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SYSTEMATIC REVIEW

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Posterior tibial nerve electrical stimulation in chronic constipation: a systematic review and meta-analysis

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ABSTRACT

Aim: A systematic review and meta-analysis were performed to investigate posterior tibial nerve electrical stimulation application methods in patients with chronic constipation.
Background: Posterior tibial nerve electrical stimulation is a management procedure for chronic constipation.
Methods: A comprehensive search was conducted on Ovid, PubMed, Scopus, ProQuest, Web of Science, and The Cochrane Library based on the PICO formation of the study. All randomized controlled trials and quasi-experimental studies in which patients with chronic constipation were treated with transcutaneous tibial nerve stimulation (TTNS) or percutaneous tibial nerve stimulation (PTNS) were included in this study. Two independent reviewers screened all titles, abstracts, and full texts. The selected studies' quality was assessed critically using the Joanna Briggs Institute checklists. The data synthesis was conducted using Review Manager Software.
Results: Out of 1016 records, 11 studies were included in this study. The results showed that TTNS was effective in improving constipation symptoms (SMD: -1.52, CI 95%: -2.81 to -0.22, p< 0.0001) and reducing defecation time of patients with chronic constipation (SMD: -0.86, CI 95%: -1.60 to -0.13, p= 0.17). Additionally, PTNS was found to improve the quality of life of these patients (SMD: -1.32, CI 95%: -2.05 to -0.59, p< 0.00001).
Conclusion: Both TTNS and PTNS can be effective interventions for chronic constipation. To suggest a definitive and standard treatment plan, further research is needed to determine optimal parameters for TTNS and PTNS applications.

Keywords: Posterior tibial nerve electrical stimulation, Constipation, Meta-analysis.

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Introduction

Chronic constipation is a prevalent health problem defined by reduced bowel movements, incomplete defecation, need for manual maneuvers to facilitate evacuation, excessive straining, prolonged attempts to evacuate, hard stools, and abdominal distension (1, 2). It occurs in 2% to 26.9% of the general population and 18.9% of older people (3, 4). Constipation significantly impacts patients' psycho-social status and quality of life (QOL) and imposes high healthcare costs (5).

Primary (functional) and secondary constipation are the main types of chronic constipation (1, 2). The present management of chronic constipation consists of medications and drugs, education regarding constipation, modifying lifestyle (increasing mobility and intake of fluid and fiber), physiotherapy interventions, and surgery. Physiotherapy methods commonly used for chronic constipation include biofeedback, pelvic floor training, electrical stimulation such as interferential, electroacupuncture, and neuromodulation (2, 6).

Sacral nerve stimulation and posterior tibial nerve stimulation are two ways of neuromodulation (7). The

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posterior tibial nerve originates from the L4 to S3 nerve roots, which supply the lower gastrointestinal tract, genitourinary tract, and pelvic floor muscles. Thus, it could be possible that the posterior tibial nerve electrical stimulation can modulate sphincter function and bowel motility. Percutaneous tibial nerve stimulation (PTNS) and transcutaneous tibial nerve stimulation (TTNS) are two different methods of application of posterior tibial nerve electrical stimulation. PTNS was first introduced by Stoller in 1987 and involves inserting a needle electrode near the medial malleolus, while TTNS is performed using surface electrodes. Frequency, pulse width, amplitude, duration of treatment time, and number of treatment sessions are parameters of posterior tibial nerve electrical stimulation (6, 8, 9).

A recent systematic review evaluated the effects of various neuromodulation modalities on chronic functional constipation. The review found that the beneficial impact of neuromodulation on this condition is uncertain. However, it suggested that neuromodulation may be an alternative to more invasive treatments for intractable patients. The study by Pauwels included sacral neuromodulation, transcutaneous sacral nerve stimulation, transcutaneous interferential current therapy, and tibial nerve stimulation (PTNS and TTNS) as types of neuromodulation (6).

Several studies have considered the effects of posterior tibial nerve electrical stimulation on constipation (9–19). However, the parameters of posterior tibial nerve electrical stimulation were different. To our knowledge, there is no consensus on posterior tibial nerve electrical stimulation application methods. Therefore, a systematic review and meta-analysis were performed to investigate the effects and methods of application of the posterior tibial nerve electrical stimulation and evaluate the parameters, including frequency, pulse width, amplitude, duration of treatment time, and number of treatment sessions to suggest the best methods of application for patients with chronic constipation.

Methods

This systematic review and meta-analysis were carried out using a checklist based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA) guidelines (20) and registered in the PROSPERO (CRD42022370244).

Search strategy and eligibility criteria

A comprehensive scientific search was conducted on Ovid, PubMed, Scopus, ProQuest, Web of Science, and The Cochrane Library to identify all relevant and available studies published up to October 25, 2022. The search was updated on November 23, 2022. The search strategy for each database was designed based on the PICO formation of the study. Gray literature (unpublished data) and international congress abstracts were also hand-searched. The reference lists of included studies were also screened for additional data. The PICO formation was as follows:

Population: Patients suffering from constipation OR chronic constipation

Intervention: Posterior tibial nerve stimulation OR tibial nerve stimulation OR transcutaneous tibial nerve stimulation OR percutaneous tibial nerve stimulation OR TTNS OR PTNS

Control: Any treatment OR no treatment OR control OR sham OR placebo OR routine treatment

Primary outcomes: Severity of constipation according to the scores of different questionnaires OR defecation per week OR bowel movements per week OR painful defecation

Secondary outcomes: Quality of life OR QOL OR abdominal distension OR manometry

The full details of the PubMed search strategy were reported in Appendix S1.

