Electrical stimulation therapy for chronic constipation: a systematic review and meta-analysis

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Abstract

Introduction: Treatment of chronic constipation often is challenging, and non-traditional treatment methods, including nonpharmacological methods, may be attempted. Electrical stimulation therapy (EST) has been tried in many small and uncontrolled series. Although most results have been encouraging, validity of the method has not been established.

Material and methods: Five articles, concerning 338 patients (average age: 40.8–63.6 years) with constipation, were included in the study. Electroacupuncture or transcutaneous interferential electrical stimulation was the modality used. The causes of the constipation were stroke, slow transit, functional, opioid use, or unknown etiology. The primary and secondary outcomes were response rate and degree of constipation, respectively. Adverse events were also assessed.

Results: The results of the meta-analysis yielded a significant improvement in treatment response for EST compared with control treatment (medications or sham control), with the odds ratio 4.263 (95% CI: 1.456–12.484, \(p = 0.008\)). A significant reduction in degree of constipation also was found, with the pooled estimate of standardized difference in mean change 1.039 (95% CI: 0.315–1.763, \(p = 0.005\)). The average percentage of adverse events associated with EST was < 5%.

Conclusions: The EST with electroacupuncture or transcutaneous interferential electrical stimulation for the treatment of constipation due to various causes is effective and reasonably safe. However, further detailed studies using these methods are needed.

Key words: constipation, bowel preparation, functional GI disease, meta-analysis.

Introduction

Constipation is a common functional gastrointestinal disorder and is one of the most frequent reasons for patients to visit a physician [1]. Chronic constipation may be an idiopathic disorder or associated with various recognized conditions, such as mechanical bowel obstruction, irritable bowel syndrome, metabolic and endocrinology disorders, medications, and neurologic or myopathic disorders [1, 2]. Chronic constipation
is classified into outlet obstruction constipation, slow transit constipation, or both. Patients with chronic constipation most often can be treated effectively with simple measures, such as dietary modification or fiber supplements. Others, however, require more vigorous measures, including medications such as laxatives, stool softeners, emollients, or prokinetic agents. The clinical benefits of prokinetic agents often are suboptimal, and their adverse effects often preclude their use [2].

Nonpharmacological measures are occasionally used to treat resistant chronic constipation. Some of these measures are defecation training, behavior therapy, anorectal biofeedback, acupuncture, and electrical stimulation therapy (EST) [1, 2]. The EST, which uses brief waves of electrical stimulation to strengthen the muscles in the lower pelvis, has been associated with some success in small studies of constipation, some of which have been summarized by Thomas et al. [3]. Two types of EST are electroacupuncture and transcutaneous interferential electrical stimulation. Transcutaneous interferential electrical stimulation uses two currents that produce a beating effect, and has been used to treat a number of bowel disorders including dyspepsia, irritable bowel syndrome, slow transit constipation, and constipation in children with myelomeningocele (a type of spina bifida) [4]. In the colon, transcutaneous interferential electrical stimulation increases the colonic motility, colonic transit, the sensation of the urge to defecate and defecation frequency [4]. It also reduces soiling and bloating [4]. Electroacupuncture is a method in which an electrical current is delivered to needles inserted into acupoints [5]. Factors that influence the efficacy of electroacupuncture include acupoint group, operative technique of puncture, stimulation parameters, and treatment interval [5]. Although electroacupuncture has shown efficacy in clinical studies, the mechanism involved in these effects is unclear [5].

Because of the uncertainty about the validity of EST in treating chronic constipation, we conducted this meta-analysis to clarify the effectiveness and safety of EST in this troubling, complex condition. The primary outcome measure was response rate. The secondary outcome measure was degree of constipation. Adverse events also were also evaluated.

Material and methods

Search strategy

This systematic review and meta-analysis was conducted in accordance with PRISMA guidelines [6]. Medline, Cochrane, Google Scholar, and ClinicalTrials.gov databases were searched up to March 31, 2014. Reference lists of relevant studies were hand-searched, using these key words: constipation, electric stimulation therapy, transcutaneous electric nerve stimulation, interventional electrical stimulation, transcutaneous electrical stimulation, and electroacupuncture.

Selection criteria

Inclusion criteria

The inclusion criteria were the following: 1) randomized controlled trial; 2) participants were adults (≥ 18 years); 3) participants had the diagnosis of chronic constipation, including idiopathic constipation, or drug-related constipation; 4) interventions involved electric stimulation therapy, including sacral nerve stimulation, transcutaneous electrical nerve stimulation, electro-acupuncture, or interventional therapy; 5) the control group received sham control or medication only.

