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Percutaneous tibial nerve stimulation (PTNS) efficacy in the treatment of lower urinary tract dysfunctions: a systematic review

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Abstract

Background: Percutaneous Tibial Nerve Stimulation (PTNS) has been proposed for the treatment of overactive bladder syndrome (OAB), non-obstructive urinary retention (NOUR), neurogenic bladder, paediatric voiding dysfunction and chronic pelvic pain/painful bladder syndrome (CPP/PBS). Despite a number of publications produced in the last ten years, the role of PTNS in urinary tract dysfunctions remains unclear. A systematic review of the papers on PTNS has been performed with the aim to better clarify potentialities and limits of this technique in the treatment of OAB syndrome and in other above mentioned urological conditions.

Methods: A literature search using MEDLINE and ISI web was performed. Search terms used were “tibial nerve” and each of the already mentioned conditions, with no time limits. An evaluation of level of evidence for each paper was performed.

Results: PTNS was found to be effective in 37-100% of patients with OAB, in 41-100% of patients with NOUR and in up to 100% of patients with CPP/PBS, children with OAB/dysfunctional voiding and patients with neurogenic pathologies. No major complications have been reported. Randomized controlled trials are available only for OAB (4 studies) and CPP/PBS (2 studies). Level 1 evidence of PTNS efficacy for OAB is available. Promising results, to be confirmed by randomized controlled studies, have been obtained in the remaining indications considered.

Conclusions: PTNS is an effective and safe option to treat OAB patients. Further studies are needed to assess the role of PTNS in the remaining indications and to evaluate the long term durability of the treatment. Further research is needed to address several unanswered questions about PTNS.

Keywords: PTNS, OAB, Lower urinary tract dysfunctions, Neurogenic bladder

Background

Percutaneous Tibial Nerve Stimulation (PTNS) is a lower urinary tract neuromodulation technique performed by percutaneous electrical stimulation of the posterior tibial nerve. This technique was described by Stoller in the late 1990s for the treatment of overactive bladder syndrome [1]. The needle insertion point, situated 4–5 cm cephalad to the medial malleolus, has previously been acknowledged

as a neural access point for the regulation of bladder and pelvic floor function. Furthermore, experiments on animals demonstrated that the electrical stimulation of the hind leg produces detrusor inhibition [2]. Basing his research on these concepts, McGuire [3] showed that the transcutaneous electric stimulation of the posterior tibial nerve can suppress neurogenic detrusor overactivity.

Description of the technique

The technique consists of stimulating the nerve by means of a 34 gauge needle electrode inserted 4–5 cm cephalad to the medial malleolus. Once the current is applied, the flexion of the big toe or the movement of

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the other toes confirms the correct positioning of the needle electrode. The electric current is a continuous, square wave form with a duration of 200 μ s and a frequency of 20 Hz. The current intensity is determined by the highest level tolerated by the patient. In Figure 1 the stimulator (Urgent[®] PC, Uroplasty, Minnetonka, MN, USA) and the technique of stimulation are represented. The stimulation sessions last for 30 minutes and are performed once a week for 10–12 weeks in the majority of published papers. In a report published by Finazzi Agrò et al. [4], the possibility of a more frequent stimulation was analysed: stimulation performed 3 times a week obtained the same results obtained as a weekly stimulation protocol. The advantage of more frequent sessions is to obtain effects in 4 weeks instead of 12: results seemed to be dependent upon the number of stimulations performed and not the time elapsed from the beginning of the stimulation program [4]. In a recent study [5], a protocol of weekly PTNS sessions performed for 6 weeks was evaluated in women with overactive bladder syndrome. The Authors found that this shortened protocol obtained a positive response in 69,7% of 43 women.

Mechanisms of action

To date despite of its great clinical use, PTNS mechanism of action still remains unclear even though in the last years several studies have tried to better clarify it.

