Transcutaneous electrical nerve stimulation for relieving acute pain in the prehospital setting: a systematic review and meta-analysis of randomized-controlled trials

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Although medics in many services are equipped with pharmacological analgesia, legislative or logistical restrictions in some systems result in the need to rely on nonpharmacological avenues for the management of acute pain. Transcutaneous electrical nerve stimulation (TENS) has been proposed as an alternative to analgesic medication that could be feasible and effective in the prehospital setting. The aim of this systematic review was to determine the effectiveness and safety of TENS when administered by medics to patients with acute pain in the prehospital setting. A systematic literature review was carried out to identify randomized-controlled trials investigating the safety and efficacy of TENS compared with 'sham' (placebo) TENS in the prehospital setting. Quality assessment of included studies was carried out to identify potential for bias. Qualitative and quantitative synthesis of results was performed to determine effectiveness and safety. The studies included were meta-analysed using a random-effects model to produce pooled results for comparison of the mean post-treatment pain scores using a visual analogue scale (VAS). Four studies were included in the analysis, all of which were prospective clinical trials of good methodological quality. Meta-analysis indicated that TENS produced a clinically significant reduction in severity of pain [mean VAS reduction 38 mm (95% confidence interval 28–44); $P<0.0001$] for patients with moderate-to-severe acute pain. TENS produced post-treatment mean pain scores that were significantly lower than 'sham' TENS [33 mm VAS (95% confidence interval 21–44); $P<0.0001$]. TENS was also effective in reducing acute anxiety secondary to pain. No safety risks were identified. When administered by medics in the prehospital setting to patients with acute pain, TENS appears to be an effective and safe nonpharmacological analgesic modality that should be considered by emergency medical services organizations in which pharmacological pain management is restricted or unavailable. *European Journal of Emergency Medicine* **21:10–17 © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Introduction

Provision of analgesia to patients with acutely painful presentations is a common function of ambulance medics. In most developed countries, ambulance medics have pharmacological analgesics available to them; however, there are many situations in which the administration of medicinal drugs lies outside medics' scope of practice. Developing countries, for example, may not be in a position to provide trained prehospital providers with inhaled or parenteral pain relief agents. Some countries, for example those operating under a Franco-German model of emergency medical services provision, also place legislative restrictions on medics that render provision of pharmacological analgesia infeasible [1]. Against this background, novel nonpharmacological avenues of analgesia such as active warming [2–5], acupressure [6–8] and transcutaneous electrical nerve stimulation (TENS) [6–9] have been explored in the prehospital setting to enhance frontline pain management capability.

TENS first came to prominence in the 1970s, quickly proliferating as an analgesic across a range of pain aetiologies. Its mechanism of action is grounded in the 'gate control' theory of pain transmission as described by Melzack and Wall [10]. The analgesic effects arise from the electrical stimulation of non-noxious afferent nerve fibres in the skin, acting to inhibit the transmission of nociceptive responses through the dorsal horn of the spinal cord. This effectively 'closes the gate', thereby decreasing transmission of pain signals from the source of acute pain in the periphery to the central nervous system [11].

Although shown to be effective in some individual studies, rigorous systematic reviews investigating the effectiveness of TENS for arthritic pain, cancer pain, labour pain, back pain and acute traumatic pain have been unable to show a clear benefit [12–16]. Despite being the subject of several prehospital clinical trials, no systematic review has, to the best of our knowledge, investigated the effectiveness and safety of TENS when administered by medics in the prehospital setting.

The aim of this systematic review was to investigate the effectiveness of TENS, compared with 'sham' (i.e. placebo)

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TENS, for relieving acute pain and anxiety when performed by medics in the prehospital setting.

Methods

This systematic review and meta-analysis was carried out and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines [17].

