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SYSTEMATIC REVIEW

Transcutaneous electrical nerve stimulation and interferential current demonstrate similar effects in relieving acute and chronic pain: a systematic review with meta-analysis



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KEYWORDS

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Transcutaneous electrical nerve stimulation

Abstract

Background: Transcutaneous electrical nerve stimulation and interferential current have been widely used in clinical practice. However, a systematic review comparing their effects on pain relief has not yet been performed.

Objectives: To investigate the effects of transcutaneous electrical nerve stimulation and interferential current on acute and chronic pain.

Methods: We use Pubmed, Embase, LILACS, PEDro and Cochrane Central Register of Controlled Trials as data sources. Two independent reviewers that selected studies according to inclusion criteria, extracted information of interest and verified the methodological quality of the studies made study selection. The studies were selected if transcutaneous electrical nerve stimulation and interferential current were used as treatment and they had pain as the main outcome, as evaluated by a visual analog scale. Secondary outcomes were the Western Ontario Macmaster and Rolland Morris Disability questionnaires, which were added after data extraction.

Results: Eight studies with a pooled sample of 825 patients were included. The methodological quality of the selected studies was moderate, with an average of six on a 0–10 scale (PEDro). In general, both transcutaneous electrical nerve stimulation and interferential current improved pain and functional outcomes without a statistical difference between them.

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Conclusion: Transcutaneous electrical nerve stimulation and interferential current have similar effects on pain outcome. The low number of studies included in this meta-analysis indicates that new clinical trials are needed.

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Introduction

The American Chronic Pain association (ACPA) defines chronic pain as “ongoing or persistent pain lasting beyond the usual course of an acute illness or injury, or pain that lasts 3–6 months or more, and which adversely affects the individual’s well-being” or simply “pain that continues when it should not”.¹ Due to its elevated economic cost, prevalence, and influence on the quality of life of individuals and their families, chronic pain is considered a global public health problem.² It is estimated that approximately 30% of the world’s population suffers from some type of chronic pain.³

Currently, pain management mainly consists in the use of pain medications, pain neuroscience education,⁴ psychological counseling, exercises, manual therapy, and electrical stimulation (ES).¹ Regarding ES, interferential current (IFC) and transcutaneous electrical nerve stimulation (TENS) have been used to manage chronic pain.⁴ TENS units, which typically deliver pulsed currents in the 1–200 Hz frequency range, with a pulse duration of 100–200 μ s,⁵ are widely used due to their low cost and simple use and can be used as an independent method of treatment.^{6,7} IFC delivers medium-frequency alternating currents which pass through the tissues simultaneously and cross with each other, producing interference and resulting in an amplitude-modulated frequency of 1–200 Hz.⁸ It has been claimed that IFC decreases skin impedance, reducing the discomfort normally associated with low-frequency currents,⁵ although this assertion has been challenged.⁹ In fact, the differences between TENS and IFC for the management of pain remain unclear.^{10–12}

IFCs added advantage of generating an amplitude-modulated frequency (AMF), which is a low-frequency current that is able to penetrate more deeply into the tissues, has been claimed as the main analgesic component of IFC.⁵ Theoretically, the benefits of IFC stimulation could be achieved without the associated unpleasant side effects like pain, discomfort and skin irritation.¹³ Unfortunately, IFC has been known to have these side effects. Nonetheless, Rutjes et al.¹⁴ have observed significant effects of IFC for pain control. Despite presenting the theoretical advantages associated with the medium frequencies of IFC compared to TENS,^{6,10,11} previous studies have found that IFC generated a similar effect to control pain and improve function over time compared to TENS (low frequency) in osteoarthritis (OA)¹⁵ and in patients with chronic low back pain.¹⁵

In fact, the results of these studies do not present a clear consensus on which current type is the best for pain control. A narrative review has shown that IFC and TENS have similar effects on pain relief.¹² However, these authors reported numerous experimental biases resulting from

sub-optimal designs (such as unblinded and non-randomized trials), results from healthy subjects using experimental pain (ischemic pain, cold pressure pain or mechanical pain), small sample sizes, and mainly the heterogeneity of IFC or TENS parameters, that could affect the main outcomes.^{12,13}

According to these conflicting results, the clinical application of IFC and TENS to control pain and increase functional outcomes should be investigated in order to determine the best parameters to induce analgesic effects with minimum discomfort. Therefore, a systematic review comparing IFC to TENS would thus be useful to help guide rehabilitation clinicians in the optimal use of ES. We conducted a systematic review of randomized controlled trials to compare the effects of IFC and TENS on pain control and functional outcomes.

