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REVIEW ARTICLE

Transcutaneous electrical nerve stimulation in the treatment of pain in breast cancer patients: systematic review

Estimulação elétrica nervosa transcutânea no tratamento da dor em pacientes com câncer de mama: revisão sistemática

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ABSTRACT

BACKGROUND AND OBJECTIVES: Breast cancer is the second most common type of cancer affecting the female population worldwide. Its treatment is multidisciplinary and entails a series of adverse effects such as acute or chronic pain. The objective of this study was to evaluate the effectiveness of transcutaneous electrical nerve stimulation (TENS) in the treatment of pain in breast cancer patients.

CONTENTS: The indexed databases Pubmed, Web of Science, Embase, Latin American Health Sciences (LiLACS), ProQuest, gray literature, Google Scholar and Open Grey were included. There were no limitations on the search period or language. The risk of bias was assessed using the Cochrane ROB2 tool. The primary outcome was pain intensity and the secondary outcome was quality of life. Initially, 501 records were found, 392 in the main indexed databases and 109 in the gray literature. Finally, 4 studies were included in this review, all randomized clinical trials.

CONCLUSION: The findings of this review indicate that TENS current can be an effective approach to reducing pain in breast cancer patients, without interfering with quality of life.

KEYWORDS: Breast neoplasms, Electric stimulation, Pain measurement.

RESUMO

JUSTIFICATIVA E OBJETIVOS: O câncer de mama é o segundo tipo de câncer que mais afeta a população feminina no mundo todo. Seu tratamento é multidisciplinar e acarreta uma série de efeitos adversos, como a dor aguda ou crônica. O objetivo deste estudo foi buscar avaliar a eficácia da estimulação elétrica nervosa transcutânea (TENS) no tratamento da dor em pacientes com câncer de mama.

CONTEÚDO: Foram incluídas as bases de dados indexadas, Pubmed, *Web of Science*, Embase, Ciências da Saúde da América Latina (LiLACS), *ProQuest*, e literatura cinzenta, *Google Scholar e Open Grey*. Não houve limitação de período para busca e nem idioma. O risco de viés foi avaliado utilizando a ferramenta da Cochrane ROB2. O desfecho primário foi a intensidade da dor e o desfecho secundário foi qualidade de vida. Inicialmente foram encontrados 501 registros, sendo 392 nas principais bases de dados indexadas e 109 na literatura cinzenta. Ao final, foram incluídos 4 estudos nesta revisão, todos ensaios clínicos randomizados.

CONCLUSÃO: Os achados deste estudo indicam que a corrente TENS pode ser uma abordagem eficaz para a redução da dor em pacientes com câncer de mama, sem interferências na qualidade de vida.

DESCRITORES: Estimulação elétrica, Medição da dor, Neoplasias da mama.

HIGHLIGHTS

- Breast cancer can cause painful complications and functional limitations, requiring effective pain management strategies
- TENS appears to be a promising physiotherapeutic resource for reducing neuropathic pain in women with breast cancer, although results on quality of life are still inconclusive
- The available evidence is limited and at risk of bias, indicating the need for more robust studies to define protocols and confirm the efficacy of TENS in this population

INTRODUCTION

Breast cancer (BC) is characterized by the disordered multiplication of breast cells, leading to the formation of a tumor. This is a more common type of cancer and causes the highest number of deaths in women[1]. It is a heterogeneous disease with environmental and genetic factors involved, and therefore, several therapies based on genetic and molecular developments have been studied[2]. The most common forms of treatment to contain the disease are surgery, radiotherapy, and chemotherapy, in addition to endocrine therapy[3].

