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Review Article

Percutaneous Tibial Nerve Stimulation in Urology: Overview

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Introduction

Tibial Nerve Stimulation (TNS) was first introduced by McGuire and colleagues in 1983, who observed symptomatic relief of lower urinary tract symptoms (LUTS) using transcutaneous adhesive electrodes over the common peroneal or posterior tibial nerve[1]. In 1990, Stoller and colleagues adjusted this method and described the Stoller Afferent Nerve Stimulation(SANS) for the treatment of overactive bladder (OAB) syndrome via percutaneous stimulation of the posteriortibial nerve (PTNS); they observed at least a 50% improvement in symptoms in 80% of their cohort of 90 patients[2]. It has been used as minimally invasive option for various forms of bladder dysfunction, ranging from OAB to neurogenic bladder to pelvic pain syndrome; however, a paucity of level 1 evidence limits its adoption in today's urologic practice [3]. In this review, the authors seek to analyze and summarize the current literature regarding the use of PTNS for various urologic conditions.

Neuroanatomy and principles of PTNS

The tibial nerve, also called the posterior tibial nerve due to its close association with the posterior tibial artery,is a mixed nerve containing motor and sensory fibers originating from the L4-S3 nerve roots; these nerve roots also provide innervation to the detrusor, urinary sphincter, and pelvic floor muscles.To clarify the anatomical course of the tibial nerve at the level of ankle joint, we dissect the medical side of the lower leg (Figure 1). The tibial nerve is 3-4 cm from the medial malleolus (halfway between medial malleolus and the Achilles tendon).

Neuromodulatory therapies are presumed to improve or restore normal control of an imbalanced voiding reflex by affecting the central afferents [4]. The aim of this treatment modality is to achieve detrusor inhibition by acute electrical stimulation of

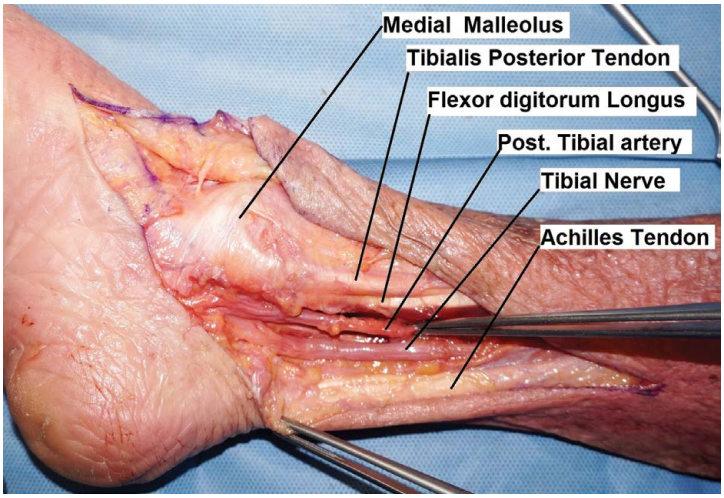

Figure 1: Anatomy of the tibial nerve in relation to the medial malleolus

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afferent somatic sacral nerve fibers by means of PTNS. Although the exact mechanism of neurostimulation is still unclear, it is suggested that TNS modulates afferent and efferent signals through the sacral plexus (S2-S3) [5,6].

Inhibition of spinal micturition centers can be achieved by electrical stimulation of either the pelvic nerve, afferent sensory fibers in the pudendal nerve, or muscle afferents from the limbs[7-9]; most of the current literature on mechanism, however, is limited to animal studies.Tai and colleagues have found that irritation induced bladder over activity is suppressed by tibial nerve stimulation in cats[10]. A 30 minute stimulation at both low (5 Hz) and high (30 Hz) frequencies was able to significantly increase bladder capacity for greater than 2 hours. Danisman and colleagues found that PTNS reduced mast cell count in female rat bladders[11]. Another study by Chang and colleagues demonstrated that electrical stimulation of the hind legreduced C-fos (a marker of neuronal metabolic activity) expressionin rat sacral spinal cords[12]. Choudhary and colleagues recently found PTNS increases bladder compliance and, subsequently, pressures at which the voiding reflex is initiated in rats with overactive detrusors stimulated by acetic acid; increased bladder storage capacity was achieved via inhibition of afferent signaling [13].

