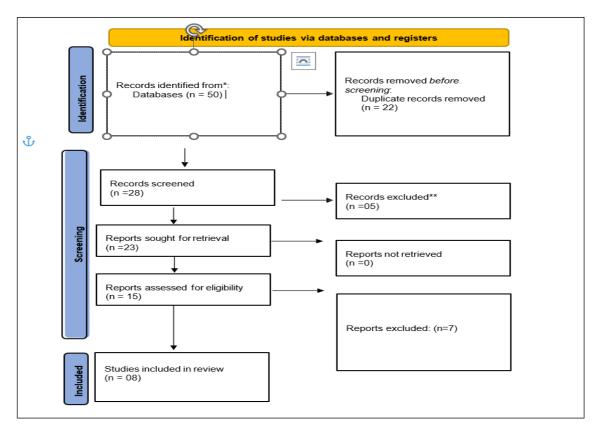


Figure 1: Selection process for PRISMA Flowchart

3. Summary of Articles Review

Table 1: Summary of the Article reviewed

Author and Year of Publication	Participants	Study Setting	Inclusion Criteria based on Neck pain	Interventions	Duration	Outcome Measures	Conclusion
Jose Vicente Leon Hernandez et al (2021)	Total (n=40) patients with chronic neck pain were randomly assigned into high frequency percutaneous electrical nerve stimulation and low frequency percutaneous electrical nerve stimulation	La Salle Centro Universitario, Madrid, Spain	Aged 18 – 65 years, neck pain perceived in the posterior region of the cervical spine, from the superior nuchal line to the first thoracic spinous process with more than 12 weeks of evolution, the presence of active trigger points in the trapezius muscle	1. Group A (n=20) receives received high frequency percutaneous electrical nerve stimulation 2. Group B (n=20) received low frequency percutaneous electrical nerve stimulation for 2 weeks	Once a week for 2 weeks	1. visual analogue scale (VAS) 2.the pressure pain threshold (PPT) 3. Neck Disability Index and Kinesiophobia	Low and high frequency percutaneous electrical nerve stimulation combined with deep dry needling showed similar effects, since no differences between groups were observed on any of the outcome measures
Gustavo Plaza- Manzano et al (2020)	Total (n=16) patient with heterogenous musculoskeletal condition receives percutaneous electrical nerve stimulation.	Department of Physical Therapy, Spain	Older than 18 years of age.	Group receives Percutaneous Electrical Nerve Stimulation for musculoskeletal pain.	-	Pain OR related disability or function	There is low level of evidence suggesting the effects of PENS alone or in combination for pain, but not related disability, in musculoskeletal pain.
Debra K.	Total (n=200)	Geriatric	Age>65, English	The	Twice a	1. McGill Pain	GCAE was