There are several complications associated with the disease and also sequelae from treatment, such as limited range of motion of the ipsilateral shoulder, scar adhesion, seroma, dehiscence, lymphedema, dysesthesia and pain in the shoulder, axillary, and lateral chest wall[4,5]. In other words, the treatment of BC can lead to various complications, including persistent pain and functional limitations, with pain reported in 21% to 55% of cases, affecting patients before and after surgery, which is often related to concentrations of pro-inflammatory cytokines, as well as postoperative repercussions related to neuropathic pain, myofascial pain, rotator cuff dysfunction, and adhesive capsulitis, in addition to lymphovascular disorders[6-8]. Pain, being a subjective and multifactorial experience, can significantly impact quality of life of the patient, requiring effective approaches for its managemen[9].

Among the strategies available in the field of physical therapy, transcutaneous electrical nerve stimulation (TENS) has stood out as a noninvasive therapeutic resource capable of modulating pain signals and improving functionality[10-12]. However, despite evidence pointing to benefits in reducing neuropathic pain, such as post-mastectomy pain syndrome[13], there is still debate in the literature about its real effectiveness and the mechanisms involved, such as analgesic effects through the gate control theory, action on serotonin and β-endorphin, on peripheral and central sensitization, and even anti-inflammatory drugs, based on a possible rebound effect on the dorsal root reflex[14-20]. Thus, it is important to further study this approach in order to optimize protocols and expand its use in the context of rehabilitation of patients with BC. Therefore, the present study's objective was to conduct a systematic review on the use of TENS for pain reduction in women undergoing treatment for BC.

CONTENTS

Study design

This study was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement and registered with the Open Science Framework (OSF) under DOI 10.17605/OSF.IO/PC9T2.

Eligibility criteria

The acronym PICOS was used to formulate the question focused on in this study: P - population (women with breast cancer); I - intervention (TENS); C - comparison (placebo, sham, or pharmacological group); O - outcome (primary outcome - pain intensity; secondary outcome - use of drugs); S - study type (randomized clinical trials).

Women with BC, aged over 18, who complained of pain during treatment (chemotherapy or post-surgery), regardless of the time of diagnosis, and who had undergone TENS intervention were included in the study. The Visual Analog Scale (VAS) was used to evaluate pain. Studies were included without time or language restrictions for the search. Studies whose texts were not available in full were excluded. Duplicate studies that did not present results were also excluded.

Information source

The indexed databases used were: PubMed, *Biblioteca Virtual em Saúde* (BVS - Virtual Health Library), Web of Science, Embase, PEDro, and LiLACS. The gray literature was also searched using Google Scholar.

Search strategy

The keywords from Medical Subject Headings (MeSH) and Health Sciences Descriptors (DeCS) from the BVS website were used: "Breast Neoplasms" or "Breast Neoplasm" or "Breast tumor" and "transcutaneous electrical nerve stimulation" or "TENS."

Study selection

The software Rayyan QCRI (Qatar Computing Research Institute) and EndNote Web were used to collect references and exclude duplicates.

The included records were selected by two independent reviewers (R1 and R2) in two phases. In the first phase (phase 1), the two reviewers evaluated the titles and abstracts according to the eligibility criteria; in the second phase (phase 2), the reviewers analyzed the full texts and selected the articles according to the same criteria as in phase 1. In cases of disagreement, a third reviewer (R3) participated before the final decision was made in both phases.

Individual assessment of risk of bias in studies

Risk of bias was assessed using the Cochrane tool, ROB 2, by two blinded reviewers, R1 and R2. Disagreements were resolved by R3. All included studies were assessed in five domains: deviations from planned interventions, lack of data in the results, measurement of results, selection of reported studies, and overall result of bias analysis. Each domain had an overall result: low risk, some concerns, or high risk.

RESULTS

This review included four primary studies that met the eligibility criteria on the effectiveness of TENS for pain control in patients with BC.

Study selection

During the search, 501 records were found, 392 in the main indexed databases and 109 in the gray literature. The search was conducted on December 20, 2024, in all databases. Of the total, 50 duplicate studies were automatically and manually excluded. Finally, 342 studies remained for Phase 1 (reading of titles and abstracts) and four studies for Phase 2 (full text reading), all of which were included (Figure 1).