Methods

Protocol and registration

The study selection process included screening of titles, reading of abstracts, checking for duplicated studies, evaluating inclusion criteria and full text reading. (PROSPERO Registration number: CRD42017056606, accessed at <https://www.crd.york.ac.uk/PROSPERO/>).

Eligibility criteria

We included randomized controlled trials (RCTs) that compared the use of TENS and IFC on individuals with chronic or acute pain and that use a VAS (visual analog scale) for the main outcome. The secondary outcome assessed was specific questionnaires for functional outcome analysis such as the Western Ontario Macmaster (WOMAC) and the Roland Morris Disability Questionnaire for osteoarthritis and lower back pain, respectively. It is also important to emphasize that pain and function are considered core outcomes on chronic pain evaluation along with emotional function, life satisfaction, participant ratings of improvement and satisfaction with treatment, symptoms and adverse events, work ability, illness perception and participant’s disposition.^{16–19}

Information sources

A literature search was conducted from November of 2016 to April of 2017 on the following databases: Pubmed, Embase, LILACS, PEDro and Cochrane Central Register of Controlled Trials (CENTRAL). A manual search was conducted by checking the reference list of eligible articles. Contact with

authors was made when additional data was required. Year of publication was not used as a limit.

Search strategies

The search terms were selected according to the Medical Subject Headings (MeSH) of the United States National Library of Medicine (NLM) and were: "Interferential Current AND Transcutaneous Electrical Nerve Stimulation AND Pain", "Interferential current AND transcutaneous Electrical Nerve Stimulation AND Chronic Pain", "Interferential current AND transcutaneous Electrical Nerve Stimulation AND Analgesic Effects" and "Interferential current AND transcutaneous Electrical Nerve Stimulation AND rehabilitation". In order to increase the effectiveness and encompass a greater number of articles, those terms were combined in each database and "Transcutaneous electrical nervous stimulation" was modified to "Transcutaneous nervous stimulation" during EMBASE searching.

Study selection

The exclusion criteria were: 1) not related to the object of study; 2) non RCT; 3) utilized induced pain models on healthy subjects; 4) did not compare both currents; 5) did not use VAS as a main or secondary outcome; 6) published in a language other than English, Portuguese or Spanish; 7) unable to find full version; 8) missing data. One independent reviewer performed the selection of the studies and, in case of disagreement; a second and third reviewer were consulted, and consensus was reached through discussion.

Data collection process

Two authors independently assessed trials for inclusion, evaluated risk of bias, assessed with to the PEDro scale¹⁹ and extracted data. One author was responsible for the final review. Continuous variables were extracted as mean and standard deviation when available; for studies with missing data, an initial contact was attempted in order to obtain its information. For those which data were not provided, data were estimated using a transformation method according to Cochrane Review Manager Software version 5.2.²⁰

The following data were assessed: year of publication, sample size, subject's age and gender; current characteristics, pulse duration, current frequency, duty cycle, electrode size, intensity; treatment area and duration; main outcomes and dysfunction; VAS, values pre-and post-intervention and results.

Risk of bias in individual studies

In order to evaluate the quality of the studies, two authors independently assessed the selected studies using one instrument: The 11-item PEDro scale, which quantitatively includes the following 11 item: 1) eligibility criteria were specified (not used to calculate score); 2) subjects were randomly allocated to groups; 3) allocation was concealed; 4) the groups were similar at baseline regarding the most important prognostic indicators; 5) there was blinding of all

subjects; 6) there was blinding of all therapists who administered the therapy; 7) there was blinding of all assessors who measured at least one key outcome; 8) measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups; 9) all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by "intention to treat"; 10) the results of between-group statistical comparisons are reported for at least one key outcome; 11) the study provides both point measures and measures of variability for at least one key outcome. Each of the items were marked as "yes (1/0)" or "no (0/0)" and provided a 0 to 10 scale. Four of the seven eligible articles already had final scores published at <http://www.pedro.org.au/>, so the authors assessed the remaining three.