Some papers have shown that an effect of detrusor inhibition can be found after hind leg or pudendal electric stimulation in animal models [2,6]. In two very recent studies [2,7] Tai and co-workers have found that irritation induced bladder overactivity is suppressed by tibial nerve stimulation in cats. A 30 minute stimulation at both low (5 Hz) and high (30 Hz) frequencies was able to induce

prolonged poststimulation inhibition of bladder activity, which lasted for more than 2 h and significantly increased bladder capacity.

Danisman [8] found that after PTNS the mast cells count in the bladder of female rats diminished.

Another study, as described by Chang and colleagues [9], shows that PTNS could produce effects on the (sacral) spinal cord by reducing C-fos expression (a marker of neuronal metabolic activity), in rat sacral spinal cord, after electrical stimulation of the hind leg.

An effect on supraspinal centers, has also been demonstrated in humans in a paper published by Finazzi Agro [10]. The Authors found a significant increase in amplitude of long latency somatosensory evoked potentials (LL-SSEP) recorded 24 hours after the end of a 12 session PTNS program. This finding could reflect a modification in elaboration mechanisms of sensory stimuli and it suggests a possible reorganization of cortical excitability after PTNS.

In conclusion, data available do not permit to draw definitive conclusions about PTNS mechanisms and sites of action; the results of this treatment can be due to effects on different areas of the central nervous system, but also to a peripheral effect on the target organ.

Aim of study

Despite the lack of certainty about the mechanism of action of PTNS, in the last decade this technique has been widely used for the treatment of overactive bladder syndrome (OAB) and results of PTNS on non-obstructive urinary retention (NOUR), neurogenic bladder, paediatric voiding dysfunctions and chronic pelvic pain/painful bladder syndrome (CPP/PBS) have been described as well.



Figure 1 Stimulator and technique for percutaneous tibial nerve stimulation (PTNS).

Aim of this systematic review, reported accordingly to the PRISMA statements [11], was to assess PTNS efficacy not only in OAB but also in other common urological conditions and to underline gaps in the present knowledge where research is still needed.

Methods

Eligibility criteria

All studies published on international peer reviewed journals have been considered. Only papers in English language were included in the review. Papers with only abstract were excluded. No publication date restriction was imposed. Participants of any age, sex, affected by any pathology of urological interest were considered. Only study describing effects of a percutaneous electrical stimulation of the posterior tibial nerve were considered. Primary outcome measure was the percentage of patients considered improved, independently by the definition of improvement used by the Authors. Several secondary outcome measures were considered.

Information sources

A literature search using MEDLINE and ISI web was performed. The last literature search was run on December 2012. The search was conducted by two physicians independently.

Search

Search terms used were “tibial nerve” combined with each of the following: “overactive bladder syndrome”, “urinary retention”, “neurogenic bladder”, “voiding dysfunction”, “chronic pelvic pain”, “painful bladder syndrome”, “Stoller afferent nerve stimulation”. Related articles of pertinent papers were also searched.

Study selection

Eligibility assessment was performed independently by two reviewers who screened papers titles and abstracts. Case Reports were excluded.

Data collection process

One review author extracted the following data from included studies and the second author checked the extracted data. Disagreements were resolved by discussion between the two review authors; if no agreement could be reached, it was planned a third author would decide.

Data items

Information was extracted from each included study on: condition treated, type of study, mean or median age of patients population, percentage of female patients, definition of improvement, number and percentage of improved patients, treatment of control group (if present).

Risk of bias across studies

An evaluation of level of evidence (based on the Oxford Centre for Evidence-Based Medicine criteria [12] of PTNS efficacy) was performed for each paper.

Our search strategy is shown in Figure 2.

Results

Evidence synthesis

We included 32 studies, with a total of 1087 adult participants between 18 and 82 years of age and 62 children between 1 and 17 years old. There were 6 Randomized clinical trial (RCT) studies: two compared PTNS with Sham studies, two compared PTNS with anticholinergic therapy, one compared PTNS with placebo therapy and one with ‘no treatment’ group.