Table 1 summarizes the most important findings from the clinical trials included in this study (n=04).

Studies characteristics

With regard to the population analyzed, the studies included only women affected by BC, who had undergone mastectomy or not, aged between 38 and 69 years, totaling 122 individuals. A reference study[21] analyzed patients who suffered from chemotherapy-induced peripheral neuropathy after mastectomy, summing up a total of 30 participants. Reference authors[22] analyzed 41 patients with a history of BC and chronic pain for at least six months after cancer treatment. Other authors[5] included women who underwent mastectomy associated with axillary lymphadenectomy (AL), totaling 33 participants. Finally, another group of researchers[23] analyzed patients who reported pain resulting from intercostobrachial nerve (ICBN) injury, totaling 18 women.

Assessment instruments and intervention protocol

The authors[21] compared, over a period of 12 weeks, treatment with ice packs on the ankles three times a week in two 15-minute sessions separated by a 45-minute interval. The other group received TENS on the lower limbs, with one electrode positioned at the lower edge of the medial tibial condyle and the other three inches above the medial malleolus, with the second channel following the same parameter on the contralateral limb. The device was turned on and adjusted to create contraction under the electrodes (moderate intensity), with a frequency of 15 Hz and a phase duration of 250μs, for 30 minutes, three times a week. The VAS was used as the measurement instrument in this study. Although there was a reduction in pain and improved sural nerve conduction velocity in the TENS group, the use of cryotherapy showed better results.

In the study[22], all volunteers received three interventions (TENS, TSE, and placebo) in a cross-over manner. The authors mention that TENS was used continuously, generating strong but comfortable paresthesia, with no indication of other parameters. For transcutaneous spinal electroanalgesia (TSE) and placebo, patients were instructed to place two electrodes at the paravertebral level of C3-C4 and two electrodes on the spinous processes of T1 and T10, for 10 to 30 minutes, at maximum intensity and frequency varying according to the moments of experienced pain.

A three-week period was stipulated for each intervention, with one week of "cleaning." Patients were also instructed to keep a diary with the date and time of use, parameters used, percentage of pain relief, and analgesics used. They received weekly phone calls during the intervention and a personal evaluation after the three weeks described above. The Brief Pain Inventory (BPI), Hospital Anxiety and Depression Scale (HAD), VAS, and analgesic consumption were used as measurement instruments. All interventions had beneficial effects on pain and quality of life, with little evidence that active therapies were better than placebo.