Inclusion and exclusion criteria

All randomized controlled trials (RCTs) and quasi-experimental studies in which patients with chronic constipation were treated with PTNS or TTNS were included in this review.

Exclusion criteria included animal studies, study types other than quasi-experimental and RCTs, and studies with children's participants. Also, all RCTs and quasi-experimental studies in which patients with constipation were treated by electroacupuncture, interferential stimulation, or sacral nerve modulations were excluded. Studies that didn't provide access to treatment details and parameters through the full text of the article or communication with the authors via email were also excluded.

Study selection

All citations were exported to EndNote, and duplicate studies were removed. Two independent reviewers screened all titles, abstracts, and full texts to find the eligible studies. A third reviewer solved disagreements during each step of the selection process. The PRISMA flow diagram presented the search results (Figure 1) (21).

Quality assessment

The selected studies' quality was assessed critically using the Joanna Briggs Institute (JBI) checklist for RCTs and quasi-experimental studies (https://jbi.global/critical-appraisal-tools). According to the consensus, if the score of the appraisal checklist exceeded 60% of the total score, it was considered acceptable for inclusion in this study. The selected studies' quality assessment results are presented in Figure 2 and Figure 3.

Data extraction

Data such as the author's name, publication year, study design, disease, sample size, type of intervention (PTNS/TTNS), outcomes, and methods of application of posterior tibial nerve electrical stimulation were

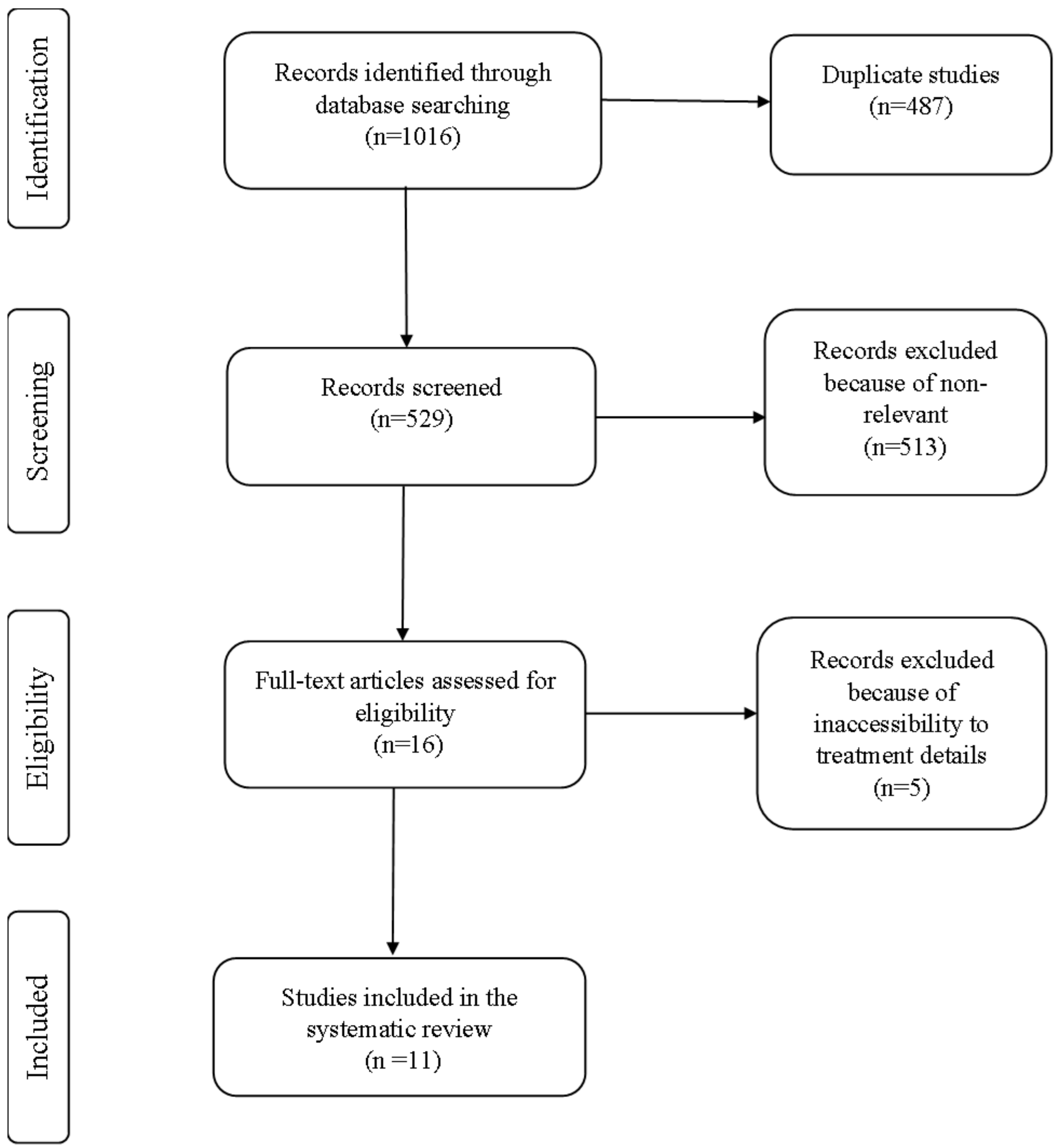

Figure 1. Search and selection process of systematic review.