There are 16 studies about OAB, 4 studies about NOUR, 9 studies about CPP/PBS, 3 studies about neurogenic bladder. Four studies are in children (1 with OAB, 1 OAB and NOUR and a OAB and Dysfunctional voiding). Only 6 studies are Randomized clinical trials: 4 in the OAB group and 2 in the CPP/PBS group. In the OAB RCT studies, control groups are different: Tolterodine, placebo, sham, oxybutynin. In the CPP/PBS group one RCT study uses sham and one has ‘no treatment’. There are 9 multicenter studies.

The inclusion criteria were:

- Participants: patients (adults and children) with idiopathic OAB, NOUR, CPP/PBS and neurogenic bladder;
- Intervention: Percutaneous tibial nerve stimulation (PTNS);
- Comparison: Sham nerve stimulation; anticholinergic medications; placebo;
- Outcome measures: cure/improvement in symptoms at the end of initial treatment program.

The exclusion criteria were:

- Papers with only abstract;
- Non-English Articles;
- Case reports;
- Papers about PTNS non reporting clinical results.

Participants and intervention

OAB studies involved a total of 640 treated patients and 189 control patients, NOUR studies involved 81 treated patients, CPP/PBS involved 233 treated patients and 56 control patients. Children studies are on 62 patients and Neurogenic bladder studies are on 72 patients.

In all studies the rate of female patients is higher than the rate of male patients. Two studies are only on female. In five studies sex is not specified. In adult studies mean age ranges between 45 and 65 years old.

