available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Collaborative Review – Voiding Dysfunction

Efficacy and Safety of Sacral and Percutaneous Tibial Neuromodulation in Non-neurogenic Lower Urinary Tract Dysfunction and Chronic Pelvic Pain: A Systematic Review of the Literature

Manuela Tutolo[a,b,*], *Enrico Ammirati*[c], *John Heesakkers*[d], *Thomas M. Kessler*[e], *Kenneth M. Peters*[f], *Tina Rashid*[g], *Karl-Dietrich Sievert*[h,i], *Michele Spinelli*[j], *Giacomo Novara*[k], *Frank Van der Aa*[a], *Dirk De Ridder*[a]

[a] *Department of Urology, University Hospitals Leuven, Leuven, Belgium;* [b] *Department of Urology, URI, IRCCS Ospedale San Raffaele, Milan, Italy;* [c] *Department of Urology, Ospedale San Giovanni Battista, Turin, Italy;* [d] *Department of Urology 610, Radboud University Medical Center, Nijmegen, The Netherlands;* [e] *Department of Neuro-Urology, Balgrist University Hospital, Zurich, Switzerland;* [f] *Department of Urology, Beaumont Hospital, Royal Oak, MI, USA;* [g] *Functional Urology and Gender Services, Imperial College Healthcare NHS Trust, Charing Cross Hospital, London, UK;* [h] *University of Rostock Urology Clinic, Rostock, Germany;* [i] *Department of Urology, Comprehensive Cancer Center, Medical University Vienna, Vienna General Hospital, Vienna, Austria;* [j] *Spinal Unit, Division of Neurourology, A. Zanollo Center for Sacral Area Disfunction, Ospedale Niguarda, Milan, Italy;* [k] *Department of Surgery, Oncology, and Gastroenterology – Urology Clinic, University of Padua, Padua, Italy*

Article info

Article history:
Accepted November 3, 2017

Associate Editor:
Jean-Nicolas Cornu

Keywords:
Sacral neuromodulation
Tibial nerve stimulation
Overactive bladder
Chronic non-obstructive urinary retention
Lower urinary tract dysfunction

Abstract

Context: Neuromodulation is considered in patients with non-neurogenic lower urinary tract dysfunction (LUTD) not responsive to conservative treatment.
Objective: To systematically review the available studies on efficacy and safety of sacral neuromodulation (SNM) and percutaneous tibial nerve stimulation (PTNS) in non-neurogenic LUTDs not responsive to conservative treatments.
Evidence acquisition: A literature research was conducted in PubMed/Medline and Scopus, restricted to articles in English, published between January 1998 and June 2017, with at least 20 patients and 6 mo of follow-up.
Evidence synthesis: Twenty-one reports were identified. Concerning SNM, the improvement of $\geq$50% in leakage episodes ranged widely between 29% and 76%. Overall dry rate ranged between 43% and 56%. Overall success/improvement rate in PTNS varied between 54% and 59%. Symptom improvement or efficacy in interstitial cystitis/bladder pain syndrome patients appeared to be lower compared with other indications in both techniques. Safety data showed fewer side effects in patients submitted to PTNS.
Conclusions: Neuromodulation gives good results and is a safe therapy for patients with overactive bladder or chronic nonobstructive urinary retention with long-lasting efficacy. Moreover, PTNS has been shown to have good success rates and fewer side effects compared with SNM. These data have to be confirmed with long-term follow-up.
Patient summary: Sacral neuromodulation can improve low urinary tract symptoms in selected patients; it appears to be a safe therapy for nonresponders to standard medical therapies. Percutaneous tibial nerve stimulation (PTNS) is a less invasive technique that gives good results in short time with fewer side effects. However, we must consider that PTNS has not been tested in the long term and results are lower if compared with SNM.

* Corresponding author. Department of Urology, University Hospitals Leuven, Herestraat 49, Leuven 3000, Belgium. Tel. +32 16 34 69 30; Fax: +32 16 34 69 31.
E-mail address: tutolo.manuela83@gmail.com (M. Tutolo).

https://doi.org/10.1016/j.eururo.2017.11.002
0302-2838/

1. Introduction

Sacral neuromodulation (SNM) has been approved by the US food and Drug Administration for overactive bladder (OAB) syndrome (urinary urgency, urinary frequency, nocturia, urgency urinary incontinence [UUI]) and chronic nonobstructive retention (CNoUR) [1–3]. However, the published data on effectiveness of SNM are scarce and contradictory. Moreover, no long-term data from well-designed studies are currently available [4–8].