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Score
Zhang-2014	U	U	Y	Y	N	N	Y	N	Y	Y	Y	Y	Y	8/12
Wu-2019	U	U	Y	Y	N	N	Y	N	Y	Y	Y	Y	Y	8/12
Saba-2022	Y	Y	Y	N	N	Y	Y	N	Y	Y	Y	Y	Y	10/12

U: Unclear/ Y: Yes/ N: No

Since the fifth question of the checklist (blindness of the therapist) was not relevant in these studies, the final score was calculated out of 12.

1. Was true randomization used for the assignment of participants to treatment groups?
2. Was allocation to treatment groups concealed?
3. Were treatment groups similar at the baseline?
4. Were participants blind to treatment assignment?
5. Were those delivering treatment blind to treatment assignment?
6. Were outcomes assessors blind to treatment assignment?
7. Were treatment groups treated identically other than the intervention of interest?
8. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?
9. Were participants analyzed in the groups to which they were randomized?
10. Were outcomes measured in the same way for treatment groups?
11. Were outcomes measured in a reliable way?
12. Was appropriate statistical analysis used?
13. Was the trial design appropriate, and were any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?

Figure 2. Quality assessment of RCTs.

extracted from each included study. The characteristics of the included studies are presented in Table 1.

Data synthesis

The meta-analysis was carried out based on the results of included studies that compared pre- and post-intervention (PTNS or TTNS). Data synthesis was conducted using Review Manager statistical software (version 5.4). The standardized mean difference (SMD) with a 95% confidence interval (CI) was calculated using mean ± standard deviation (SD) for all continuous variables. Statistical heterogeneity was assessed by the I2 index and the chi-square test. An I2>50% and P<0.05 for Cochran's Q were considered as heterogeneity. Statistical analysis was performed using the randomized effect model. The meta-analysis results were displayed on a forest plot if there were at least two pooled studies for the same outcome. Publication bias was not evaluated by using the funnel plot due to the insufficient number of studies included in the meta-analysis.

Results

Literature search and description of studies

A total of 1016 relevant records were found based on the search strategy. After removing 487 duplicate records, the titles and abstracts of 529 articles were carefully screened. Subsequently, 16 studies were eligible for full-text assessment. Five articles were excluded due to the unavailability of treatment details and parameters in the full text or through communication with the authors. In the end, 11 studies were selected for the critical appraisal process. The PRISMA flowchart of the current study is shown in Figure 1.

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Score
Collins-2011	Y	Y	Y	N	Y	N	Y	Y	Y	7/9
Kumar-2016	Y	Y	Y	N	Y	N	Y	Y	Y	7/9
Stundiene-2014	Y	Y	Y	N	Y	N	Y	Y	Y	7/9
Iqbal-2015	Y	Y	Y	N	Y	N	Y	Y	Y	7/9
Madbouly-2017	Y	Y	Y	N	Y	N	Y	Y	Y	7/9
Ge-2018	Y	Y	Y	Y	Y	Y	Y	Y	Y	9/9
Gokce-2019	Y	Y	Y	N	Y	Y	Y	Y	Y	8/9
Gokce-2022	Y	Y	Y	N	Y	Y	Y	Y	Y	8/9

U: Unclear/ Y: Yes/ N: No

1. Is it clear in the study what is the 'cause' and what is the 'effect' (i.e., there is no confusion about which variable comes first)?
2. Were the participants included in any comparisons similar?
3. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?
4. Was there a control group?
5. Were there multiple measurements of the outcome both pre and post the intervention/exposure?
6. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed
7. Were the outcomes of participants included in any comparisons measured in the same way?
8. Were outcomes measured in a reliable way?
9. Was appropriate statistical analysis used?

Figure 3. Quality assessment of quasi-experimental studies

The risk of bias in the included studies

Eleven studies were appraised by the JBI appraisal checklists for possible biases. According to the consensus, if the score of the appraisal checklist exceeded 60% of the total score, it was considered acceptable for inclusion in this study. Therefore, all 11 selected studies were included in the review because of the acceptable scores. Additionally, seven studies were entered into the meta-analysis. The results of this assessment are shown in Figure 2 and Figure 3.

Summary of evidence

Selected studies used posterior tibial nerve electrical stimulation with different parameters. Two of the 11 included studies used PTNS, and the remaining used TTNS for managing chronic constipation. These studies were designed as RCT or quasi-experimental. Some of the measured outcomes including patient assessment of constipation symptoms (PAC-SYM), defecation time, patient assessment of constipation-quality of life (PAC-QOL), maximum tolerated volume (MTV), maximum squeezing anal pressure, and desire of defection or defecatory desire volume (DDV) were assessed before and after the intervention. The outcomes are presented in Table 1. The subgroup analysis was conducted to compare the effects of the intervention (PTNS and TTNS) on the quality of life of patients with constipation.