Eligibility criteria

To be considered eligible for inclusion, studies were required to fulfil five criteria: (a) use a prospective parallel randomized-controlled trial design; (b) compare 'real' TENS with 'sham' TENS; (c) be performed by medics in the prehospital setting; (d) report an outcome of pain reduction; and (e) have a patient population older than 18 years of age presenting with acute pain.

Literature search and study selection

A systematic literature search was carried out to identify potentially relevant studies by two investigators with postgraduate training in literature searching. Exhaustive electronic searches were performed of the following databases: Cochrane Database of Systematic Reviews (inception to December 2012); ACP Journal Club (1991 to December 2012), Cochrane Database of Abstracts of Reviews of Effects (inception to 4th Quarter 2012); Cochrane Central Register of Controlled Trials (inception to December 2012), Cochrane Methodology Register (to 4th Quarter 2012); Medline and Pre-Medline (inception to December Week 4, 2012); EMBASE (inception to 15 December 2012); and CINAHL (to December, 2012). Keywords ('tens', 'pain', 'analgesia', 'sham') and exploded MeSH terms ('pain', 'analgesia', 'transcutaneous electrical nerve stimulation') were used as required to create a PICO-based search strategy with a validated prehospital specific search filter [18]. A methodological search filter was not used. The search was last run on 15 December 2012. The reference lists of these studies were handsearched to identify additional studies that may not have registered on the electronic search. We restricted the search to studies published in English and French as the authorship team had no further capacity for translation and to published studies. We excluded conference abstracts as they were deemed to contain insufficient information to allow a proper methodological assessment of validity and bias.

Selection of studies for inclusion was performed independently by two investigators and arbitrated by a third in the event of disagreement. The online citations of studies identified in the search were screened for relevance and full-text copies of potentially relevant studies were retrieved for assessment of eligibility against the previously mentioned criteria. All authors agreed on the final selection.

Data extraction

Data extraction was performed independently by two authors. Where discrepancies in data were identified, a third author reviewed the data.

Assessment of risk of bias

Risk of bias assessment was performed independently by two authors, and arbitrated by a third in the event of disagreement, using Cochrane Collaboration's tool for assessing bias in randomized trials [19]. Potential for bias was assessed across several domains and classified as low, moderate or high risk for each domain. The domains assessed were random sequence generation, allocation concealment, blinding of personnel, blinding of participants, blinding of outcome assessment, incomplete outcome assessment and selective reporting.

Assessment of heterogeneity

Before being included in the quantitative synthesis of data (i.e. meta-analysis), studies were assessed for clinical heterogeneity. For those included in the meta-analysis, visual assessment of heterogeneity was carried out using a forest plot and statistical assessment was carried out using Higgins' I^2-statistic [20].

Outcomes

The primary outcome was difference in the mean final pain score between real and sham TENS, reported in millimetres using a visual analogue scale (VAS), determined on arrival at hospital. The mean reduction in pain score for patients who received 'real' TENS was also calculated. The secondary outcome was safety of TENS, determined by the frequency and type of adverse effects and impact of TENS on physiological variables.

As all studies included reported data on pain-related anxiety, a post-hoc decision was made to analyse the difference in the mean final anxiety score between real and sham TENS and the mean reduction in anxiety following treatment with real TENS.

Statistical analysis

Statistical analysis was carried out using Revman 5.1 [21]. The meta-analysis was carried out using a random-effects model to report the difference in the mean final pain and anxiety score in millimetres (VAS) with a 95% confidence interval (CI) for real compared with sham TENS and for mean reduction in pain and anxiety following real TENS. Statistical assessment of publication bias was not performed because of the unreliability of these methods with small numbers of included studies [22].

Ethical approval

As this study was a review of published studies, none of which used potentially identifiable information, ethical approval from a lead human research ethics committee was not required.