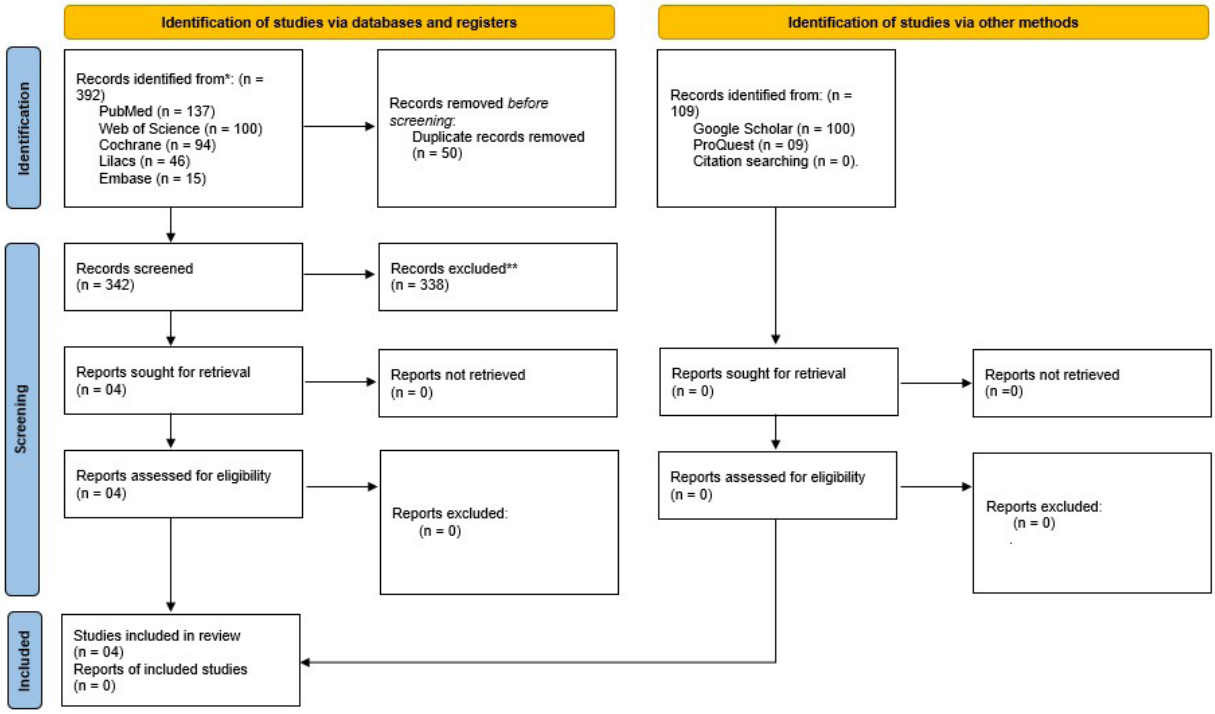

Figure 1. PRISMA flowchart, showing searchs, refinement, and the total number of analyzed studies.

Table 1. Selection of included studies.

Eligible studies/ Country	Sample description	Intervention protocol	Body area	Period of evaluation	Outcomes/ Measuring instruments	Post-intervention results (Mean + Standard deviation/p-value)	Conclusion
Elshinnawy et al.[21] Egypt	n= 30. CG: (n=15) EG: (n=15) Gender: Female Mean Age: (45 an 65 years).	GC: Cold + drug. GE: TENS.	LL	T0: Start. T1: 12 weeks.	VAS	CG: Pain reduction of 70.83%, 44.12% increase in sural nerve amplitude (p<0.05). EG: Pain reduction of 55.17%, increase in sural nerve amplitude of 26.87% (p<0.05).	The application of cold has a better effect on pain in post-mastectomy PDIC.
Robb et al.[22] United Kingdom	n= 41 GP1= 9 GP2=6 GP3=9 GP4=10 GP5=7 GP6=8 Gender: Female Mean Age: (38 to 60 years).	Gp1) TENS, TSE, Pl; Gp2) TENS, Pl, TSE; Gp3) TSE, TENS, Pl; Gp4) TSE, Pl, TENS; Gp5) Pl, TSE, TENS; Gp6) Pl, TENS, TSE.	Thoracic region and upper limb.	T0: 3 months. T1: 6 months. T2:12 months.	HAD, BPI, VAS and analgesics intakes.	No statistically significant difference between groups (p>0.05). All groups reported pain relief and improved quality of life, possibly due to placebo effect and psychophysical interactions of the treatment.	None of the interventions were superior to placebo. More research is needed to prove the effectiveness of TENS and TSE in chronic pain associated with breast cancer.
Mendonça et al.[5] Brazil	n= 33 EG: (n=16) CG: (n=17) Gender: Female Mean Age: (40 to 62 years).	GE: TENS GC: placebo	ICBN	T0 T1: After 20 days.	VAS	Dysesthesia decreased significantly in the active TENS group (p<0.006). There were no statistically significant differences in quality of life between the groups (p>0.05).	TENS reduced dysesthesia in the ICBN, but did not improve patients' quality of life.
Silva et al.[23] Brazil	n=18 GA: (n=9) GB: (n=9) Gender: Female Mean Age: 43 to 69 years old.	GA: acupuncture TENS. GB: burst TENS.	Intercostobrachial region (shoulder and armpit area affected by mastectomy).	T0: before application. T1: after application.	VAS	The TENS Acupuncture group showed an 88.4% reduction in pain, while the TENS Burst group showed a 66.3% reduction. There was electrical modification in the somatosensory cortex.	TENS promoted electrocortical changes and pain relief in patients with intercostobrachial pain. Future studies should investigate other brain wave patterns.