Statistical analysis

Data from each study was converted into standardized between-group mean differences and 95%CI (IFC vs TENS) and pooled using a random-effects model. We determined statistical heterogeneity of data with an I^2 test and interpreted the results according to Higgins et al.,²¹ which considers values above 25 and 50% as moderate and high heterogeneity, respectively. Outcomes considered for analysis were pain evaluated by a visual analog scale. A p -value <0.05 was considered significant. All analyses were conducted using Review Manager Software version 5.2.²¹

Results

Study selection

Eight of 4384 articles met all inclusion criteria and made the detailed data extraction (Fig. 1). Most articles were excluded as they were duplicated from different databases and for not being related to the search subject.

Study characteristics

All of the characteristics of the studies are presented in Table 1 as supplementary material. A total of 825 patients were evaluated from 2005 to 2017.

Risk of bias within studies

The methodological quality of the included studies using the PEDro score is presented in Table 2. PEDro total scores ranged from 4 to 9 and had an average score of 6. Most the studies used concealed allocation (75%) and similarity at baseline characteristics (87.5%). None of the studies performed therapist blinding. Most studies performed subject follow-ups (62.5%) and variability reports (75%). All studies reported between-group differences.

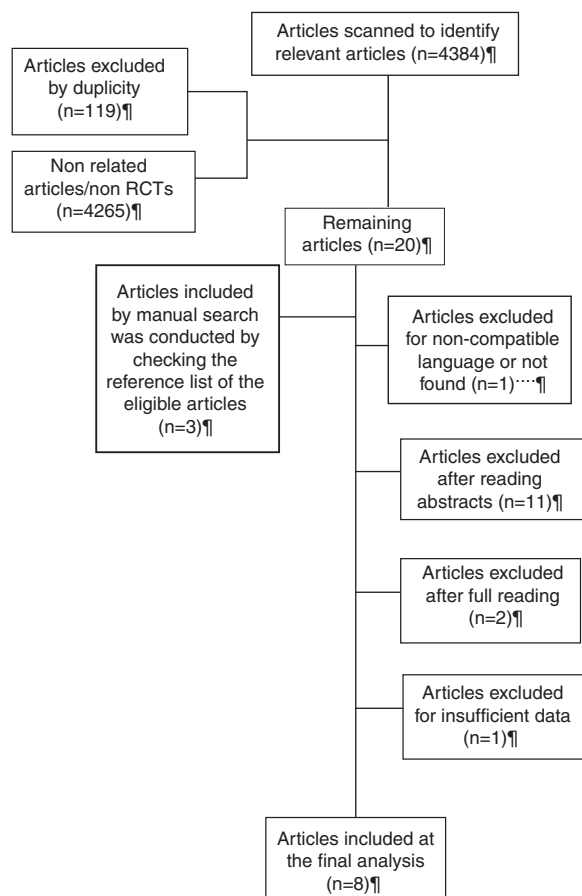


Figure 1 Flowchart of the literature review process. *Abbreviations:* RCTs, randomized controlled trial.

TENS and IFC modalities

The studies contained variations in the settings for the parameters used, especially regarding current pulse duration and frequency, which ranged from 80 to 330 μ s and 0.2 to 120 Hz, respectively. The most used frequency was 100 Hz. For IFC, carrier frequency was set at 4000 Hz in six studies and it was not mentioned in two studies.

Considering duration of application, 20 min was the most frequently used (51.14%) followed by 30 min (28.57%) and a single study utilized a total of 60 min. Intensity was generally established by touch sensation and lack of visual contraction. Total duration of the treatment varied from acute (one day) to chronic (8 weeks). None of the studies mentioned any type of familiarization or adjustments of current intensity due to sensory habituation.

VAS

Statistical analysis demonstrated heterogeneity with considerable variation across the studies and no difference between the use of TENS or IFC (0.36, CI -0.56 to 1.27 , $I^2 = 91\%$) (Fig. 2).