Recent literature suggests both sensory and motor neuromodulatory effects of PTNS. Changes in the brain cortex during PTNS similar to those reported by sacral nerve stimulation(SNS) have been described [14,15]. Data from Finazzi-Agroand colleagues suggests plastic reorganization cortical signaling following PTNS in patients with OAB [16]. Several very recent studies have also suggested a role of certain neurotransmitter receptors in the in mechanism of action for PTNS. Matsua and colleagues found that intravenous (IV) inhibition of the metabotropic glutamate receptors and opioid receptors reduced PTNS efficacy in cat bladders [17]. Ferroni and colleagues, similarly, found that naloxone reduced PTNS effect in OAB when injected IV;interestingly, they also found an effect of naloxone when applied directly to the rostral brain stem [18]. To build on this, Zhang and colleagues investigated the role of individual opioid receptors and found a larger role of μ and κ receptors than δ for PTNS-induced detrusor inhibition [19]. Xiao and colleagues found that PTNS ineffective in animals with acute spinal cord transection, further suggesting the role of the brain stem in PTNS mechanism [20].

PTNS procedure

The procedure consists of stimulation of the tibial nerve by 34 gauge needle electrode inserted 4–5 cm cephalad to the medial malleolus[2]. Interestingly, this site is the same one used in traditional Chinese acupuncture (SP6) to relieve dysfunction of the pelvic floor and pelvic organs[21-23].

Patients are positioned either supine or sitting with the soles of the feet together and their knees abducted and flexed ("frog position"). A pad is placed at the medial face of the ipsilateral calcaneus as grounding. The needle electrode connected to an external low voltage (9 V) pulse generator, which delivers the electrical pulse. Once the electrode needle is correctly placed and pulse is applied, patient response is confirmed by involuntary toe flexion orextension of the entire foot accompanied by a sensation in the ankle and sole of the foot. Toe flexion occursfrom direct stimulation of the S3 nerve root, which is also responsible for bladder innervation. A current level of 0.5-9 mA at a fixed frequency of 20 Hz and pulse width of 200 μs is selected and adjusted based on the patient's tolerance to the associated discomfort. Commonly used PTNS protocol consists of weekly sessions lasting approximately 30 minutes for 10-12 weeks. Reports of longer lasting sessions and/or frequently stimulation achieving the same results in less timehave also been described in the literature [24,25]. Others found that daily sessions may be more effective than twice weekly sessions[26].

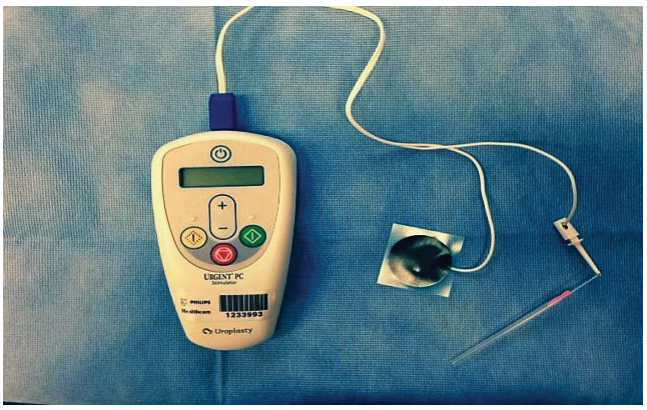

Figure 2. Urgent PC Neuromodulation System (Courtesy of Uroplasty, Inc., Minnetonka, MN)

In general, PTNS is a low-risk procedure with complications consisting mainly of minor bleeding, pain, and skin inflammation from needle placement[26]. Other less common adverse events including leg cramps, foot pain, a vasovagal response; in contrast to SNS, PTNS avoids direct painful electrical impulses near the pelvic region, as well as the morbidity and cost associated a surgical procedure for definitive implant placement. The need of repeated stimulation sessions, however, is a major limitationof PTNS.

PTNS use for the treatment of OAB was approved by the FDA in 2000. The Urgent PC Neuromodulation System (Uroplasty, Inc., Minnetonka, MN) is currently the only device commercially available, which received the CE(Conformity marking by European area) mark for OAB and fecal incontinence in 2005(Figure 2).

TNS can be achieved either by adhesive electrode transcutaneous stimulation (TTNS), which has been demonstrated to be effective for urinary and bowel dysfunction, or by PTNS, which has been shown to be more effective than TTNS likely because the needle electrode is directly in contact with the tibial nerve [27].

PTNS Uses in Urology

A. Overactive Bladder Syndrome

Overactive bladder (OAB) is a syndrome of urinary urgency, usually accompanied by frequency, nocturia, and possible urge incontinence which afflicts approximately 12% of the population [28]. "Dry" OAB without incontinence is more prevalent in males, while "wet" OAB with incontinence is more common in females [28]. OAB is a significant economic burden on our healthcare system, as well a physical, psychological, and social stressor for patients[29].

The AUA/SUFU guidelines recommend PTNS as a third-line therapy for highly motivated patients who are willing to comply with the frequent office visits required. PTNS may be better for those with less refractory, mild to moderate OAB symptoms[30].