Its use is indicated, in general, in patients who have failed conservative standard measures. Recent studies indicate that over 50% of individuals with OAB discontinue pharmacotherapy at 12 mo (regardless of the particular agent) due to lack of efficacy or due to intolerable side effects [2–9].

The mechanism of action of SNM is still not totally understood. Practically its function is based on mild electrical stimulation of the sacral nerves that can modulate neural reflexes that influence bladder and pelvic floor behaviour.

Patients who have at least 50% improvement in the main symptoms are considered to be a success and are candidates for implantation of a permanent implantable pulse generator [10].

Percutaneous tibial nerve stimulation (PTNS) is an alternative accepted neuromodulation therapy for non-neurogenic lower urinary tract dysfunction (LUTD) [11]. The believed working mechanism is that this approach can give a neural access to target the sacral plexus from an accessible, minimally invasive entry point into the nervous system via the posterior tibial nerve [12–16]. Both techniques have also shown beneficial effects in interstitial cystitis/bladder pain syndrome (IC/BPS), and the simplicity of the surgical technique and low patient morbidity associated with it make this an attractive option before cystectomy and urinary diversion [4–7].

Previous reviews have already demonstrated great discrepancy in terms of outcomes, symptom assessment, definition of cure/improvement, and range of treatments received before SNM or PTNS. Moreover, severity of symptoms was often not well described [17].

To try to clarify this situation and give the highest evidence available for the performance of neuromodulation in refractory LUTDs, we conducted a systematic review of neuromodulation efficacy and safety outcomes in the context of non-neurogenic LUTD management after a minimum follow-up of 6 mo.

2. Evidence acquisition

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement [18,19].

A literature search was conducted on PubMed/Medline and Scopus in June 2017. The search strategy included the following terms: “sacral neuromodulation” AND “tibial neuromodulation” AND “lower urinary tract symptoms” AND “overactive bladder” AND “urinary retention” AND “chronic pelvic pain” AND “painful bladder syndrome”.

For pragmatic reasons, we limited our search to randomised and/or prospective trials and retrospective studies, written in English, with at least 20 human adult patients and 6 mo of follow-up, published between January 1998 and June 2017 (Supplementary material). To be included, the studies had to assess the efficacy and/or safety of the aforementioned techniques and/or predictors of success.

Articles were first screened and selected based on their abstract and then studied in detail. Two independent researchers evaluated the articles and discussed eligibility with one researcher, making the final decision. For every paper, we evaluated the following aspects: study design, baseline patient evaluation, reports of perioperative data, study outcome criteria for efficacy and safety, follow-up, drop-out rate (if applicable), ethics, and results. Efficacy and safety results were reported for each paper and pooled together according to each neuromodulation technique. Results of the systematic review were analysed regarding study methods, ethics, and outcome assessment in the context of currently active clinical research recommendations provided by the fourth International Consultation on Incontinence [20].

3. Evidence synthesis

3.1. Literature search results

The flow diagram is presented in Figure 1. Using the aforementioned research strategy, 2302 studies were identified. After applying the eligibility criteria, a total of 147 papers were assessed for eligibility.

Many studies included patients without preoperative stratification for different types of incontinence. These heterogeneous studies providing potentially confounding results were excluded from our analysis. After a second detailed selection, 21 papers reporting efficacy and/or safety outcome of SNM and PTNS were identified and included. The supplementary material shows the detailed reasons for exclusion of particular studies.

3.2. Risk of bias assessment

For assessing the risk of bias, we evaluated each paper at study and outcome level. At the study level, we evaluated any bias in the selection of patients enrolled, with the lowest risk in prospective randomised clinical trials with adequate methods of randomisation that guarantees concealment of the allocation of patients in each group; we also evaluated the risk of bias linked to the blindness towards the treatment of participants and personnel. At the outcome level, we evaluated any detection bias linked to the blindness of the outcome assessment, the completeness of outcome data or, on the contrary, the possible effect of missing data on the outcome measure, and the bias linked to possible omission of data (Fig. 2).

For nonrandomised studies, we applied the ROBINS-I tool to assess the methodological quality of observational studies [21]. We evaluated the presence of baseline

Please cite this article in press as: Tutolo M, et al. Efficacy and Safety of Sacral and Percutaneous Tibial Neuromodulation in Non-neurogenic Lower Urinary Tract Dysfunction and Chronic Pelvic Pain: A Systematic Review of the Literature. Eur Urol (2018), https://doi.org/10.1016/j.eururo.2017.11.002