Results

Study selection and search results

The initial search strategy used for the Medline database produced 11 citations for screening. Of these, seven were excluded because of not fulfilling the eligibility criteria. Hand-searching of the remaining three articles identified another study that fulfilled the criteria for inclusion. The additional searches of other resources detailed previously produced duplicates of the four identified articles, but no new studies. At completion of the literature-searching process, there were four randomized-controlled trials eligible for inclusion, enrolling a total of 261 patients [6–9]. The results of the search strategy are detailed in Fig. 1.

Study characteristics

The characteristics of the studies included are summarized in Table 1. All studies were published in English and were from European countries. All studies were homogenous with respect to study design and methodology using similar procedural protocols for the study process. All studies used the same high-frequency (100 Hz), low-amplitude (2 mA) 'dose' of TENS. In all four studies, the placebo (sham) group had the equipment applied but received no electrical stimulation. The outcomes (reduction in pain severity and reduction in anxiety) and their measurement were common across all studies, using a VAS to rate before and after pain and anxiety severity. The initial and final pain score was determined by the same medic who was blinded to group allocation throughout. No concurrent analgesics were administered in any study and all excluded patients who had received any analgesic within the previous 48 h. Although the initial pain severities were similar across the included studies, each study investigated a different aetiology of pain: acute renal colic [6], acute lower back pain [7], traumatic hip pain [8] and pelvic pain in women [9]. The duration of treatment and transport was similar for all studies. There was wide variation in the mean age of enrolled patients across studies. Initial pain severity and anxiety level was comparable across studies.

Risk of bias across included studies

The potential for bias was low in all included studies in the domains of random sequence generation, allocation concealment, blinding of personnel, incomplete outcome data and selective reporting. Randomization and group allocation were robust in all studies, with no differences in baseline characteristics for groups in each study. However, a moderate risk of bias was identified in relation to blinding of participants and outcome assessment. With respect to blinding and outcomes assessment, each study used a similar procedural protocol to incorporate blinding of the medic assessing outcomes and the patient. The medic assessing pain after treatment did not know which treatment the patient received, and had left the vicinity of the patient before treatment was initiated. On arrival at hospital, the medic blinded to the treatment allocation performed the outcome assessment in the absence of the treating medic. The patients were told that they may or may not experience a sensation during their treatment, and so were apparently unaware of the group to which they had been allocated. With respect to incomplete outcome data, none of the studies included carried out an intention-to-treat analysis, with all describing an 'a priori' decision to analyse using a 'per protocol' approach. In each study, a notable number of patients who had been enrolled randomized and had outcomes measured were retrospectively excluded if hospital diagnosis did not match the specific condition of interest. Lang and colleagues enrolled and randomized patients with acute traumatic hip pain, but excluded all those who did not have a confirmed fracture after hospital diagnosis. Similarly, Mora and colleagues enrolled patients with a history of kidney stones and acute lower back or lower abdominal/flank pain, but later excluded those not confirmed to have kidney stones. Again, Barker and colleagues enrolled female patients with acute severe pelvic pain, but later excluded those with confirmed nongynaecological aetiology. Finally, Bertalanffy and colleagues enrolled patients with lower back pain, but then excluded those who were diagnosed in the hospital as having pain not of spinal or musculoskeletal origin.

Primary outcome – effectiveness of transcutaneous electrical nerve stimulation for relieving pain