BPI = Brief Pain Inventory; VAS = Visual Analog Scale; CG = control group; EG = experimental groups. HAD = Hospital Anxiety and Depression; LL = lower limbs; ICBN = intercostobrachial nerve; TENS = transcutaneous electrical nerve stimulation; TSE = transcutaneous spinal electroanalgesia.

In another study[23], the authors placed electrodes on the intercostobrachial nerve dermatome in women undergoing axillary lymphadenectomy. Using a portable TENS device, they set the parameters to a frequency of 100 Hz and a phase duration of 100 μs, and the current was increased to the maximum sensory level tolerated by the patient. In the placebo TENS group, the device was set to interrupt the current after 45 seconds of stimulation. For evaluation, the following measurement instruments were used: esthesiometer, dysesthesia intensity with VAS, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - EORTC QLQ-C30, and breast cancer module - EORTC QLQ-BR23 questionnaires. A reduction in pain intensity was observed, but no improvement in quality of life.

Finally, another group of authors[24] chose to use burst TENS and acupuncture TENS methods. The acupuncture TENS device was preprogrammed for automatic frequency and intensity, with a descending phase duration of 275 to 175 μs and a progressive increase in frequency from 5 to 25 Hz over a period of 12.5 seconds. The TENS burst, in turn, was programmed with 7 pulses of 28 ms cycle-on and 472 ms cycle-off (2 Hz) and a phase duration of 150 μs. The study used electroencephalograms to visualize brain activity and VAS to assess pain as evaluation instruments. They report that there was a change in electrical activity in the parietal region, and a reduction of pain.

Risk of bias analysis

The risk of bias evaluation showed that 50% of the studies had a low risk and the other 50% had some concerns regarding randomization. In deviations from intended interventions, the result was 75% of some considerations and 25% of high risk. Regarding missing outcome data, all studies presented low levels of risk. For outcome measures, all studies presented high risk. For outcome selection, 50% presented a high risk, 25% presented some concerns, and the other 25% presented low risk of bias.

Thus, the result was that 25% of the studies presented some concerns and the other 75% presented high risk (Figure 2).

Figure 3 presents an individual assessment of bias risk, highlighting methodological quality in five domains of Rob2.