Specific questionnaire evaluation

The WOMAC and Rolland Morris Disability Questionnaire quantitative analysis were not assessed here since we

included only three and two studies for each questionnaire, respectively; therefore, we described the qualitative aspects for osteoarthritis and lower back pain. The WOMAC questionnaire is a validated instrument designed for evaluating pain, stiffness and physical function in patients with osteoarthritis in the knee or hip. Adedoyin et al.¹¹ demonstrated improvements in pain and WOMAC total score (pain, stiffness and function) with ES in addition to exercise, but not equivalent with exercise-alone effects. Burch et al.²⁶ observed a significant decrease in all categories when IFC was applied and Atamaz et al.²⁴ reported a significant decrease in pain and physical function with no difference in stiffness using either TENS or IFC.

Concerning chronic low back pain, three studies utilized the Rolland Morris Disability Questionnaire (RMDQ) for baseline evaluation, originally published in 1983 to quantitatively measure lower back influence on an individual's daily activities. Dohnert et al.²⁸ and Facci et al.²⁵ studies reported positive effects on RMDQ with no difference between currents; however, Rajfur et al.¹⁵ found that IFC therapy was better than TENS in this outcome.

Discussion

Summary of evidence

This systematic review summarizes the current evidence on TENS and IFC used primarily for global evaluation of acute and chronic pain. In general, TENS and IFC both provided significant pain decreases and lead to positive effects in function in both WOMAC and RMDQ questionnaires. The findings presented here have important implications for rehabilitation. As both parameters reduced pain equally, physical therapists could choose either TENS or IFC and expect similar treatment effects.

Six out of eight studies demonstrated equal improvements in VAS regardless of the current type (TENS or IFC) and frequency.^{15,22,24-27} When comparing pain levels between TENS and IFC, previous studies found divergent results. It is notable that pain assessment is a complex and multidimensional process and that VAS evaluation is a one-dimensional instrument. Considering this, only Tugay et al.²⁷ performed other forms of evaluation such as specific questionnaires and clinical aspects. Moreover, most studies^{15,23,24,26,27} included male and female individuals in the same therapy group. As chronic pain is prevalent in female patients,²⁹ this fact could add bias to the results interpretations, as ratio differences were taken into consideration instead of risk in all studies.³⁰ A better understanding of such differences, along with the identification of evidence that considers sex differences in pain and similar comparison groups, will help guide researchers to develop ES to control pain.

Considering that different TENS modalities, such as low-frequency TENS,^{26,27} acupuncture-like TENS,^{15,28} and burst-TENS²² were used, this systematic review did not show a dependency on frequency in terms of pain and functional outcomes. Considering that frequency did not determine TENS efficacy, current evidence shows that intensity is the key factor for achieving optimal pain reduction as observed by Bjordal et al.³¹ Even though the current literature did not provide a clear statement regarding pain modulation

Table 1 Studies characteristics. *Abbreviations:* TENS, transcutaneous electrical stimulation; IFC, interferential current therapy; VAS, visual analog scale; WOMAC, Western Ontario and McMaster University Osteoarthritis Index; RMQ, Rolland Morris Questionnaire.