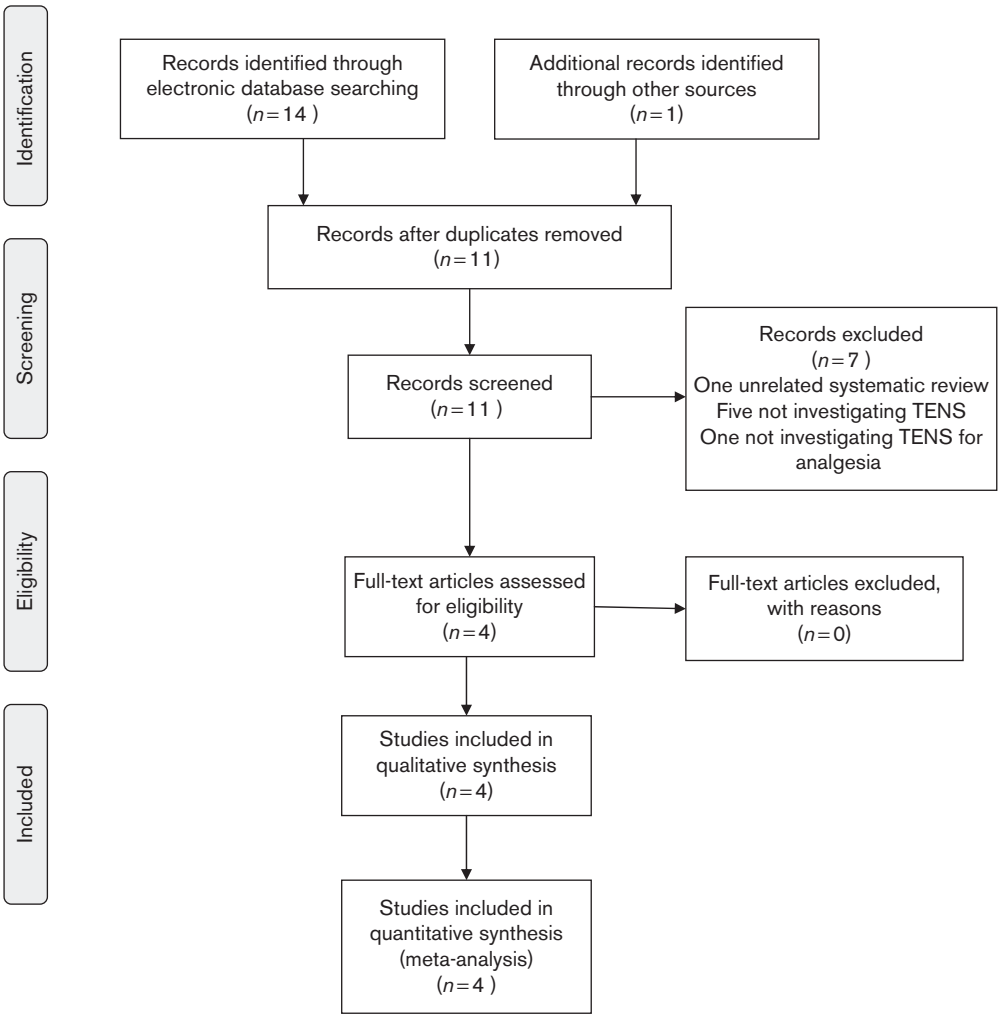
All studies included found that TENS led to statistically and clinically significant reduction in pain severity (Fig. 2). The smallest mean reduction was 30 mm, whereas the largest (50 mm) was seen in patients with renal colic [6]. In a pooled analysis of 128 patients who received real TENS in the included studies, TENS produced a reduction in the mean pain severity of 38 mm (95% CI 28–48; $P < 0.0001$). Significant heterogeneity was present ($I^2 = 94\%$). Sensitivity analysis showed that heterogeneity was most likely because of the study by Mora *et al.* [6], without which the heterogeneity reduced to a moderate level with little change to the summary estimate. The cause for the heterogeneity was uncertain, with no methodological or clinical differences across the included studies other than aetiology of pain.

Each study found significant differences in the mean final pain scores favouring TENS compared with sham treatment (Fig. 3). In the pooled analysis consisting of 261 patients, the difference in the mean final pain score between sham and real TENS was 33 mm (95% CI 21–4; $P < 0.0001$). There was a high level of heterogeneity ($I^2 = 94$).

Secondary outcome – effectiveness of transcutaneous electrical nerve stimulation for relieving anxiety

All four studies found TENS to be more effective than sham treatment in reducing patient-reported anxiety secondary to pain, with each reporting statistically

Fig. 1



Flow chart describing the identification and selection of studies. TENS, transcutaneous electrical nerve stimulation.