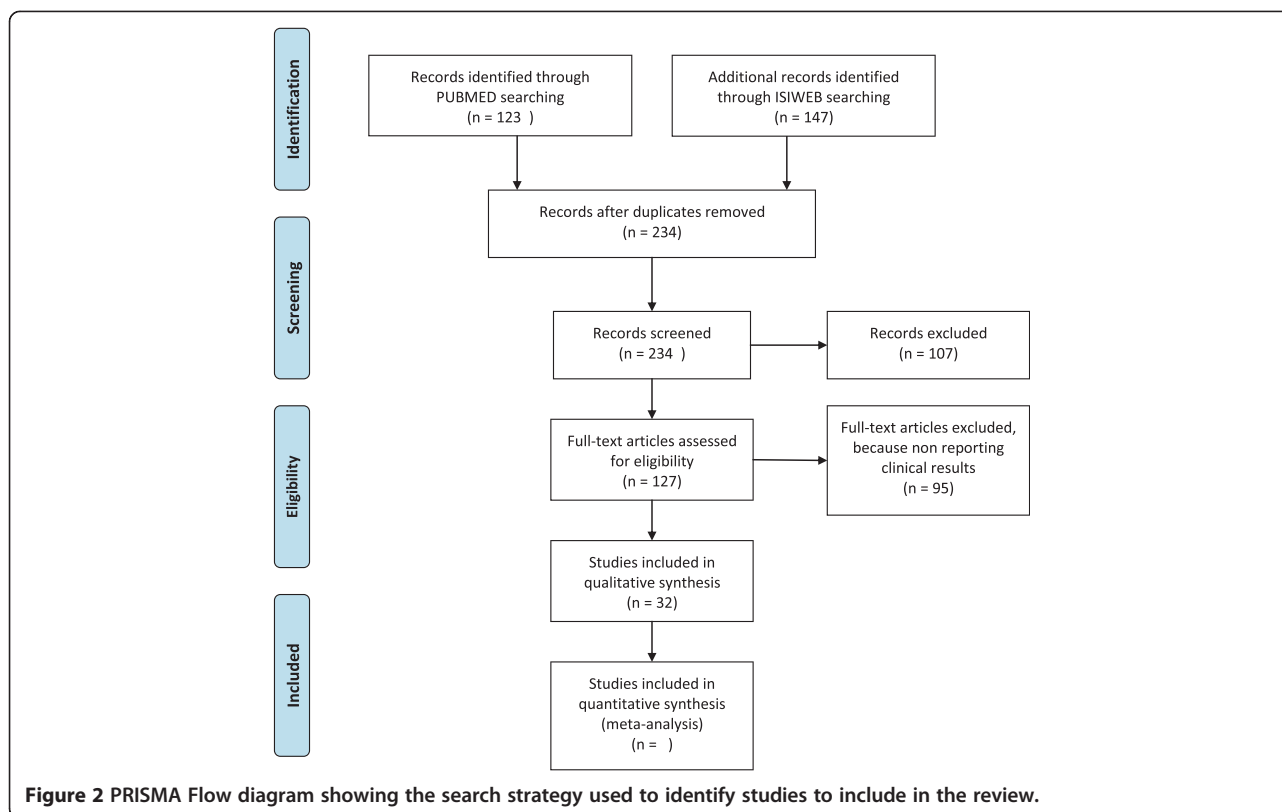


Figure 2 PRISMA Flow diagram showing the search strategy used to identify studies to include in the review.

Comparison

Two studies compared PTNS with Sham nerve stimulation, two studies compared PTNS with anticholinergic medications, one with placebo and one with 'no treatment' group.

Outcomes

Six studies evaluate only urodynamic outcome, 20 only clinical outcome and 6 urodynamic and clinical outcome.

Results in overactive bladder syndrome

Several studies have been published evaluating the effects of PTNS on OAB [13-19]. According to these studies, the overall percentage of patients classified as "successfully treated" was 54.5-79.5%. Of note, the definition of "success" differs among studies from the use of urodynamic data to clinical parameters and quality of life measures. In spite of these differences, the reported success rates are of clinical interest, especially because many were obtained from a population of patients who were already non responsive to conventional therapies. Improvements are reported not only in symptoms, but also in urodynamic observations. Klingler [13] reported a reduction of detrusor overactivity and Vandoninck showed an increase of the cystometric capacity and of the threshold of appearance of involuntary detrusor contractions [17].

Randomized controlled trials on OAB More recently, some randomized controlled studies on PTNS as treatment of OAB have been published. Peters et al. [20] provided the results of a randomized controlled study comparing PTNS to tolterodine 4 mg extended release. The subjects' global response assessments of overactive bladder symptoms was improved from baseline in a significantly higher percentage of patients in the PTNS arm compared to the tolterodine arm (79.5% reporting cure or improvement vs. 54.8%, $p = 0.01$). Objective measures (reductions in urinary frequency, incontinence episodes, urge severity and night-time voids; improvement in voided volume) improved similarly in both groups. The Authors state that PTNS is safe and offers improvements of OAB symptoms, with objective effectiveness comparable to pharmacotherapy.

After first developing a validated sham for PTNS [21], Peters randomized a total of 220 adults with OAB to PTNS or sham therapy [22]. PTNS subjects achieved statistically significant improvement in bladder symptoms with 54.5% reporting moderately or markedly improved responses compared to 20.9% of sham subjects from baseline ($p < 0.001$). According to Authors, PTNS therapy is safe and effective in treating OAB and superior to a placebo.

More recently, Finazzi Agrò [23] provided a prospective double blind, placebo controlled study aimed to investigate the possible placebo effects of PTNS on

detrusor overactivity incontinence. Patients were randomly assigned either to PTNS or to placebo group. Patients showing a reduction >50% of urge incontinence episodes were considered "responders". A statistically significant difference between responders' rates was found (71% in PTNS group vs 0% in placebo group, $p < 0.0001$). Improvement in the number of incontinence episodes, number of voids, voided volume and Incontinence quality of life (I-QoL) score were statistically significant in the PTNS group but not in placebo group. The authors concluded that the relevance of a placebo effect was negligible in this patients' population.

Results for OAB are reported in Table 1: positive data on the efficacy of PTNS in this condition are reported by all Authors. Three randomized controlled trials (level of evidence 1) are available for PTNS as treatment for this condition.

Results in non-obstructive urinary retention

PTNS has been used also in the treatment of non-obstructive urinary retention (NOUR) and the experience in this field is limited to few published papers. According to these papers, the percentage of patients successfully treated is good, varying from 41 to 100%, according to the parameters chosen to classify "success" [13,24,25]. In a study published by Vandoninck [24], the primary outcome measure was a reduction of the total catheterized volume per 24 hours. Using a reduction of >50%, the percentage of responders was 41%; using a reduction rate of >25%, the percentage of responders was 67%.