Exclusion criteria

The exclusion criteria were the following: 1) the intervention involved only acupuncture, without electric stimulation; 2) non-English or non-Chinese publication; 3) letters, comments, editorials, case reports.

Study selection and data extraction

Studies were identified according to the search strategy by two independent reviewers. Where there was uncertainty regarding eligibility, a third reviewer was consulted. Data extraction was also performed by two independent reviewers, and a third reviewer was consulted to resolve any uncertainties.

The following information was extracted from studies that met the inclusion criteria: the name of the first author, year of publication, study design, demographic data of subjects, information of intervention, length of follow-up, definition of outcome measures, outcomes before and after intervention, and adverse events.

Quality assessment

We used the Cochrane Risk of Bias Tool to assess the quality of included studies [7]. The quality assessment also was performed by independent reviewers, and a third reviewer was consulted to resolve discrepancies.

Outcome measures

The primary outcome measure was response rate. The secondary outcome measure was degree of constipation. Adverse events also were also evaluated.
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Statistical analysis

To evaluate the efficacy of EST for constipation, we used the pooled odds ratio for the likelihood of treatment response and for standardized difference in mean change of degree of constipation between EST and control treatment (defined as medication or sham control).

Heterogeneity among the studies was assessed by use of the two statistics of Cochran Q and I²; if either a Q statistic with $p < 0.1$ [8] or an $I^2$ statistic $> 50\%$ [9] was found, we applied the random-effects model (DerSimonian-Laird method) [10]. Otherwise, the fixed-effects model was used (Mantel-Haenszel method).

To determine the robustness of the pooled estimate, a sensitivity analysis based on the leave-one-out approach was performed. Publication bias analysis was not performed because the number of studies was too small ($< 10$) to detect an asymmetric funnel [11]. A two-sided $p$-value $< 0.05$ was considered to indicate statistical significance. All statistical analyses were performed using Comprehensive Meta-Analysis statistical software, version 2.0 (Biostat, Englewood, NJ, USA).

Results

Literature search

Figure 1 is a flowchart for study selection. After the initial identification of 387 records, 325 articles were excluded for not being relevant, leaving 63 studies for full-text review. Fifty-seven studies were excluded after the full-text review for not meeting the inclusion/exclusion criteria.

Study characteristics

Five articles, concerning 388 patients (average age: 40.8–63.6 years) with constipation, were included in the study [12–17]. The basic characteristics of the included studies are summarized in Table I. Among the five included studies, two had treatment durations of 4 weeks [12–14], two of 2 weeks [16, 17], and one of 5 days [15]. Details of the treatments, definitions of response, and the scales for degree of constipation are summarized in Table II.

Meta-analysis for treatment response

Four of the five included studies reported the treatment responses of EST and control treatments (medication or sham). All of the studies reported a better response to EST than to the control treatment, but in only two of the studies [14, 16] were the differences significant. A random effect model was performed when pooling the reported odds ratios since obvious heterogeneity was observed among the studies ($Q = 8.2$ with $p = 0.042$ and $I^2 = 63.5\%$). The results of the meta-analysis revealed that EST for constipation resulted in significant improvement in treatment response compared with control treatment (med-
ications or sham control); the pooled estimate of odds ratio was 4.263 (95% CI: 1.456–12.484, \( p = 0.008 \)) (Figure 2 A).

Sensitivity analysis based on the leave-one-out approach was performed to evaluate the robustness of the pooled estimates. When each study was removed in turn, the direction of the pooled estimates did not change (all pooled odds ratios > 1); although removal of Wand et al. resulted in the difference between EST and control groups becoming non-significant. Overall, the sensitivity analysis indicated that the findings are reliable (Figure 2 B).

Meta-analysis for degree of constipation

Four of the included studies reported the degree of constipation with EST and control treatments (medication or sham). Across the four studies, a greater reduction in the degree of constipation was observed in the EST group compared with the control group; in three of the studies, the difference was statistically significant [14, 16, 17]. A random effect model was performed when pooling the reported standardized differences of mean change since obvious heterogeneity was observed among the studies (\( Q = 19.3 \) with \( p < 0.001 \) and \( I^2 = 84.5\% \)). The results of the meta-analysis revealed that EST reduced the degree of constipation significantly more the control treatment, with the pooled estimate of standardized difference in mean change in degree of constipation 1.039 (95% CI: 0.315–1.763, \( p = 0.005 \)) (Figure 3 A).