Table 1 Characteristics of included studies

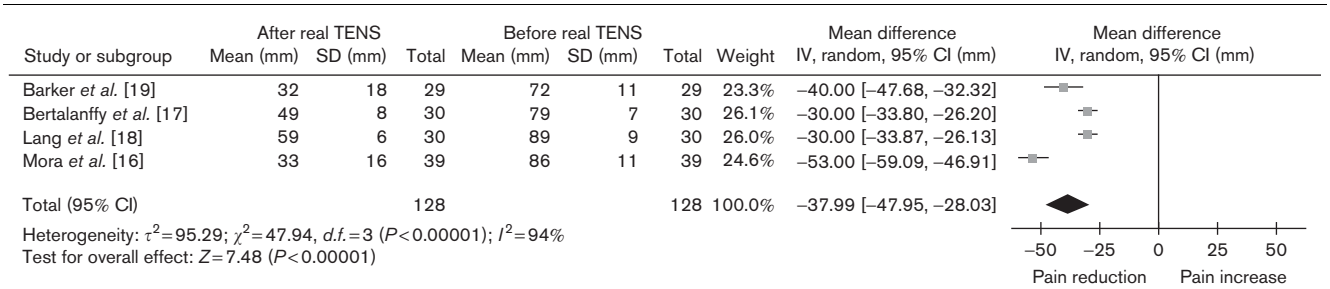
References	Country	Participants (*n*)	Population	Mean age (mean±SD) (years) (real/sham)	Initial pain (mm±SD) (real/sham)	Initial anxiety (mm±SD) (real/sham)	Concurrent use of analgesic drugs (Y/N)
Lang *et al.* [8]	Hungary	63	Adults >19 years with acute pain secondary to hip fracture of >60 mm severity	82±7/79±14	89±9/86±12	72±9/75±7	N
Mora *et al.* [6]	Austria	73	Adults (age range not stipulated) with acute renal colic >60 mm severity (VAS) secondary to urolithiasis presenting to paramedics	29±7/27±7	86±11/86±18	69±8/72±21	N
Bertalanffy *et al.* [7]	Austria	63	Adults >19 years with first episode of lower back pain with >60 mm severity (VAS) presenting to paramedics	47±7/49±6	79±7/76±16	82±8/85±6	N
Barker *et al.* [9]	Hungary	62	Women (age range not reported) with acute pelvic pain presenting to paramedics	24±5/26±4	72±11/69±13	59±11/57±9	N

N, no; VAS, visual analogue scale; Y, yes.

significant reductions in anxiety following real TENS (Fig. 4). In the pooled analysis involving four studies and 128 patients, real TENS produced a mean reduction in anxiety of 20 mm (95% CI 10–30; $P < 0.00001$).

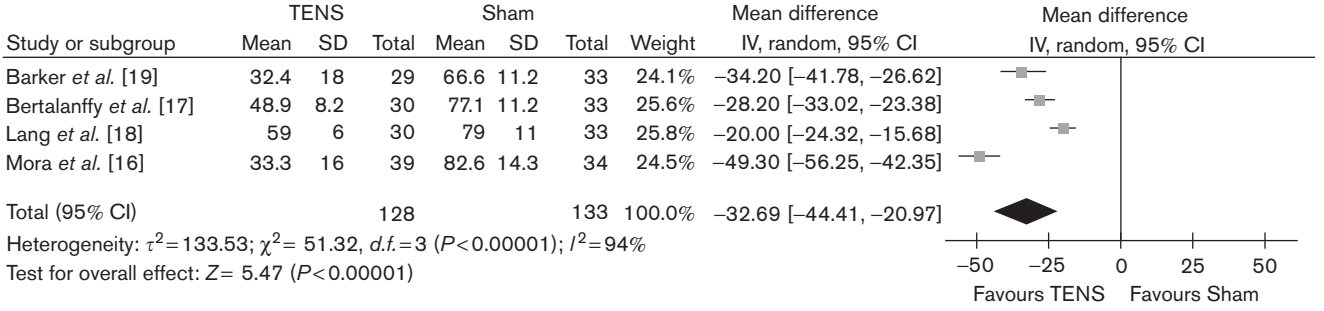
Each study found significant differences in the mean final anxiety score favouring TENS compared with sham treatment. In the pooled analysis of 261 patients (Fig. 5), real TENS produced a mean final anxiety score