Author and Year of Publication	Participants	Study Setting	ing based on Neck Interventions Durat		Duration	Outcome Measures	Conclusion	
Weiner, Subashan Perera et al (2018)	patients were randomly assigned to 1. PENS 2. control-PENS 3. PENS + GCAE 4. control-PENS + GCAE	Research Education and Clinical Centre, VA Pittsburgh	speaking, Low back pain "every day or almost every day"> moderate intensity >3 months	randomization groups were (1) PENS, (2) control- PENS, (3) PENS + general conditioning and aerobic exercise (GCAE), and (4) control- PENS + GCAE for twice a week for 2 weeks	week for 2 weeks	Questionnaire 2. self-reported disability with the Roland and Morris questionnaire 3. Self- reported physical function 4. Performance- based physical function 5. Geriatric Depression Scale 6. Self-rated health	more effective than PENS alone in reducing fear avoidance beliefs, but not in reducing pain or in improving physical function.	
Hong Li, MB, Qiao-rong Xu et al (2018)	Total (n=62) patients with at least 2 migration attacks each month randomly divided into a verum PENS group and a sham PENS group	Department of Neurology, The People's Hospital of Yan'an, Yan'an	Age 18 to 70 years old, have a history of migraine longer than 3 months, have at least 2 attacks each month	Group A receives (n=31) Verum PENS while Group B (n=31) receives Sham PENS for 12 weeks of the treatment.	12 weeks for treatment	1. Monthly migraine days (MMD) 2. 50% of responder rate 3. Monthly Migraine attacks 4. monthly headache days 5. monthly acute antimigraine drug intake	The results of this study demonstrated that verum PENS is more effective and safer than Sham PENS for the treatment of migraine.	
Alan R. de Azevedo et al (2018)	Case series of 4- 14 years overactive bladder in children received PENS therapy for 1 week.		1. children with pure OAB 2. uroflowmetry with a bell or tower-shaped curve 3. post-void residual urine <20 ml 4. presence of urgency or urge incontinence	all the children with age of 4-14 years receives PENS therapy for 1 week	once a week for 20 minutes	1. Questionnaire on lower urinary tract dysfunction 2. Visual Analog Scale (VAS)	PENS seems to be an effective and safe treatment for OAB over the short term	
Hesham E. Ahmed, et. Al (2017)	Total (n)= 30 patients with headache were received PENS or needle alone according to the crossover study design.	McDermott Centre for Pain Management, Department of Anaesthesiology and Pain Management, University of Texas Southwestern Medical Centre, Dallas	A history of severe headache occurring four or more times per week	For Active PENS group, the needle probe was connected to five bipolar leads, with low power output and frequency of 15 Hz and 30 Hz. For Needle- only group, probes and leads were connected in identical manner with zero amplitude.	30 minutes, 3 times per week for 2 consecutive weeks	1. Short form health status survey (SF-36) 2. Physical component summary (PCS) 3. Mental component summary (MCS)	PENS therapy would appear to be a useful complementary therapy for the short-term management of patients with debilitating recurrent headache symptoms.	
El - Sayed A. Ghoname et al (2017)	Total (n)= 64 patients were randomly to three groups as	McDermott Centre for Pain Management, Department of	Age greater than 18 yrs, absence of any acute or chronic illness,	1. Group A receives PENS 2. Group B receives TENS	30 mins 3 times per week	1. Short form health status survey (SF-36) 2. Physical	Sham- controlled study demonstrates that PENS is	



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Author and Year of Publication	Participants	Study Setting	Inclusion Criteria based on Neck pain	Interventions	Duration	Outcome Measures	Conclusion	
	Sham-PENS, PENS and TENS	Anaesthesiology and Pain Management, University of Texas Southwestern Medical Centre, Dallas	History of sciatica, constant pain with one leg, positive SLR test	3. Group C receives Sham for 30 mins 3 times per week		component summary (PCS)	more effective than TENS in improving short-term outcome in patients with sciatica.	
Debra K.	Total (n=34)	Department of	NOT	Group A	2 times	1. on site with	PENS may be a	
Weiner, MD et	English	Manipulative	MENTIONED	receives PENS	weekly for	a history and	promising	
al (2017)	speaking, community- dwelling adults were randomized to receive Group A PENS and physical therapy (PT) or Group B sham PENS and physical therapy	Medicine, Texas		and physical therapy (PT) while Group B receives sham PENS and physical therapy for 2 times weekly for 6 weeks	6 weeks	physical examination to validate the exclusion criteria obtained by telephone 2. Folstein Mini-Mental State Examination	treatment modality for community dwelling older adults with CLBP	

PENS: Percutaneous Electrical Nerve Stimulation, MCS: Mental component summary, MTrPs: Myofascial Trigger Points, WOMAC: Western Ontario and McMaster Universities Arthritis Index, MT: Manual Therapy, EX: Exercise, ROM: Range of Motion, VAS: Visual Analogue Scale, NPRS: Numerical Pain Rating Scale, PPT: Pain Pressure Threshold, NDI: Neck Disability Inde

4. Results

Study Selection:

The first electronic database search produced 28 articles. One more possibly relevant article was found through manual searches of reference lists, web searches, and discussions with experts. After eliminating duplicates and reviewing the titles, abstracts, and full texts, we selected 08 RCTs, as depicted in Figure 1, which also details the reasons for exclusion. Substantial differences in study designs and techniques uncovered during the initial full-text screening led us to determine that performing a formal meta-analysis was not possible.

Participants:

446 individuals were part of the analysis, all of whom had myofascial trigger points and had received treatment through Percutaneous Electrical Nerve Stimulation. Out of the five studies, five were conducted on outpatients, five focused on home exercises, and one involved in patients. The inclusion criteria specified individuals aged 18 and above. The analysis covered both current and past recipients of Intramuscular Manual Therapy. The majority of participants in the studies were female.