Results	Both therapies appear to be effective	Significant pain decrease in both groups	IFC was greater than TENS in VAS	Significant improvements in both groups	Significant improvements with no difference between currents	Appears to be a promising therapy	Both appear to be effective	Neither IFC or TENS produced additional effects compared to exercise alone
Main dysfunction/disease	Chronic low back pain	Neck discomfort	Carpal tunnel syndrome	Osteoarthritis of the knee	Chronic low back pain	Osteoarthritis of the knee	Menstrual pain; lower limb pain; low back pain	Osteoarthritis of the knee
Main outcomes	VAS; RMQ; VAS clinical evaluations	VAS	VAS;	VAS; WOMAC	VAS; RMQ	VAS; WOMAC	VAS	WOMAC; VAS
Treatment duration	3 weeks	5 days	3 weeks	3 weeks	2 weeks	8 weeks	1 day	4 weeks
Intensity (mA)	Subjective dosage	Tactile sensation threshold	Not mentioned	Tactile sensation threshold	Strong but comfortable	60 mA	Tolerated level without contraction	Started from 0 to muscle contraction threshold of each subject
Electrode size (cm)	Not mentioned	Not mentioned	35 × 45 mm	TENS 5 × 5; IFCs 8 × 6	5 × 5	Not mentioned	Not mentioned	8 × 6
Duty cycles	TENS = 60 min IFC = 20 min	30 min bilateral	20 min	20 min	30 min	IFC: 15 min TENS: 35 min	20 min	20 min
Frequency (Hz)	TENS = 100 IFC = 50–100	Both 100	TENS = 100 IFC = 20	TENS = 80 IFC = 100	Both 20	TENS: 0.2 IFC = 1–150	TENS = 120 IFC = 0–100	Both 80
Width (μs)	TENS = 100 IFC = 100	TENS = 150	TENS: 80	Not mentioned	TENS = 330; IFC = not mentioned	TENS = 300 IFC = not mentioned	TENS: 100	Both 200
Age (years)	18–73	18–40	35.4 ± 4.2 34.2 ± 4.8 34.9 ± 4.9	50–80	49.63 ± 50.88	62.6 ± 10.5	31.5 ± 1.7	55.41 ± 9.21
Sample size (n)	123	64	63	203	150	116	32	46
Author (years)	Rajfur et al. (2017) ¹⁵	Acedo et al. (2015) ²²	Koca et al. (2014) ²³	Atamaz et al. (2012) ²⁴	Facci et al. (2011) ²⁵	Burch et al. (2008) ²⁶	Tugay et al. (2007) ²⁷	Adedoyin et al. (2005) ¹¹

Table 2 Methodological quality of the included articles (PEDro scale).

Author (years)	Rajfur et al. (2017) ¹⁵	Acedo et al. (2015) ²²	Koca et al. (2014) ²⁷	Atamaz et al. (2012) ²⁴	Facci et al. (2011) ²⁵	Burch et al. (2008) ²⁶	Tugay et al. (2007) ²⁷	Adedoyin et al. (2005) ¹¹
Between-group difference reported	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Intention to treat analysis	No	No	No	Yes	Yes	No	No	No
>85% follow up	Yes	No	No	Yes	Yes		Yes	Yes
Assessor blinding	No	No	No	Yes	Yes	Yes	No	Yes
Therapist blinding	No	No	No	No	No	No	No	No
Subject blinding	No	No	No	Yes	No	Yes	No	No
Similarity at baseline	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Concealed allocation	Yes	Yes	Yes	Yes	Yes	Yes	No	No
Randomized allocation	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

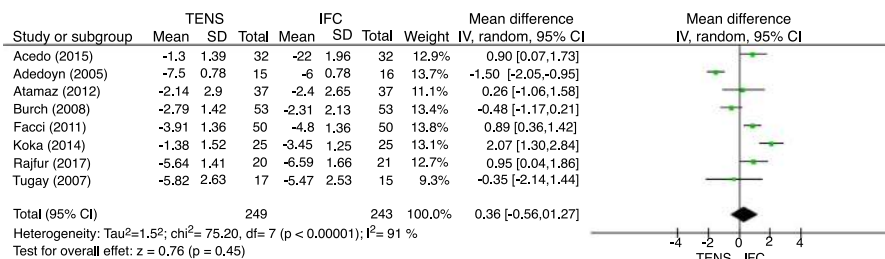


Figure 2 Comparison between IFC and TENS modalities for pain – visual analog scale (VAS).

mechanisms involved in IFC therapy, it is well known that TENS therapy reduces hyperalgesia using central as well as peripheral mechanisms.³²

Curiously enough, some studies,^{22,23,26,27} found that IFC therapy has a tendency to be better than TENS in controlling pain^{23,27} regarding WOMAC scores²⁶ and in reducing pain medication intake,²⁴ however, a statistical difference was not detected. IFC therapy used to treat carpal tunnel syndrome was able to significantly improve functional capacity, pain severity and even median nerve latency and conduction velocity.²⁷ Considering acute effects, Tugay et al.²⁷ found statically superior effects of IFC in reference to low back pain immediately after ES and 8 h after its application, but that difference disappeared 24 h after ES application. Zeng et al.³³ have considered the benefits of TENS, but concluded that IFC appears to be a more promising therapy for pain relief. As no consistency was found, studies evaluating both currents and its mechanisms of control could help elucidate this matter.