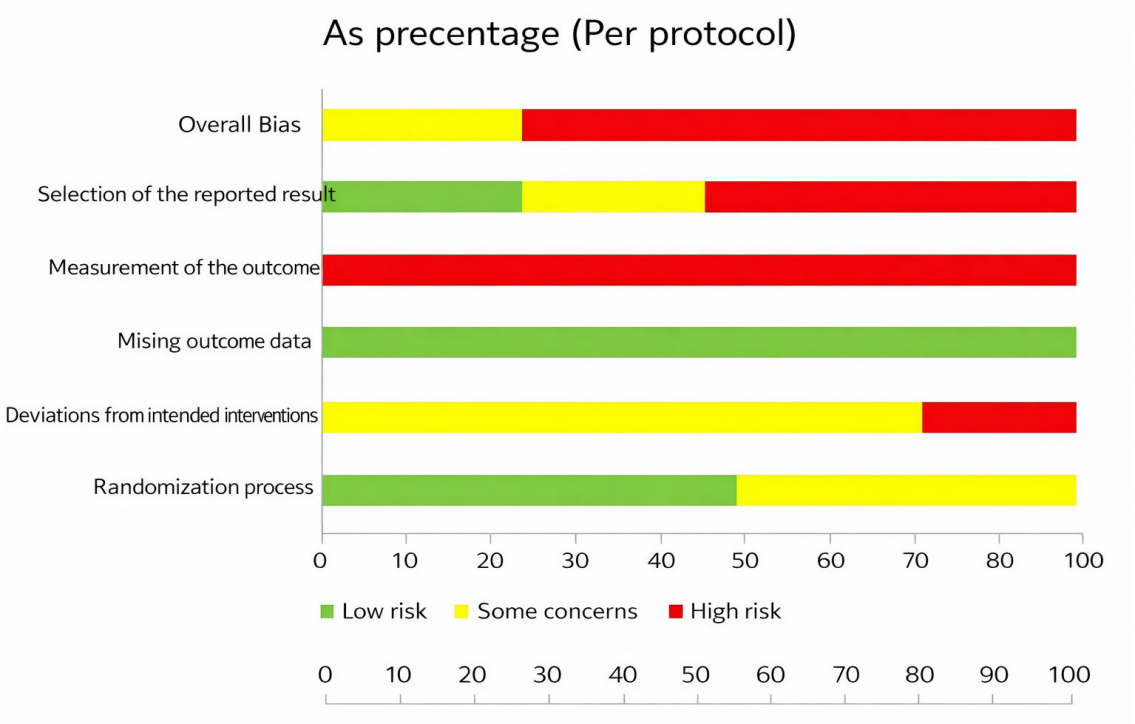

Figure 2. Risk of bias: review of the authors' judgments on each risk of bias item presented as percentages in all included studies.