According to another paper from the same authors [25], an improvement of the urodynamic parameters of the voiding phase (maximum flow, detrusor pressure at maximum flow, post-void residual urine) was also observed.

Van der Pal [26] showed that PTNS has an effect in QoL of all patients investigated and a reduction of at least two pads/day recorded in the bladder diary.

Results for NOUR are reported in Table 2: positive data on the efficacy of PTNS in this condition are reported by all Authors. No randomized controlled trial is available for PTNS as treatment for this condition; only prospective non randomized trials are available (level of evidence 2–3).

Results in chronic pelvic pain/painful bladder syndrome

Few studies have evaluated the effect of PTNS on CPP/PBS [27-32]. According to Van Balken [27], this technique seems to be effective in as much as 42% of patients with CPP. In the same group of patients, Kim [28] found that 90% showed an improvement >25% in the VAS score for pain, with 60% reaching improvement >50%. Kabay [29] evaluated the efficacy of PTNS in the treatment of patients with category IIIB chronic non-bacterial prostatitis. 89 patients were randomized to receive either PTNS ($n = 45$) or sham treatment ($n = 44$). A complete response on pain

and symptoms was observed after PTNS in 40% and 66.6% of the patients, whereas a partial response was observed in 60% and 33.3% of the patients, respectively; no significant results were seen after sham treatment.

Two studies from Zhao [30,31] evaluated PTNS for the treatment of PBS/interstitial cystitis (IC). In the first one [30], after a prospective evaluation in 14 patients with refractory IC, the authors concluded that PTNS had no significant clinical effect over 10 weeks of treatment. In a more recent study [31], the same author evaluated the efficacy of PTNS performed twice a week in 18 female patients with IC. 44.4% of patients evaluated the trial effective and showed a significant improvement in bladder capacity. Baykal [32] evaluated the effect of intravesical heparin and PTNS in 10 subjects with IC. After 2 and 12 months of treatment, patients showed significant reduction of symptoms and of Wisconsin pain scores as well as an increase of cystometric capacity. The authors concluded that the combination of intravesical heparin and peripheral neuromodulation seems to be an alternative for patients with IC who were not responsive to other treatments.

Congregado [33] described a significant improvement in all lower urinary tract irritative symptoms of 51 female patients studied. Gokylidiz [34] reported a 100% of clinical success in 12 patients with chronic pelvic pain treated with PTNS.

Results for CPP/PBS are reported in Table 3: positive data on the efficacy of PTNS in this condition are reported by all but one Authors. Only one randomized controlled trial is available for PTNS as treatment for CPP (level 1, one paper); several prospective non randomized trials are available (level of evidence 3).

Results in children

PTNS seems to be effective in the treatment of non-neurogenic lower urinary tract dysfunctions of children: 60-80% of children with OAB and 43-71% of children with urinary retention showed a significant improvement [35-37]. De Gennaro [36] found that PTNS is generally well accepted by children, with low scores of a visual analog scale for pain, that further decreased during the treatment. Efficacy at 2 year follow up was maintained [37].

Results in children are reported in Table 4: no randomized controlled trial is available for PTNS as treatment for dysfunctional voiding/OAB in children; only prospective non randomized trials are available (level of evidence 2–3).

Results in patients with neurogenic bladder

Few reports have been published on the effects of PTNS in patients with neurogenic bladder. Acute urodynamic effect of PTNS were observed in a mixed population of OAB patients, most of whom neurologically impaired (multiple sclerosis -MS-, spinal cord injury -SCI-, Parkinson's disease -PD-). During stimulation, an increase