Sensitivity analysis based on the leave-one-out approach was performed to evaluate the robustness of the pooled estimate. The pooled estimates retained the same directions regardless of removal of any given study (all pooled standardized difference in mean change > 0), indicating that the findings were robust (Figure 3 B).

Quality assessment

The results of quality assessment are shown in Figure 4. Generally, the included studies had a high risk of selection bias and performance bias because most of them did not clearly describe the process of randomization and did not sufficiently blind the participants and outcome assessors. Only two of the five studies described the sham control.

Adverse events

The percentage of reported adverse events with EST was low, less than 5%. Peng et al. [12], in a study using electroacupuncture, reported no adverse events in patients treated with shallow puncture, but pain in two (3.2%) treated with deep puncture. Wang et al. [14] had no adverse events among 71 patients treated with electroacupuncture (48 deep needling, 23 shallow needling). Wang et al. [17] had no adverse events in 9 patients treated with electroacupuncture. Zhang et al. [15] found no adverse events in 66 patients treated with electroacupuncture for narcotic-induced constipation. Wang et al. [16] did not report adverse events.

### Table I. Summary of basic characteristics of included studies

| Study ID | Population | Treatments and control | Treatment duration | Number of patients | Age [years] | Male, n (%) |
|----------|------------|------------------------|--------------------|--------------------|------------|-------------|
| Peng (2013) | Slow transit constipation | Electroacupuncture, deep puncture | 4 weeks | 64 | 53 (13) | 16 (25) |
| | | | | 33 | 52 (17) | 14 (42.4) |
| | | Electroacupuncture, shallow puncture | | | | |
| | | Medication | | 31 | 59 (12) | 14 (45.2) |
| Wang (2010) | Functional constipation | Electroacupuncture, deep puncture | 4 weeks | 48 | 48.85 (13.30) | 10 (20.83) |
| | | | | 23 | 44.69 (15.29) | 4 (17.39) |
| | | Electroacupuncture, shallow puncture | | | | |
| | | Medication | | 24 | 40.83 (13.30) | 1 (4.17) |
| Zhang (2009) | Cancer patients with morphine-induced constipation | Electroacupuncture | 5 days | 33 | 59.61 (12.49) | 17 (51.5) |
| | | | | 33 | 63.55 (11.01) | 19 (57.6) |
| Wang (2008) | Post-stroke constipation | Electroacupuncture | 2 weeks | 40 | 63.2 (3.74) | 22 (55) |
| | | | | 40 | 61.9 (4.65) | 23 (57.5) |
| Wang (2008) | Type 2 diabetes with gastroparesis of more than 3 months | Electroacupuncture | 2 weeks | 9 | 57.7 (7.4) | 8 (88.9) |
| | | | | 10 | 57.1 (9.9) | 8 (80) |

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### Table II. Summary of treatments and clinical outcomes of included studies

| Study ID | Treatments and control | Treatment duration | Response | Degree of constipation |
|----------|------------------------|-------------------|----------|------------------------|
| Peng (2013) | Electroacupuncture, deep puncture* | 4 weeks | Weekly stool frequency ≥ 4 | NR |
| Peng (2013) | Electroacupuncture, shallow puncture* | 4 weeks | Weekly stool frequency ≥ 4 | NR |
| Wang (2010) | Electroacupuncture, deep puncture* | 4 weeks | Weekly stool frequency ≥ 4 | Numeric rating scales for straining, incomplete relief after defecation, stool consistency, rumbling, abdominal pain, abdominal distension, diarrhea, fecal incontinence | 11.77 (3.01) |
| Wang (2010) | Electroacupuncture, shallow puncture* | 4 weeks | Weekly stool frequency ≥ 4 | | 6.27 (2.75) |
| Zhang (2009) | Electroacupuncture | 5 days | Complete response and significant response and partial response | Numeric rating scales for frequency, stool consistency, straining, defecation time | 9.21 (1.41) |
| Wang (2008) | Electroacupuncture | 2 weeks | Complete response and significant response and partial response | Numeric rating scales for major symptoms (the first defecation time, interval, defecation speed, stool consistency, straining, desire to defecate) and minor symptoms (abdominal pain, abdominal distension, dizziness, lethargy, bitter taste in mouth, irritability, poor appetite, painful sacrum) | 20.03 (2.37) |
| Wang (2008) | Medication | | | | 20.34 (3.02) |
| Wang (2008) | Sham control | | | | 2.38 (0.56) |