Fig. 2



Forest plot for the outcome of difference in the mean reduction in pain score (mm) for patients receiving real TENS, reported on a VAS. CI, confidence interval; IV, inverse variance; TENS, transcutaneous electrical nerve stimulation; VAS, visual analogue scale.

Fig. 3



Forest plot for the outcome of pooled difference in the mean final pain score between real and sham TENS. CI, confidence interval; IV, inverse variance; TENS, transcutaneous electrical nerve stimulation.

26 mm lower than placebo TENS (95% CI 17–35; $P < 0.0001$). There was a high level of heterogeneity ($I^2 = 88\%$). As for the primary outcome, sensitivity analysis indicated the heterogeneity could be attributed to the study by Mora and colleagues, without which the heterogeneity reduced to a moderate level with little change to the summary estimate.

Secondary outcome – adverse effects and safety of transcutaneous electrical nerve stimulation

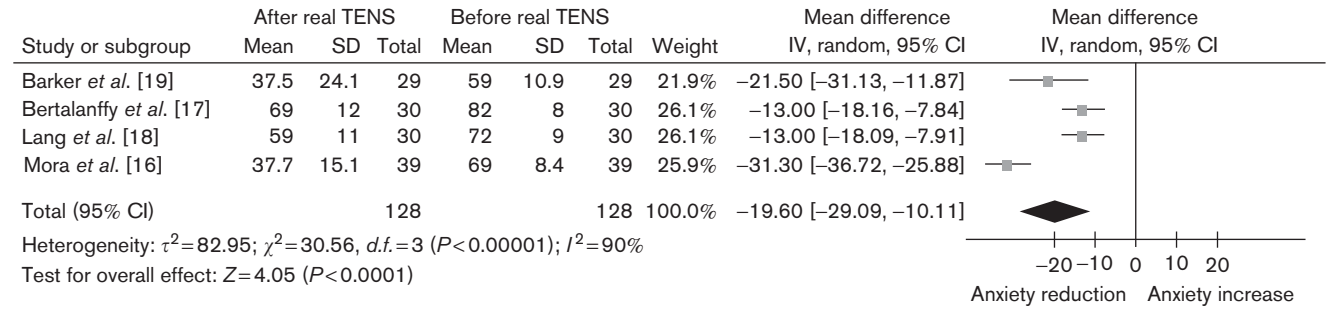
None of the studies included reported detailed data on adverse effects or complications arising from TENS, and none defined what type of adverse effects or complications, if any, were monitored for. No adverse effects were described in any study. Each study did report effects of TENS on vital signs, none of which appeared harmful. Statistically significant reductions in heart rate were reported for those who received TENS across all studies. Nonsignificant differences in blood pressure following TENS were reported across all studies.

Discussion

This systematic review provides evidence that, when compared with sham treatment, TENS could be an effective prehospital analgesic modality that leads to clinically meaningful reductions in acute pain for patients with moderate-to-severe pain of musculoskeletal and visceral aetiology.