Table 1 Results of the use of PTNS in OAB Patients

Authors	Years	Control group	PTNS			Other			RCT	Methods	Level	Results	Female n(%)		Mean age		Multicenter	
			n	Positive	%	n	Positive	%					R	PTNS	Control group	PTNS group		Control group
Klingler HC	2000 [13]	N/A	15	10	67				N	Urodynamic and clinical	3	<10 voids/day <2voids/night PadTest (g) 10	73		N/A		N	
Govier FE	2001 [14]	N/A	47		71				N	Urodynamic	2-3	25% reduction in mean daytime voiding frequency	90		57.4 (24–80)		Y	
van Balken MR	2001 [15]	N/A	37	22	59				N	Clinical	2-3	Request for continued chronice treatment	73		52.5 (23–74)		Y	
Vandonink V	2003 [16]	N/A	35	24	69				N	Clinical	2-3	Continuing treatment	71		57 (29–82)		Y	
Vandonink V	2003 [17]	N/A	60	34	57				N	Urodynamic	2-3	50% reduction					Y	
Peters KM	2009 [20]	Tolterodine	44	35	80	42	23	55	0.01	Y	Clinical	2-3	Improvemtn for cure in 79.5% compared to 54.8% in the tolterodine arm	96	92	57.5	58.2	Y
Peters KM	2010 [22]	Sham	110	60	55	110	23	21	<0.001	Y	Clinical	1	Improvement in overall bladder symptoms	78	80	62.5	60.2	N
Finazzi-Agro E	2010 [23]	Placebo	17	12	71	15	0	0	<0.001	Y	Clinical	1	50% reduction	100	100	44.9	45.5	N
Amarenco G	2003 [38]	N/A	44	22	50					N	Clinical	1		66		53.3		N
van Der pal F	2005 [26]	N/A	11	11	100					N	Clinical		Improvement in overall bladder symptoms	54.5		51 (33–66)		N
Karademir K	2005 [18]	Oxybutynin + PTNS	21	13	62	22	18	82	<0.0001	Y	Clinical		Improvement in overall bladder symptoms					Y
de Séze M	2011 [45]	N/A	70	58	82.8					N	Urodynamic and clinical		Improvement in 82.6% and 83.3% of the patients on day 30 and day 90 regarding symptoms and QoL					N
van Balken MR	2006 [44,47]	N/A	132	43 O/68 S	32,6 O/51,5 S					N	Clinical		Improvement QoL	61.3		53 (21–82)		N
Nuhoglu B	2005 [19]	N/A	35	19	54					N	Urodynamic and clinical		Improvement Urgency and QoL	100		47.3 (35–57)		

Table 2 Results of PTNS in Patients affected by non obstructive urinary retention

Authors	Years	Control group	PNT		RCT	Methods	Level	Results	Female (%)	Mean age	Multicenter	
			n	Positive %								
van Balken MR	2001 [15]	N/A	12	7	58	N	Clinical	2-3	Request for continued chronice treatment	58	58, 8	N
Vandoninck V	2003 [16,17]	N/A	39	16	41	N	Clinical	2-3	50% reduction of catheterized volume	69	53 (28–77)	Y
Vandoninck V	2004 [24]	N/A	39	16	41	N	Urodynamic	3	50% reduction of catheterized volume	69	53 (28–77)	Y
van der pal F	2006 [26]	N/A	30	29	100	N	Bladder Diary and QoL	2-3	Improvement BD and QoL	86.6	51 (20–72)	N

of first involuntary detrusor contraction volume and of cystometric capacity was found [38]. Similar results were observed by Kabay [39] in PD patients with detrusor overactivity. On the other hand, Fjorback [40] failed to obtain acute urodynamic reductions of detrusor overactivity in MS patients.

Kabay and Gobbi [41,42] investigated the effect of PTNS on the lower urinary tract symptoms in MS patients with detrusor overactivity and lower urinary tract symptoms (LUTS), respectively. After 12 weeks, statistically significant improvements in several urodynamic and clinical parameters were observed. Both authors concluded that PTNS is effective to improve LUTS in MS patients.

Results in neuropathic bladder are reported in Table 5: positive data on the efficacy of PTNS in this condition are reported by all Authors. No randomized controlled trial is available for PTNS as treatment for this condition; only prospective non randomized trials are available (level of evidence 2–3).

Complications

No major complications are reported in literature, following PTNS treatment. Only mild to moderate pain in the site of the puncture was reported by some authors; the majority of patients, with the inclusion of children [35–37], seem to tolerate perfectly the positioning of the needle and the subsequent stimulation.