Patient Assessment of Constipation Symptoms (PAC-SYM)

Three studies used TTNS, which assessed constipation symptoms using the PAC-SYM questionnaire (11, 14, 16). The meta-analysis revealed a significant improvement in constipation symptoms (SMD: -1.52, CI 95%: -2.81 to -0.22, p-value< 0.0001). However, these studies had high statistical heterogeneity (I2:87%, p-value= 0.0004) as shown in Figure 4.

Defecation time

Regarding defecation time, two studies (10, 15) were reviewed that used TTNS as a treatment method. The result of the meta-analysis indicated that TTNS could be an effective intervention for reducing the defecation time (SMD: -0.86, CI 95%: -1.60 to -0.13, p-value= 0.17). Additionally, the studies had moderate heterogeneity (I2:46%, p-value= 0.17) (Figure 5).

Patient Assessment of Constipation-Quality of Life (PAC-QOL)

Five studies used the PAC-QOL questionnaire to evaluate the effect of constipation on the quality of life of patients with chronic constipation. One study (9) used PTNS, while the others (10, 11, 14, 16) used TTNS. The result of the meta-analysis came up with SMD: -0.41, CI 95%: -1.08 to 0.25, p-value= 0.001, which showed the interventions were not accompanied by significant improvement in the quality of life of patients with chronic constipation. Also, heterogeneity in the studies was high (I2:78%, p-value= 0.001). However, subgroup analysis revealed that PTNS was effective in the improvement of the quality of life (SMD: -1.32, CI 95%: -2.05 to -0.59, p-value< 0.00001). Heterogeneity analysis indicated p-value= 0.03, and I2 was 80.1% (Figure 6).

The Manometric Maximum Tolerated Volume (MTV)

Two studies (13, 15) were included in the meta-

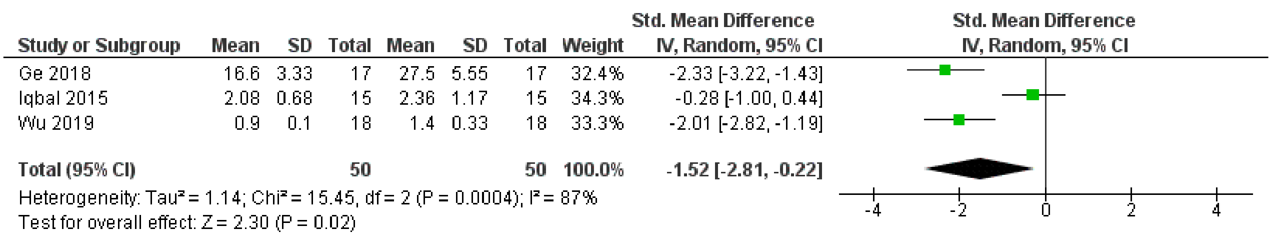

Figure 4. Forest plot of comparison before vs. after TTNS on PAC-SYM.

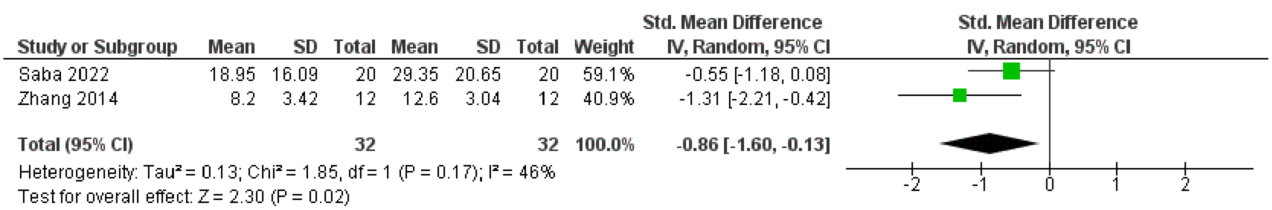

Figure 5. Forest plot of comparison before vs. after TTNS on defecation time.