Methodological Quality

Four studies included in the analysis were considered to have inadequate methodological quality. A comprehensive summary of the research attributes can be found in Table 2. The primary methodological concerns identified were limited sample sizes and absence of masking (or blinding), especially among participants. Table 2 outlines a thorough analysis of the studies' attributes. Version 1: Four of the studies that were part of the analysis were determined to possess subpar methodological quality. A detailed summary of the research features is available in Table 2. The main methodological challenges observed were small sample sizes and a lack of masking (or blinding), particularly with regards to participants. Table 2 showcases an in-depth breakdown of the studies' characteristics.



Sr. No.	Study	1 (not included in score)	Rating for Criterion							Total score	Main concerns			
			2	3	4	5	6	7	8	9	10	11		
1	Jose Vicente Leon Hernandez et al (2021)	√	√	√	√	=	=	=	√	√	√	√	08	No Masking (blinding)
2	Gustavo Plaza- Manzano et al (2020)	√	*	=	✓	✓	=	=	*	=	✓	✓	07	There is no hidden allocation, blinding, or intention-to-treat analysis in this study
3	Debra K. Weiner, Subashan Perera et al (2018)	✓	√	√	√	=	=	√	√	√	√	√	09	No masking of participants and therapist
4	Hong Li, MB, Qiao-rong Xu et al (2018)	✓	✓	√	√	=	=	√	√	√	√	√	09	No masking of participants and therapist
5	Alan R. de Azevedo et al (2018)	✓	√	√	√	=	=	√	√	√	√	√	09	No masking of participants and therapist
6	Hesham E. Ahmed, et. Al (2017)	√	✓	✓	=	✓	=	=	✓	✓	✓	✓	08	Baseline outcome measures are not taken. The therapist and assessor are not blind
7	El - Sayed A. Ghoname et al (2017)	✓	✓	✓	✓	√	=	=	√	=	✓	✓	08	The study did not involve blinding of the therapist and assessor. Additionally, there needed to be more intention to treat analysis.
8	Debra K. Weiner, MD et al (2017)	√	√	=	√	√	=	=	√	√	√	√	08	No allocation concealment. There was no blinding of the therapist and assessor.

1. Criteria for eligibility 2. Randomized assignment 3. Concealment allocation 4. Initial measurements of Baseline outcome for each group were similar 5. Participants are kept unaware of the treatment they receive 6. Therapist are blinded to the treatment. 7. Key endpoint are assessed for over 85% of the subjects 8. Data- analysis to be carried out 9. Group Comparisons are presented using statistical Analysis 10. Provides both point measures and measures of variability for at least one key outcome.

Efficacy of Head and Neck Massage for Myofascial Trigger Points:

Albert Moraska conducted a study to evaluate the efficacy of targeted head and neck massage for recurrent tension-type headaches. The research involved 56 participants diagnosed with this condition, with one group receiving massage therapy and the other a placebo. While there was no significant difference in headache frequency between the two groups, statistical data showed variations over time. Both groups experienced a reduction in headache frequency, but there was no significant variance between the effects of massage therapy and the placebo. Subjects reported a greater decrease in headache pain following massage compared to the placebo or wait-list groups.



Efficacy of Kinesio-Taping, Trigger Point Injection, and Neural Therapy on Myofascial Trigger Points:

Saime conducted a randomized controlled trial to assess the efficacy of Kinesio-taping (KT), trigger point injections, and neural therapy (NT) in treating myofascial trigger points. The research was carried out in physical medicine and rehabilitation outpatient clinics, involving 136 patients with active myofascial trigger points. Group 1 (n=35) received Kinesio-tape treatment, Group 2 (n=35) underwent a single trigger point injection in the trapezius muscle, and Group 3 (n=34) received neural therapy injections with the same local anaesthetic mixture. Prior to the injection, the skin was cleaned with an antiseptic solution. By the third day post-treatment, all groups exhibited improvements in pain and impairment (p<0.001) without significant variances between the groups. Nevertheless, significant differences in pain pressure threshold (PPT) values were observed when comparing the TrPs injection and NT groups across all time periods, while changes in the KT group were not statistically significant over time. The efficacy of KT in myofascial pain syndrome (MPS) has been extensively studied. Öztürk et al. investigated the immediate and long-term effects of KT on the trapezius muscle in MPS. They compared KT with a sham application on the trapezius muscle, with both groups following additional athome exercise routines. Muscle strength, visual analogue scale (VAS), and algometry scores were evaluated immediately after therapy and one month later. While all groups displayed enhancements in VAS and algometry scores, only the KT group exhibited a lasting effect during the one-month follow-up period. Furthermore, only the KT group demonstrated an improvement in muscle strength. The study concluded that the positive outcomes in the sham group were attributed to the psychological and sensory feedback effects of the taping.