Long term durability

The only available long term study on results of PTNS on the treatment of overactive bladder was published by MacDiarmid et al in 2010 [43]. Subject global response assessments showed sustained improvement from 12 weeks at 6 and 12 months, with 94% and 96% of responders, respectively.

Patients in this trial were receiving periodic PTNS sessions. Van der Pal [44] found that, 6 weeks after initial PTNS therapy, 64% of patients showed a worsening of symptoms, thus underlining the need of a maintenance stimulation protocol. The need for repeated stimulation sessions could be less common in children: according to

Capitanucci, maintenance stimulation sessions are needed only in 29% of children with dysfunctional voiding and in 50% of children with overactive bladder [37].

The need of repeated stimulation sessions, possibly for long time or lifelong, is probably the major limit of PTNS, requiring either periodic office based procedures, or a home based treatment. Transcutaneous stimulation, as proposed by McGuire [3], could be an alternative for chronic treatment. Some very recent papers evaluated the efficacy of transcutaneous tibial nerve stimulation (TTNS) in the treatment of OAB in multiple sclerosis patients [45] and of urgency incontinence in older women [46].

Discussion

Recommendations for further research

Efficacy of PTNS

Level 1 evidence is produced by few studies for efficacy of PTNS in the treatment of OAB/urge incontinence. PTNS seems to be an efficacious and safe treatment for OAB that could be highly recommended. Nevertheless, this evidence needs to be confirmed by further good quality randomized controlled studies and meta-analysis of them.

For all the remaining indications considered in this systematic review only 2–3 level of evidence of efficacy is available for PTNS (only one RCT for CPP/PBS is available). RCT for PTNS in these indications are highly recommended.

Stimulation protocol

Little is known about the effects of the electric stimulation parameters and the stimulation protocols on PTNS efficacy. Further studies are needed to identify the best electric parameters and the best protocols for every indications as well as possible effects of a combination therapy with drugs (e.g. antimuscarinics for OAB or intravesical glycosaminoglycans for painful bladder syndrome).

Safety

According to published data, PTNS is safe and well tolerated. Nevertheless, future studies will have to include safety data of the technique.

Table 3 Efficacy of PTNS in chronic pelvic pain/painful bladder syndrome

Authors	Years	Control group	PNT			Other			RCT	Methods	Level	Results	Female (%)		Mean age (range)		Multicenter
			n	Positive	%	n	Positive	%					PNT group	Control group	PNT group	Control group	
van Balken MR	2003 [27]	N/A	33	14	42				N	Clinical	3	Mean VAS for pain	33		51.6 (25–79)		N
Kim SW	2007 [28]	N/A	15	9	60				N	Clinical	3	VAS score for pain reduction >50%			60 (41–78)		N
Kabay S	2009 [29]	Sham	45	18	40	44	0	0	Y	Clinical	1	VAS score for pain reduction >50%	0	0	37.9 (range 24–51)	38.5 (range 25)	N
Zhao J	2004 [31]	N/A	14	0	0				N	Clinical	3	VAS Scale reduction	93				N
Zhao J	2008 [31]	N/A	18	8	44				N	Clinical	3	Bladder capacity increases	100		60		N
Baykal K	2005 [32]	N/A	10	10	100				N	Clinical	3	Wiscosin pain score	80		49 (40–62)		N
Congregado Ruiz B	2004 [33]	N/A	51	51	100				N	Clinical		Improvement QoL	100		55 (18–74)		N
Gokyildiz S	2012 [34]	No treatment	12	12	100	12	0	0	Y	Clinical		Improvement QoL	100	100	/	/	N

Table 4 Efficacy of PTNS use in children

Authors	Years	Control group	PNT			RCT	Methods	Level	Results	Female (%)	Mean age	Multicenter
			n	Positive	%							
Hoebeke P	2002 [35]	N/A	31	27	87		Clinical and Urodynamic findings	2-3	Clinical and shape of the uroflowmetry curve	48	11, 7	N
De Gennaro M	2004 [36]	N/A	10	8	80	N		2-3	Clinical and Urodynamic findings	60	9	N
De Gennaro M	2004 [36]	N/A	7	5	71	N		2-3	Clinical and Urodynamic findings	57	12	N
Capitanucci ML	2009 [37]	N/A	14	12	86	N	Clinical and Urodynamic findings	2-3	Clinical findings	NS	NS	N
Capitanucci ML	2009 [37]	N/A	14	14	100	N		2-3	Clinical findings	NS	NS	N

Predictive factors of PTNS success

Very few data on predictive factors of success of PTNS are available.