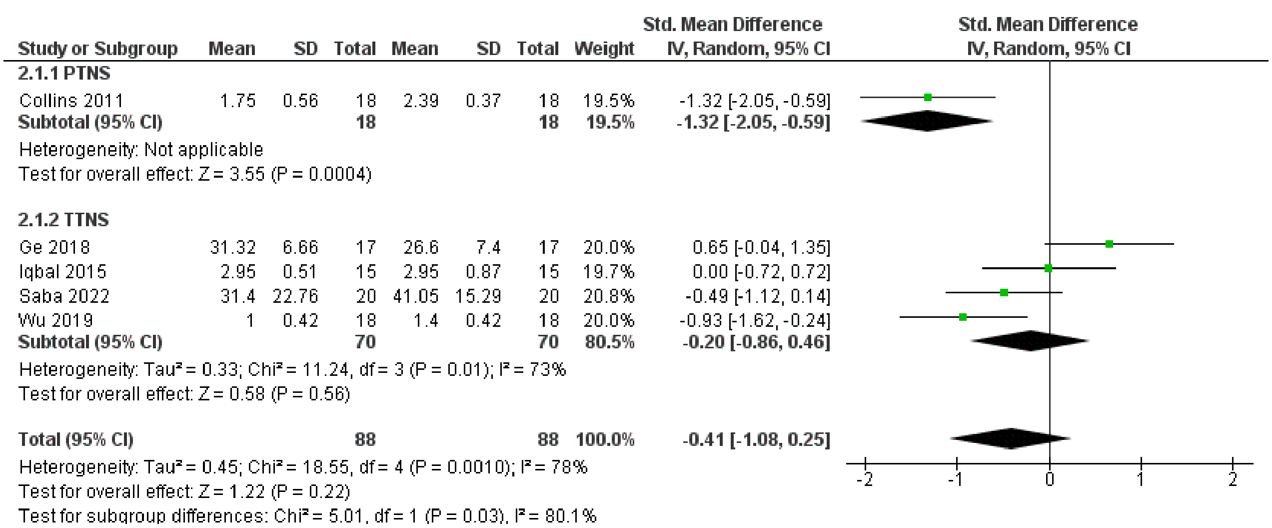

Figure 6. Forest plot of comparison before vs. after TTNS on PAC-QOL.

analysis regarding MTV that used TTNS. There was no evidence of benefit in reducing MTV before and after the intervention (SMD: -2.40, 95% CI: -5.22 to 0.42, p-value< 0.00001). Furthermore, there was a high level of heterogeneity among the studies (I2:96%, p-value< 0.00001) (Figure 7).

The manometric maximum squeezing anal pressure

Maximum squeezing anal pressure was evaluated in three studies (10, 14, 15). The findings demonstrated no significant differences before and after the TTNS (SMD: 0.23, CI 95%: -0.17 to 0.63, p-value =0.99). In addition, heterogeneity in the studies was low (I2:0%, p=0.99) (Figure 8).

The Manometric Desire of Defection or Defecatory Desire Volume (DDV)

Two studies (13, 15) entered the meta-analysis related to DDV. The results of the meta-analysis indicated that TTNS could not be an efficient intervention in reducing DDV (SMD: -2.38, CI 95%: -6.15 to 1.39, p-value< 0.00001). Also, there was a high level of heterogeneity among the studies (I2:98%, p-value< 0.00001) (Figure 9).

Discussion

The present systematic review and meta-analysis aimed to investigate the effects and methods of application of posterior tibial nerve electrical stimulation and evaluate the parameters, including frequency, pulse width, amplitude, duration of treatment time, and number of treatment sessions, to suggest the best application methods for chronic constipation patients.

Eleven studies with different posterior tibial nerve electrical stimulation parameters were included in this review. The main findings indicated that TTNS could be an effective intervention for improving constipation symptoms, as measured by the PAC-SYM score. Additionally, TTNS was found to reduce defecation time when compared to PTNS. On the other hand, PTNS was found to be effective in improving the quality of life of patients with chronic constipation compared to TTNS. However, there were no statistical changes observed in QOL and manometric parameters such as MTV, maximum squeezing anal pressure, and DDV when using TTNS.

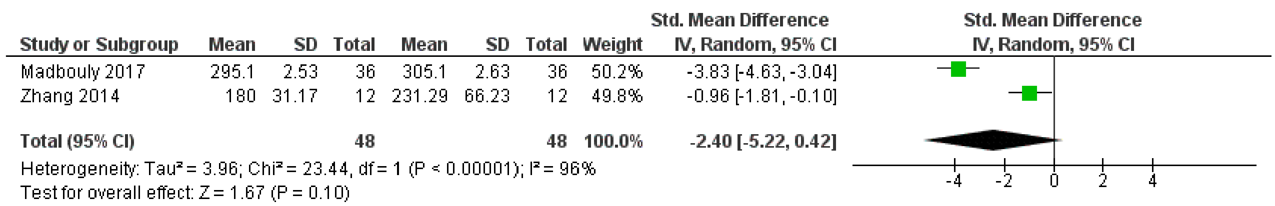

Figure 7. Forest plot of comparison before vs. after TTNS on MTV.

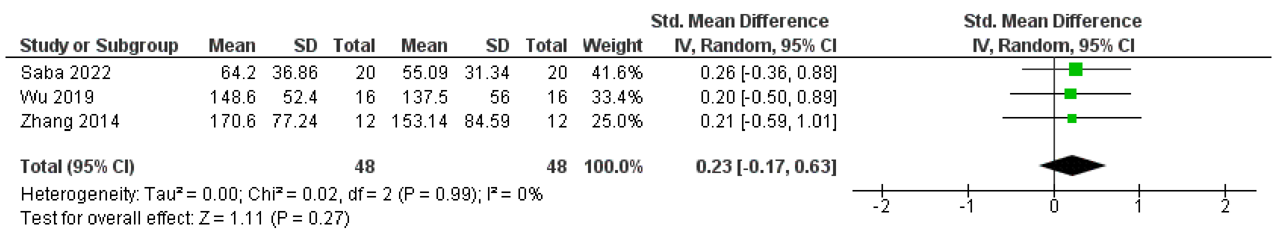

Figure 8. Forest plot of comparison before vs. after TTNS on maximum squeezing anal pressure.