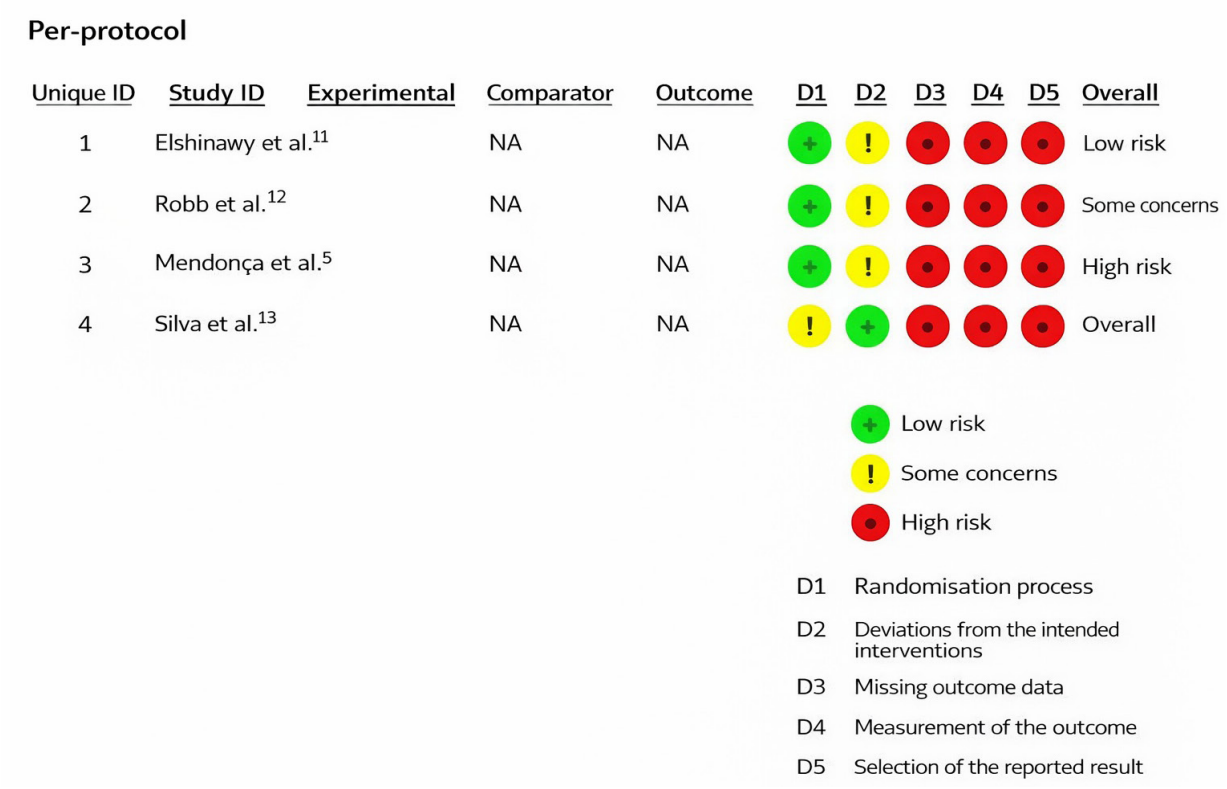

Figure 3. Summary of bias risk: analysis of the authors' judgments on each bias risk item for each included study.

DISCUSSION

TENS has been used as a treatment option for pain relief in cancer patients, both due to the direct pain caused by cancer and the effects of therapies such as chemotherapy[25]. Thus, the present study reviewed studies in which TENS was used in patients with BC, seeking to analyze its effectiveness in reducing neuropathic pain and improving patients' quality of life.

TENS is a non-invasive technique widely used in physical therapy for the relief of acute and chronic pain. Its mechanism of action is based on the gate control theory of pain, which suggests that electrical stimulation of large-diameter afferent nerve fibers can inhibit the transmission of pain signals to the brain. There is evidence that TENS may be effective in managing neuropathic pain, such as post-mastectomy pain syndrome, contributing to the reduction of dysesthesia and improvement in patient functionality.

Furthermore, there is evidence that TENS can induce electrocortical modifications, reducing neural activity associated with pain and promoting analgesia[25-28]. Stimulation of endogenous opioid release has also been shown to be related to the use of TENS, thus producing descending analgesia[20]. In addition, repeated stimulation may be able to reduce pain related to peripheral and central sensitization[17]. Peripherally, it can even produce effects by reducing the dorsal root reflex, thus having possible anti-inflammatory effects[14,15]. However, despite these mechanisms, it should be understood that pain arising from cancer is not only complex but also multidimensional, and to date, there is no clarity about the effects of TENS for adult patients[29].

The study[21] compared cryotherapy with TENS in chemotherapy-induced peripheral neuropathy in post-mastectomy patients. The results showed that cold application was more effective in reducing pain (70.83%) compared to TENS (55.17%). In study[22], no significant differences were found between TENS, TSE, and placebo in pain reduction. Study[5] researched the effectiveness of TENS on dysesthesia and quality of life in women after BC surgery. The conclusion was that, although TENS significantly reduced the intensity of dysesthesia, there was no significant improvement in the participants' quality of life. Finally, study[23] evaluated the effects of TENS on post-mastectomy intercostobrachial pain. The results indicated a significant reduction in pain in the groups treated with TENS.

In this systematic review, only four studies were included, which presented in general a high risk of bias. It can be inferred that TENS may be an effective tool in reducing post-mastectomy neuropathic pain, especially for the treatment of intercostobrachial pain and dysesthesia. However, its influence on quality of life has not yet been shown to be beneficial, suggesting that it should be used in conjunction with other treatment approaches for more effective management of symptoms associated with BC.

The limitations of this study include the small number of primary articles, as well as the lack of delimitation of the use of TENS as a therapy for pain caused by cancer or as a sequela of its treatment, which would result in an even smaller number of primary articles for analysis. Thus, more high-quality primary studies are needed to better understand the neurophysiological mechanisms involved and determine optimized protocols for different patient profiles. It is suggested that studies with dosimetric standards be conducted to obtain more evidence on the actual therapeutic effects.

CONCLUSION

The findings of this review indicate that TENS may be an effective approach for pain reduction in patients with BC, especially for intercostobrachial pain and postmastectomy dysesthesia. However, its influence on quality of life did not result in therapeutic advantages. Caution should be exercised with these findings, as there was a limited response from the literature search.

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AUTHORS' CONTRIBUTIONS

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