The urodynamic characteristics of OAB patients seem to be relevant: OAB patients not showing detrusor overactivity (or showing it only at higher bladder volumes) seem to be more prone to respond to treatment [17]. In NOUR, patients with milder symptoms seem to respond better [25]. Bad mental health (as measured with the SF-36 Mental Component Summary) seems to be a negative predictive factor for success of PTNS in patients with OAB, NOUR or CPP/PBS [47].

Studies on subgroups of patients in the different indications considered are needed, to find patients more prone to respond to this treatment, with the aim to reduce the number of patients unsuccessfully treated, thus reducing the costs.

Long term durability

Only one long term (12 months) study on results of PTNS on the treatment of overactive bladder is available [43]. No long term studies are available for the remaining indications. Further long term studies are needed.

As already mentioned, the need of repeated stimulation sessions is an important drawback of PTNS, making this technique time consuming for the patients and the health professionals. Further studies on alternative possible treatments (e.g. home based transcutaneous stimulation) are needed.

Mechanisms of action

Few data are available about possible mechanisms of action of PTNS. Studies on animal models and on humans, possibly using central nervous system functional imaging techniques are to be encouraged.

Economic data

Analysis of the costs of PTNS both in the short and in the long term, in relation with the patients' quality of life improvement, would be very useful to understand the cost-effectiveness of this treatment.

Conclusions

PTNS is an effective treatment for patients with OAB syndrome non responding to conservative therapies. Results from randomized controlled studies demonstrate that the success rate of PTNS is statistically superior to that of placebo. The durability of the improvement obtained by PTNS has also been demonstrated with periodic stimulations to sustain the therapeutic effects. Finally PTNS is safe, with no major complications reported in literature. In consideration, of these potentialities, as suggested by some authors [48], PTNS could be offered early in the course of OAB treatment.

Promising results, to be confirmed by randomized controlled studies, have been obtained in non-obstructive urinary retention, CPP/PBS and urinary disorders in children. Further studies are needed to assess the exact role of PTNS in these indications and to evaluate the long term

Table 5 Results of the use of PTNS in Patients affected by neurogenic bladder

Authors	Years	Control group	PNT			RCT	Methods	Level	Results	Female (%)	Mean age	Multicenter
			n	Positive	%							
Kabay S	2009 [29,39,41]	N/A	32	15	47	N	Urodynamic	2-3	50% improvement cystometric capacity	41	64 (44-78)	N
Gobbi C	2011 [42]	N/A	21	16	76	N	Clinical	2-3	Patient perception of Bladder Cond	76	46 (29-62)	N
Kabay S	2009 [29,39,41]	N/A	19	19	100	N	Urodynamic		Custometry parameters	100		N

durability of the treatment. Further research is needed as well to assess several still unanswered questions about PTNS.

Abbreviations

PTNS: Percutaneous tibial nerve stimulation; OAB: Overactive bladder syndrome; NOUR: Non obstructive urinary retention; CPP/PBS: Chronic pelvic pain/painful bladder syndrome; RCT: Randomized clinical trial; I-QoL score: Incontinence quality of life score; IC: Interstitial cystitis; MS: Multiple sclerosis; SCI: Spinal cord injury; PD: Parkinson's disease; LUTS: Lower urinary tract symptoms; TTNS: Transcutaneous tibial nerve stimulation.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

GG and VI have made substantial contributions to acquisition, analysis and interpretation of data. EFA, ADS and AA have made substantial contributions to conception and design of the study. LT has been involved in drafting the manuscript. CDN and EFA have been involved in revising the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

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