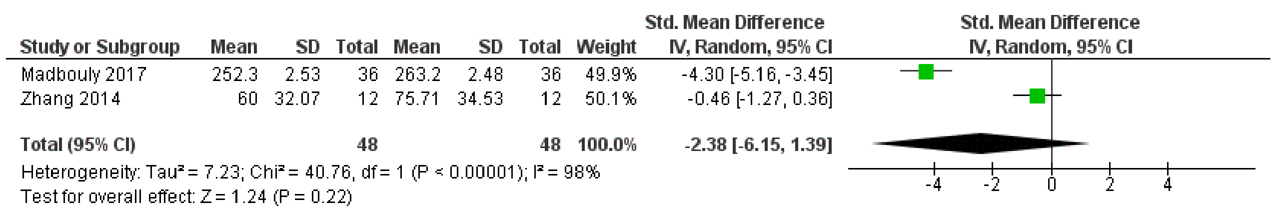

Figure 9. Forest plot of comparison before vs. after TTNS on DDV.

Table 1. Study characteristics of included studies

Author Year Study design	Disease Sample size (IG/CG)	Type of Intervention	Outcomes	Method of intervention	Results
Collins et al. (9) 2011 Pilot study	Slow transit constipation N=18 No CG	PTNS	WCS Colonic transit time Bowel diary PAC-QOL	F: 20Hz PW: 200µs Amp: sensory threshold 30 min 12 sessions (4-12 weeks)	WCS improved from the median 18 (10-24) to 14 (7-22) (p= 0.003). PAC-QOL score improved from the median of 2.31 (1.36-3.61) to 1.43 (0.39-3.78) (P = 0.008) Stool frequency increased from the median of 9 (2-48) to 16 (1-35) (p= 0.048). The median number of laxative uses decreased from 9 (0-75) to 2.5 (0-62) (p= 0.025). No change in colonic transit time (p= 0.45)
Kumar et al. (19) 2016 _	Constipation N=34 No CG	PTNS	WCS Colonic transit time Anorectal manometry (balloon expulsion test)	30 min 12 sessions (12 weeks)	No change in mean WCS (from 21.0 ± 3.2 to 19.3 ± 3.4, p= 0.1). No change in mean colonic transit time (from 31.3 ±10.3 to 30.4 ±10.0, p= 0.47). No improvement in balloon expulsion (p= 0.73).
Stundiene et al. (12) 2014 Prospective pilot study-consecutive cohort study	Constipation N=49 No CG	TTNS (bilateral)	KESS The number of bowel movements, laxatives, suppositories, and enemas uses per two weeks GIQLI	F: 20Hz PW: 200µs Amp: sensory threshold 30 min 12 sessions (6 weeks)	The mean KESS score improved from 20.88 ± 5.19 to 15.61 ± 7.19, p < 0.001 significantly. The mean stool frequency increased from 4.65 ± 2.48 to 7.47 ± 3.51 (p < 0.001). The median number of laxative uses decreased from 4 (0–44) to 0 (0–16) (p < 0.001). The mean GIQLI score improved from 92.98 ± 16.06 to 104.76 ± 18.38 (p < 0.001).
Iqbal et al. (11) 2015 Pilot study	Chronic functional constipation N=18 No CG	TTNS (bilateral)	PAC-QOL PAC-SYM Weekly bowel frequency Satisfaction of bowel movements by VAS (0-100)	F: 14Hz PW: 220µs Amp: sensory threshold 30 min 42 sessions (6 weeks)	The median PAC-QoL score improved from 2.95 (IQR: 1.18) to 2.50 (IQR: 0.70) (P = 0.047) significantly. No change in the median PAC-SYM score from 2.36 (IQR: 1.59) to 2.08 (IQR: 0.92) (P = 0.53). No significant change in weekly stool frequency (p= 0.161) and VAS score (P = 0.229).
Madbouly et al. (13) 2017 Prospective case series	Patients with rectal evacuation disorder without anatomic obstruction N=36 No CG	TTNS (bilateral)	MODS Anorectal manometry: rectal sensitivity volumes (DDV and MTV) PAC-QOL	F: 10Hz PW: 200µs Amp: - 30 min 18 sessions (6 weeks)	Responders (n=17): patients with the successful outcome The mean MODS decreased from 15. 1±2. 0 to 5. 1±1. 2, p= 0.001 in responders. The mean PAC-QOL improved from 54. 0±14. 1 to 11. 1±5. 2 p= 0.001 in responders. The mean urge to defecate volume decreased from 258. 1±21. 2 to 239. 6±15. 3, p < 0.0001 in responders. The mean maximal tolerable volume decreased from 304. 5±24. 8 to 286. 8±19. 7, p < 0.0001 in responders. Nonresponders (n=19): patients with unsuccessful outcomes No significant change in all outcomes was observed in the nonresponders.
Ge et al. (16) 2018 _	Functional constipation N=40 IG=20 CG=20 (healthy volunteers)	IG: TTNS CG: without any treatment	BSS PAC-QOL PAC-SYM Weekly bowel frequency	F: 25Hz PW: 500µs Amp: pain threshold/ 2 to 10 mA 60 min 56 sessions (4 weeks)	The BSS improved from a median of 2 (1-2) to a median of 3 (3-4) (p< 0.001). The PAC-QOL score decreased from a median of 52 (48.0-58.0) to a median of 31 (27.0-36.0) (p< 0.001). The PAC-SYM score decreased from a median of 26 (24.5-32.0) to a median of 16 (14.0-18.5) (p< 0.001) The median weekly bowel frequency increased from 2 (1-2) to 4 (3-4) (p< 0.001).
Gokce et al. (18) 2019 Prospective clinical study	Geriatric patients aged >65 years with chronic refractory constipation N=44 No CG	TTNS (bilateral)	The Constipation Severity Instrument score Time spent in the toilet Use of stool softener	F: 10Hz PW: 200µs Amp: - 30 min 18 sessions (6 weeks)	The constipation severity instrument score improved. Defecation time decreased. The use of softeners decreased from 63.6% to 15.9%.