*The two intervention groups of deep and shallow punctures were combined as one (the electroacupuncture group) in the meta-analysis. *The criteria for response were: 1) complete response: normal defecation, recovery to condition before illness, or no symptoms; 2) significant response: significantly improved constipation, stool frequency, and consistency to near normal, or mild hard stool but with defecation interval ≤ 72 h and absence of most symptoms; 3) partial response: the interval of stooling shortened by one day, or improved stool consistency with all the other symptoms improved; (4) no response: all constipation symptoms unchanged. NR – not reported.
Discussion

The major result of this meta-analysis was that EST (using electroacupuncture or transcutaneous interferential electrical stimulation) used for single-cause constipation resulted in a significant improvement in treatment response and degree of constipation compared with control treatment (medications or sham control). Also, EST was associated with a low rate of adverse events.

Many individual studies of EST have been reported. Assessment of the results is difficult because of variability in factors such as methods used, populations studied (children, adults, wom-
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Figure 4. Results of quality assessment of included studies. A – risk of bias graph, B – risk of bias summary

en), duration of treatment, outcomes measured, and causes of the constipation (drug-induced, diabetes, irritable bowel syndrome, idiopathic slow transit, evacuatory dysfunction, and central neurological disease). Etiology of the constipation may influence treatment outcomes. In our study the causes of the constipation included stroke, slow transit, functional, diabetic gastroparesis, and opioid use. Based on the cause of constipation, the response to electrical treatment may differ, leading to heterogeneity in assessed outcomes. Therefore, the results of this analysis need to be carefully interpreted.

Sacral nerve stimulation is the most common route of EST application [18–24]. Although patients in most of the included studies had some improvement in constipation, most authors urged caution in interpretation of the results. Indeed, Ortiz et al. [19] concluded that sacral nerve stimulation has limited efficacy as a routine therapy for intractable idiopathic constipation, and Govaert et al. [18] found that only about 50% of patients at follow-up had continued the therapy. Thomas et al. [3] conducted a literature review of 13 studies of sacral nerve stimulation for constipation. They concluded that stimulation appears to be an effective treatment, but that this conclusion needs to be confirmed in larger prospective studies with longer follow-up. In an interesting study, Dinning et al. [22] recorded colonic motor responses to sacral nerve stimulation with catheters positioned in the colon to the cecum. Supersensory stimulation increased the frequency of propagating sequences, whereas subsensory stimulation did not. The findings of Dinning et al. may help in the selection of optimal conditions for clinical application of EST.

Other modalities of electrical stimulation that have been reported in small series are anal canal stimulation [23] and transabdominal stimulation.
As with sacral nerve stimulation, the results of these studies are inconclusive. Two studies [26, 27] used inferential current, as was used in the studies of this meta-analysis. Other types of treatment for constipation include pharmacologic and surgical approaches [28–30].

Because of the numerous inadequacies of individual studies of EST in the treatment of constipation, our systematic review and meta-analysis is informative. Despite the rigor of our meta-analysis, however, our study has limitations. First, although several types of electrical stimulation have been used in the treatment of chronic constipation of any cause, our meta-analysis examined only transcutaneous interferential electrical stimulation and electroacupuncture. Several studies which investigated sacral nerve stimulation were excluded because they did not fit our criteria; two trials [25, 26] were excluded because they were not randomized. Thus, our results might not represent the broader spectrum of EST. Second, the study populations of the five included studies had various comorbidities, including type 2 diabetes mellitus, cancer, and stroke.

Third, the studies used various criteria to define the response and the degree of constipation, thus resulting in some heterogeneity. Fourth, the etiology for constipation and type of EST used varied across studies, which may have confounded our results. Our sensitivity analysis partially addressed this issue. Removal of each study in turn did not alter the direction of the pooled estimates, except for the removal of the study of Wand et al., which examined post-stroke constipation. It would have been of interest to perform a subgroup analysis to evaluate different etiologies and EST methods; however, this was not possible due to the limited amount of studies for each potential subgroup. Fifth, the study populations were relatively small and were followed for only a matter of weeks. For these reasons, the results of this meta-analysis must be interpreted cautiously.

We conclude from this meta-analysis that EST acupuncture can improve the symptoms of chronic constipation. However, more extensive studies, with larger and better defined populations followed for longer periods of time, will be needed in order to establish the validity of EST in this condition.

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Conflict of interest

The authors declare no conflict of interest.

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