Regarding pain type, only Tugay et al.²⁷ assessed acute pain as the main dysfunction (clinical diagnosis). Since TENS and IFC therapy could lead to muscle relaxation²² and pain reduction^{22,27,34} even for a brief period of treatment, more studies should be encouraged. Chronic pain evaluation was more consistent and overall effective, only Adedoyin et al.¹¹ reported no additional effects of TENS or IFC when compared to exercise alone as did Palmer et al.⁹ Regarding knee osteoarthritis (WOMAC), beneficial and promising results were found by Atamaz et al.²⁴ and Burch et al.²⁶ Chen et al.³⁵ and Cherian et al.³⁶ also demonstrated improvements in pain with TENS therapy, along with significant improvement in quadriceps strength.³⁶ Regarding chronic lower back pain (RMDQ), functional improvements were observed by Rajfur et al.,¹⁵ Facci et al.²⁵ and Tugay et al.²⁷ regardless of ES type. Recently, Rajfur et al.¹⁵ performed a wider evaluation and compared five ES types (conventional TENS, acupuncture-like TENS, high-voltage electrical stimulation, IFC and diadynamic current) finding no difference between them, except for diadynamic current which did not promote any such benefit.

It is important to emphasize that variations in intensity and treatment duration could have compromised these studies. Even though stimulation intensity and maintenance are key factors for the success of the treatment,³⁷ it was not described in most studies, and it was only periodically adjusted to maintain sensory threshold by two studies.^{11,15} This lack of standard may lead to analgesic tolerance³³ and to greater pain relief when given at the strongest possible intensity.³⁴ Additionally, even though the majority of the studies^{11,15,23,24,26,27} analyzed patients with a higher BMI (body mass index) and considering that subcutaneous adipose tissue appears to affect current intensity,³⁸ results were similar with eutrophic patients. Current literature on both humans and animals show that the repeated use of TENS at the same dosage and electrode position reduces a hypoanalgesic effect on the fourth and fifth consecutive days of application.^{39,40} Besides, other elements such as interaction with medication use, pain populations, timing of outcome measures, clinical design and comparison groups may also negatively influence TENS efficacy.⁴¹ In addition, four studies^{15,22,26,27} did not mention electrode sizes for each current (the remaining varied from 3.5 to 8 cm). Even though

electrode position did not appear to influence pain,³⁷ a linear and direct relationship between treatment area and energy could be conceded⁴² and results could have been influenced

Qualitative analysis of PEDro demonstrated that none of the selected studies performed a triple-blinding methodology (subject, therapist and assessor). Holman et al.⁴³ emphasizes that even though strong evidence supports blind data assignment and medical science, progress depends on high quality methodological studies, and such methodological quality is not prevalent. Since non-blinded studies often have larger effect sizes, smaller *p*-values and a higher frequency of significant results simply because researchers previously expected such conclusions,^{32,44} rigorous studies with blinded evaluations should be enforced to avoid false results.

Limitations

Finally, some limitations appear from a highly sensitive research strategy to identify trials. Following the Cochrane Collaboration recommendations,⁴⁵ it is possible that some trials were published in local databases and consequently were not included in this review; also, this study did not involve TENS or IFC therapy alone or compared to sham or control therapy analysis. Searches were supplemented by the identification of potential eligible studies from hand searching as well as from clinical trial registers. Moreover, the methods used by studies to evaluate ES effectiveness are heterogeneous, making it difficult to compare outcomes among studies. Variations in kilohertz frequency, pulse duration, electrode size and intensity⁴⁶ could have influenced the results (Table 1). The correct description of intensity, electrode size and the standardization of ES parameters used could help to determine the most effective and appropriate current for pain modulation.

Conclusion

Current evidence suggests that TENS and IFC have similar global effects on pain and positive effects on function in both WOMAC and RMDQ questionnaires. However, the methodological quality of the current literature is very heterogeneous in several key areas. Future larger, well-designed and standardized studies are needed to establish the best parameters to modulate pain.

Conflicts of interest

The authors declare no conflicts of interest.

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