Continued					
Gokce et al. (17) 2022 Prospective study	Functional constipation N=105 No CG	TTNS (bilateral)	The Constipation Severity Instrument score Time spent on the toilet Use of stool softener	F: 10Hz PW: 200µs Amp: - 30 min 18 sessions (6 weeks)	The mean constipation severity instrument total score improved from 51.4 ± 8.17 to 19.1 ± 8.66 (P < .001) Defecation time decreased (p< .001). The use of softeners decreased from 76.2% to 20% (P < .001).
Wu et al. (14) 2019 Randomized, single-blinded cross-over pilot study	Functional constipation N=18 A cross-over study with a 2-week TN at ST36 and a 2-week TN at PTN	TTNS (bilateral)	Bowel movement diary PAC-SYM PAC-QOL Anorectal manometry	F: 25Hz PW: 500µs Amp: pain threshold/ 2 to 10 mA 60 min 28 sessions (2 weeks)	No increase in the number of weekly bowel movements (from 2.7 ± 0.7 to 0.9 ± 0.3, p=0.105) with TN at PTN. The mean number of weekly bowel movements increased from 0.9 ± 0.2 to 3.5 ± 0.7, p<0.001 with TN at ST36. No improvement in the mean PAC-QOL score (from 1.4 ± 0.1 to 1.0 ± 0.1, p > 0.05 with TN at PTN. The mean PAC-QOL score decreased from 1.5 ± 0.1 to 0.8 ± 0.1, p= 0.003 significantly with TN at ST36. The mean PAC-SYM score improved from 1.4 ± 0.1 to 0.9 ± 0.1 for PTN and from 1.4 ± 0.1 to 0.6 ± 0.1 for ST36, both p≤0.001. The mean urge threshold to rectal distention decreased from 134.1 ± 14.3 to 85.6 ± 6.5, p=0.008 with TN at ST36. The mean maximum tolerance threshold decreased from 178.1 ± 14.9 to 138.1 ± 8.0, p< 0.05 with TN at ST36. No improvement in other measurements of the anorectal motility with TN at ST36 or TN at the PTN.
Zhang et al. (15) 2014 Placebo-controlled study/cross over	Chronic functional constipation N=12 2-week TN and 2-week sham TN in a crossover design	TTNS	Bowel habit diary PAC-SYM PAC-QOL Anorectal manometry	F: 25Hz PW: 500µs Amp: pain threshold/ 2 to 10 mA 60 min 28 sessions (2 weeks)	The mean number of weekly bowel movements increased from 1.1 ± 0.1 to 3.7 ± 0.4, p < 0.001 with TN which was significantly different from the sham-TN (2.3 ± 0.6, p = 0.01). Time of defecation decreased from 12.6 ± 0.88 to 8.2 ± 0.99, p = 0.02 with TN which was similar to sham TN findings. Improvement in PAC-SYM and PAC-QOL score after TN. The mean volume of distention required to achieve internal sphincter relaxation decreased from 41.43 ± 5.94 to 20 ± 4.36, p= 0.005 with TN which was significantly different from sham-TN (34.29 ± 4.81, p = 0.03). The mean rectal sensory threshold decreased from 40 ± 7.56 to 24.29 ± 4.29, p = 0.04) after TN. The mean maximum tolerance volume decreased from 231.29 ± 19.12 to 180 ± 9.0, p= 0.04 after TN.
Saba et al. (10) 2022 Prospective randomized clinical trial	Functional obstructed defecation N=42 IG=20, CG=21 Lost to follow up=1	IG: TTNS (bilateral) CG: biofeedback pelvic floor muscle training	MODS PAC-QOL Time of toileting Maximum straining anal pressure Maximum squeezing anal pressure	F: 10Hz PW: 200µs Amp: - 30 min 18 sessions (6 weeks)	Improvement in all outcomes except maximum squeezing anal pressure in both groups The mean MODS improved from 14.05 ± 6.09 to 10.00 ± 7.73 (p≤ 0.0001) in IG and from 12.71 ± 4.73 to 6.66 ± 6.06 (p≤ 0.0001) in CG. The mean PAC-QOL score improved from 41.05 ± 15.29 to 31.40 ± 22.76 (p= 0.001) in IG and from 44.71 ± 13.98 to 22.14 ± 16.80 (p≤ 0.0001) in CG. The mean time of toileting decreased from 29.35 ± 20.65 to 18.95 ± 16.09 (p≤ 0.0001) in IG and from 25.76 ± 16.90 to 14.47 ± 12.33 (p≤ 0.0001) in CG. The mean maximum straining anal pressure decreased from 43.70 ± 13.65 to 36.50 ± 12.33 (p= 0.001) in IG and from 48.71 ± 15.60 to 35.42 ± 11.85 (p=0.003) in CG. Maximum squeezing anal pressure increased from 73.45 ± 31.34 to 85.60 ± 36.86 (p≤ 0.0001) in IG and from 65.28 ± 22.82 to 92.95 ± 28.66 (p≤ 0.0001) in CG.