5. Discussion

Myofascial Trigger Points and Quality of Life: A Call for Stronger Evidence in Physical Therapy

Myofascial trigger points greatly affect patients' quality of life, and physiotherapy is a key strategy, the current literature base needs to be strengthened. Our review aimed for assessing the positive effect of dry needling for treating MTrPs, examining eight RCTs that explored various techniques including taping, ischemic compression, and myofascial release (MFR) (7) · Although the results were encouraging, the diversity of techniques prevented us from drawing a conclusion about the effective approach. A major drawback was the variety of physical therapy methods used, which complicated direct comparisons. (8)

To support more specific knowledge, further research should aim to conduct large-scale RCTs in association with adequate analytical power to determine efficacy of physical therapy interventions for trigger points. These experiments should use generalized treatment to enable comparisons between methods and increase the reliability of findings. Additionally, outcome variables and reliable outcome procedure should be employed for stronger data management. (9)

Assessing the Positive Effect of Percutaneous Electrical Nerve Stimulation and Other Physiotherapy Interventions

An analysis of studies on Percutaneous Electrical Nerve Stimulation (PENS) found its immediate efficacy to be superior to that of sham and placebo groups. (10) However, further research is needed to evaluate its effectiveness and compare it with other treatments. Thelen et al. reported that Kinesio taping (KT) increased pain-free range of motion (ROM) and reduced disability, though it did not affect pain and function. Halski et al.'s study found no significant change in bioelectric activity at the trapezius muscle trigger point, yet VAS scores significantly improved compared to the sham group. (11)

While the review identified positive variables from different physiotherapy treatments, pinpointing the most useful approach is challenging due to the differences in the techniques used across literature, such as taping, MFR, and ischemic compression. By knowing these treatments as the most useful based on literature factors, we focus to guide practitioners and researchers in choosing useful physical therapy modalities for myofascial trigger point treatment. (12)

In brief, by addressing the identified limitations of the study and providing specific suggestions for further research, we need to increase the credibility and applicability of physical therapy treatments to manage myofascial trigger points. (13)

6. Conclusion

Physiotherapy methods showed promising results, the lack of standardized methodologies and outcome measurements made it difficult to directly compare their efficacy and establish a uniform treatment plan for



myofascial trigger points. Secondly, the use of diverse outcome assessment tools further complicated to conduct reliable systemic reviews and to find out conclusions. Additionally, methodological limitations, like absence of blinding and small sample sizes may have compromised the reliability and validity of the results.

Further research should need to adopt standardized therapies, using consistent outcome measurements, with improving trail procedures to address these issues. Large no of trials with adequate analysis methods are also needed to strengthen the evidence supporting physical therapy treatments for trigger points. Establishing a uniform framework in future studies is essential for facilitating comparative effects between interventions and determining the effective physical therapy methods for managing myofascial trigger points. Developing a systematic methodology that combines various physiotherapy approaches based on patient symptoms could expedite research and improve the treatment recommendations for patients with myofascial trigger points.

7. Additional Information

Author Contributions

All authors have reviewed and approved the final version to be published, and they agree to be responsible for all aspects of the work.

Concept and Design: Dr. Maithili Deshpande, Dr. Deepali Patil

Data Acquisition, Analysis, or Interpretation: Dr. Maithili Deshpande, Dr. Deepali Patil

Manuscript Drafting: Dr. Maithili Deshpande, Dr. Deepali Patil

Critical Review for Intellectual Content: Dr. Maithili Deshpande, Dr. Deepali Patil

Supervision: Dr. Maithili Deshpande, Dr. Deepali Patil

Disclosures

Conflicts of Interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following:

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