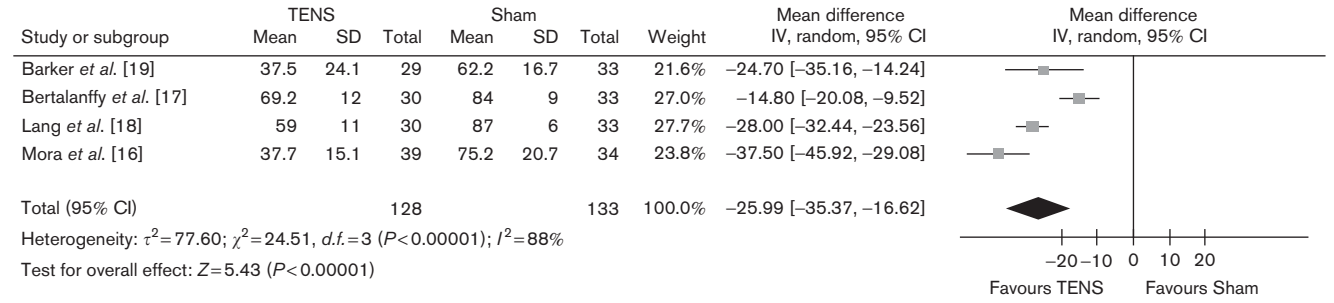
The meta-analysis of 261 patients confirms the individual findings of the four included studies in relation to pain and anxiety, and strengthens the generalizability of the results by including acutely painful presentations across a range of aetiologies. This result is in contrast to a 2009 Cochrane review by Walsh *et al*. [16], which was unable to confirm benefits of TENS for acute pain largely because of inconsistencies and missing data in the included studies. That review differs in many ways from the present study, making a comparison of findings difficult. First, we included only studies involving ambulance responses to patients with acute pain in which medics administered TENS at the scene. The Cochrane review included acute pain in diverse settings in hospital, clinics and in the patient's home, as well as TENS that was administered by healthcare providers or patients themselves. The present study examined the effectiveness of a one-off period of therapy over the short period of transportation to the emergency department, whereas the afore-mentioned review included acute pain over a period of several months with multiple, intermittent therapy

Fig. 4



Forest plot of the pooled results for the mean reduction in anxiety score (mm±SD) for patients receiving 'real' TENS. CI, confidence interval; IV, inverse variance; TENS, transcutaneous electrical nerve stimulation.

Fig. 5



Forest plot for the secondary outcome of pooled difference in the mean final anxiety score between real and sham TENS. CI, confidence interval; IV, inverse variance; TENS, transcutaneous electrical nerve stimulation.

periods. Interestingly, all four studies included in this analysis were excluded from the Cochrane review, the reason given being that the intensity of TENS stimulation delivered was below the minimum level defined in their inclusion criteria.

TENS as a prehospital intervention will have differing levels of relevance depending on the nature of the system in which it is being considered for use. Its applicability might be most relevant in prehospital systems in which pharmacological avenues for analgesia are unavailable. For example, many European ambulance systems restrict medics from using pharmacological analgesia by any route because of legislative restrictions or because of basic levels of training provided to ambulance staff [1,23–27]. The usefulness of TENS in more developed ambulance systems where medics are capable of engaging in a wider scope of practice including administration of pharmacological analgesia is less certain. For example, most Australian ambulance services adopt an aggressive approach to pain management, authorizing medics to administer a wide range of analgesics including morphine, fentanyl, methoxyflurane, ketamine and nonsteroidal anti-inflammatory analgesics [28]. This enables medics to select the most appropriate analgesic with the most suitable safety and efficacy profile that best suits the aetiology of pain and characteristics of the patient in any particular situation. However, in many instances, particularly in rural and remote areas, community responders or first aid providers may need to provide interim or 'bridging' analgesia while waiting for professional medics to arrive. TENS could be an intervention that could provide effective analgesia during such a response interval until more definitive analgesia becomes available.

In terms of effectiveness, the reduction in pain severity observed in this meta-analysis (38 mm VAS) appears to compare favourably to that produced by pharmacological analgesia. In the prehospital setting, morphine, fentanyl and methoxyflurane have been reported to produce mean reductions in pain measured by a numeric rating scale of 4.5, 4.5 and 3.2, respectively [29], whereas a recent prehospital clinical trial of nitrous oxide reported a reduction of 4 (numeric rating scale) [30].