N: Number of patients, CG: Control Group, PTNS: Percutaneous Tibial Nerve Stimulation, WCS: Wexner Constipation Score PAC-QOL: Patient Assessment of Constipation-Quality of Life, F: Frequency, PW: Pulse Width, Amp: Amplitude, IG: Intervention Group, TTNS: Transcutaneous Tibial Nerve Stimulation, KESS: Knowles–Eccersley–Scott Symptom Score, GIQLI: Gastrointestinal Quality of Life Index, PAC-SYM: Patient Assessment of Constipation-Symptoms, VAS: Visual Analog Scale, IQR: Interquartile Range, MODS: Modified Obstructed Defecation Score, DDV: Defecatory Desire Volume, MTV: Maximal Tolerable Volume, BSS: Bristol Stool Score, TN: Transcutaneous Neuromodulation, PTN: Posterior Tibial nerve

Patients with chronic constipation often experience symptoms such as incomplete defecation, excessive straining, and abdominal distension. These symptoms significantly impact the patients´ psycho-social well-being, as well as their QOL. In addition to behavioral and pharmacological management, neuromodulation is a treatment option for constipation. Among the neuromodulation methods, posterior tibial nerve electrical stimulation can be used as a safe and accessible method for patients with constipation (1, 2, 6).

Although previous systematic reviews have evaluated the effectiveness of posterior tibial nerve electrical stimulation in treating various pelvic floor disorders, there is currently no definitive recommended application method for this treatment specifically in constipation patients. Thus, the parameters of posterior tibial nerve electrical stimulation in patients with chronic constipation are discussed in the present study:

Regarding posterior tibial nerve electrical stimulation application methods, two techniques are commonly used: TTNS and PTNS. Among the studies reviewed, TTNS was utilized more frequently. In comparing the application of posterior tibial nerve electrical stimulation unilaterally or bilaterally, in six studies (10, 11, 13, 14, 17, 18) bilateral stimulation was applied. However, there was a lack of comparison between unilateral and bilateral stimulation methods in studies.

The amplitude of posterior tibial nerve electrical stimulation can vary from the sensory threshold to the pain threshold. In three studies (9, 11, 12), it was increased up to the sensory threshold, while in the other three studies (14–16), it was increased up to the pain threshold. The amplitude level was not clear in the remaining studies.

The frequency of the TTNS method was reported as 10, 14, 20, and 25 Hz. Most studies (10, 13, 17, 18) used a frequency of 10 Hz. On the other hand, for the PTNS method, a frequency of 20 Hz was used.

The pulse width of the posterior tibial nerve electrical stimulation varied among studies and was described as either 200, 220, or 500 µs. However, most studies (9, 10, 12, 13, 17, 18) used a pulse width of 200 µs.

The duration of each posterior tibial nerve electrical stimulation session was 30 minutes in most studies, except for three studies (14–16), in which the duration was 60 minutes. The total number of PTNS sessions was 12, while it was reported as 12, 18, 28, 42, and 56 in studies that used TTNS. The duration of treatment varied from two to six weeks across different studies. The treatment lasted six weeks in most studies (10–13, 17, 18).

Unfortunately, no detailed information regarding the type and shape of the stimulation was reported in any of the studies.

Therefore, a definitive and standard treatment plan couldn´t be suggested due to the various parameters.

One study noted mild pain near the needle insertion location and light bleeding after excluding the needle in the PTNS method (9). Minor side effects, including itch, local erosion, and hyperemia, were observed in the TTNS method (17), while other studies reported no adverse events during treatment.

The exact mechanisms by which posterior tibial nerve electrical stimulation affects chronic constipation are unknown. Still, potential mechanisms include modification of gastrointestinal hormones and bile acids, activation of synaptic nervous outflow caused by spinal or supraspinal somatovisceral reflex, modulation of the ascending neural pathways to the sensory cortex, and changes in vagal and synaptic activity (15, 16, 22, 23).

Limitations and Strengths

According to our knowledge, the current study is the first meta-analysis. Despite the positive results of posterior tibial nerve electrical stimulation in managing chronic constipation, the results of this review should be interpreted with caution. The number of included studies was low. There was heterogeneity observed in PAC-SYM, MTV, and DDV. Therefore, well-designed RCTs are necessary to compare PTNS with TTNS using different electrical stimulation parameters or evaluate the effects of PTNS or TTNS on chronic constipation.

Conclusion

This systematic review and meta-analysis suggest that both TTNS and PTNS can be effective interventions for chronic constipation. However, TTNS may be more beneficial in improving constipation symptoms and reducing defecation time. On the other hand, PTNS may have a greater impact on improving the quality of life for patients with chronic constipation. To suggest a definitive and standard treatment plan, further research is needed to determine optimal parameters for TTNS and PTNS applications.

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Conflict of interests

The authors declare that there is no conflict of interest.

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