Several studies have been published evaluating the effects of PTNS on OAB. PTNS was found to be effective in reducing urinary frequency, incontinence episodes, and detrusor overactivity in 37-100 % of patients with OAB[31]. In one prospective randomized, placebo-controlled trial comparing PTNS, TTNS and sham stimulation, patients undergoing PTNS had a greater reduction in the episodes of incontinence than the other groups. These improvements were maintained over a 6-month follow-up period [32]. A multicenter double-blind controlled prospective study (SumiT) compared the efficacy of the active (54.5%) and the sham therapy (20.9%) [33]. Another multicenter RCT documented comparable efficacy of PTNS vs drug therapy (OrBiT trial). At 3 months, 79.5% of the patients after PTNS vs 54.8% of patients on tolterodine were improved [34]. Other studies measuring also note improvements in OAB symptoms via urodynamic parameters [35,36].

The short-term use of PTNS have been established to improve OAB symptoms with significant evidence, but unfortunately there is no standardized protocol for maintenance therapy. Many regimes are available,rangingfrom weekly to monthly sessions depending on the patients' and clinicians' perception of symptoms control [37].

Two trials with long-term follow-up, The OrbiT and the Step trials showed that the majority of patients maintained a responder statusat 12 and 24 months, respectively, with a mean interval of treatment of about 3 weeks. The withdrawal rate was 30-33% [37-40].

The success of PTNS in OAB depends on various patient factors, including level of detrusor overactivity. Patients showing detrusor overactivity at higher filling volumes seem to be more responsive to treatment [38]. Patients with milder symptoms also may respond better [41]. 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 [42].

According to these results, PTNS is a viable alternative to drugs or implantablesacral nerve stimulation (SNS) for the long-term treatment. In contrast to SNS, patients can simply discontinue PTNS with no need to undergo surgery if they become refractory to therapy.

Finazzi Agroand colleagues showed an improvement of urodynamic parameters in 9/14 patients with neurogenic detrusor overactivity (NDO) after TTNS[43]. Other showed a significant improvement of LUTS and urodynamic filling parameters after daily 20 min sessions of TTNS for three months[44].PTNS usage, however, is more controversial for neurogenic voiding dysfunction.

B.Functional Urinary Retention

PTNS has been recommended in patients affected by idiopathic or neurogenic non-obstructive urinary retention. According to the literature, clinical success varied from 41 to 67%. Vandoninck has reported an improvement of urodynamic parameters during voiding phase [36,37]. More robust data is needed, however, to explore this application [41,45].

C.Chronic Pelvic PainSyndrome/CPPS

Few studies have been published to assess the efficacy of PTNS in treating chronic pelvic pain (CPP) syndrome. These studies show that PTNS may be considered as treatment option after failure of standard conservative therapies. It has been seen a reduction of (visual analogue scale) VAS scale and an improvement of QoL questionnaire scores. Despite that, the percentage of responders in CPPS patients seems to be lower (about 40-42 %) than that one reported in OAB patients[46,47].

Conclusion

PTNS is one form of neuromodulation that can be offered to most patients with refractory OAB who has not met their treatment goal with medication. Elderly patients, patients with neurogenic detrusor overactivity, those with nighttime frequency, those with milder symptoms, and partial responders are all excellent candidates for PTNS[48]. PTNS is a minimally invasive, office-based procedure that is safe, effective and an important therapy that ought to be considered for patients with OAB.

The evidence of the third-line OAB treatment continues to develop which can lead to improvement in the patient outcomes and QoL. Treatment success is usually based on patient expectations [41]. Communicating with and explaining all appropriate options to the patient, based on differing efficacy and side effects profile of the treatments available for OAB, as well as eliciting patient input, can enhance outcome.

In general, the site of stimulation, the S3 area of the spinal cord over the sacrum or over the tibial nerve is S3 area, is currently have consensus, but it is not clear which approach to stimulus delivery is the most effective. While the success of PTNS has been document, studies with long-term follow-up to assess its durability and efficacy are still required.

Future directions

OAB syndrome is a chronic condition that is currently treatable but not curable. Although there are many treatment options, they differ in response and durability while often having considerable side effect profiles.

Although PTNS is minimally invasive, easily applicable and well tolerated, the main disadvantage seems to be the necessity for chronic treatment. Besides that, the debate of different treatment parameters and schedules reported in the literatures, where they vary from continuous stimulation to treatment once daily or once or several times a week, for the duration of mostly some weeks or months.

All these direct the scientist and urologist to look for less invasive, more effective and more durable treatment modalities. The development of an implantable subcutaneous stimulation device may be a potential solution for this problem. Subcutaneous insertion of an implantable pulse stimulator near the tibial nerve at the lower leg may become feasible by using a small needle; in the near future, this can facilitate tibial stimulation at home without the need for the frequent visits to the urologist[27].

More high-quality trials regarding the pathology, pathophysiology, and treatment for OAB syndrome with PTNS are needed for better innovation in the following years.

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