The safety profile of TENS in the emergency setting also appears to be excellent, with essentially no risk of adverse effects regardless of patient or situational characteristics.

There are few patients in whom TENS would be contraindicated, with only those with implanted electronic devices such as pacemakers, cardiac defibrillators and spinal cord or deep brain stimulators considered unsuitable.

There were several study level issues that could bias the positive findings of the review, in particular those surrounding blinding of participants and personnel, and the choice of a 'per protocol' analysis in each of the included studies. First, blinding of participants and personnel in a study involving an intervention such as TENS is inherently difficult because of the presence of equipment and the sensation that TENS produces; all four studies appeared to make an effort to blind participants by telling them that they may or may not feel some kind of sensation even if they were allocated to the real treatment. However, although none of the studies reported previous exposure of patients to TENS, it is reasonable to assume that patients exposed to TENS previously could possibly determine which group they had been allocated to, leading to bias when reporting pain severity after treatment. Conversely, though, TENS-naive patients allocated to sham TENS would have less chance of knowing their group allocation. Blinding of personnel (medics) was addressed in each study included to the best level that could be achieved; however, potential for bias still existed as there was potential for the allocating medic to communicate the allocation to the assessing medic. These two issues constitute a moderate potential for 'detection' bias that could have influenced the magnitude of the findings at the individual study and meta-analytic level.

Second, each included study retrospectively excluded a number of patients who, after investigation in hospital, proved not to have the specific condition of interest. The decision to adopt a 'per protocol' approach to the analysis was made a priori by the various investigatory teams, with the likelihood of retrospective inclusion incorporated into the calculation of sample size; each study therefore achieved the stated sample size. However, limiting the analysis to those with the specific cause of pain significantly limits the generalizability of the results. In most instances, medics are unable to determine the specific cause of a patient's pain, but they still provide analgesia with the aim of decreasing pain irrespective of the pain aetiology.

Although there is good evidence emerging from this meta-analysis that TENS provides effective analgesia for specific painful conditions, there is scope for ongoing research exploring the effectiveness across a broader spectrum of painful presentations including nonspecific abdominal pain and musculoskeletal trauma in more distal injuries of the upper and lower limbs. Future research could also evaluate TENS in local settings and as an adjunct in combination with mild and strong analgesics across a wider range of presentations.

Limitations

There is a possibility that a selection bias could be present arising from the decision to include only English and French language studies, given that all of the studies included originated in non-English-speaking European countries. Unfortunately, the authorship team had no translational capacity to search for and appraise non-English or French studies; attempts were made to contact the primary authors of the included papers with the assumption that they would in all likelihood be aware of such studies. However, these avenues of contact, using email addresses contained within the published studies, were unsuccessful. A publication bias could be present because of limiting inclusion to published studies; however, publication bias arising from missing studies has been shown to change the conclusions in less than 10% of meta-analyses [31]. As only four studies included were in the analysis, we did not perform a statistical assessment of publication bias as such methods are not recommended because of the lack of statistical power when only a small number of trials are included [32]. The meta-analysis used aggregate data that were extracted from published studies. This can result in confounding factors inherent to each individual data set influencing the measure of effect presented in each study. In turn, this can impact on the validity of the pooled results. Accessing individual-patient data, which we could not do, would enable an individual-patient meta-analysis that would reduce the chances of such an error in the pooled result.

Conclusion

TENS appears to be an effective noninvasive prehospital treatment for acute pain and anxiety. It produces clinically meaningful reductions in pain severity and significantly lowers post-treatment pain scores compared with sham treatment, with no adverse effects reported. TENS should be considered as an effective intervention in prehospital situations where pharmacological treatment is not available or feasible. Further research is warranted to investigate the broader application of this simple nonpharmacologic pain treatment in emergency medical service provision of prehospital care.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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