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Efficacy of posterior tibial nerve stimulation (PTNS) on overactive bladder in older adults

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Abstract

Introduction The main objective of this retrospective study is to determine the efficacy of transcutaneous posterior tibial nerve stimulation (TPTNS) in older patients with overactive bladder (OAB) syndrome. The secondary objective is to look for predictive factors of efficacy of this treatment.

Methods All patients aged over 65 years with OAB syndrome for which TPTNS was introduced between 2010 and 2016 in two neuro-urology centers were included. Age, gender, etiology of OAB, urinary symptoms and detrusor overactivity (DO) were retrospectively collected. The main outcome was efficacy of TPTNS (i.e., purchase of the device between 3 and 6 months).

Results A total of 264 patients were included (mean age 74.1 ± 6.5 years; 63.3% of women), of whom 53% had neurogenic OAB. Urinary incontinence was reported by 83.7% of patients and DO was found on urodynamic studies in 154 patients. The overall efficacy of TPTNS was 45.1%. None of the tested factors were significantly predictive of efficacy, especially age (≥ 75 years, $p = 0.62$), associated stress urinary incontinence ($p = 0.69$) and presence of DO ($p = 0.60$), whether neurogenic or not.

Conclusion TPTNS is an effective treatment in older patients with OAB syndrome. No predictive factors of efficacy were found, especially age and DO. This treatment seems to be a good alternative to antimuscarinics against overactive bladder in older adults.

Keywords Overactive bladder · Aged · Tibial nerve stimulation

Introduction

Overactive bladder (OAB) is a frequent syndrome, and its prevalence increases with age. More than 30% of patients over 65 are affected by OAB symptoms (urgency, frequency, urge incontinence) [1] with important impact on quality of life but also on social activities and medical

status. Adapted care may reduce risk of falls [2], improve quality of life [3] and promote daily living's autonomy [4]. Treatment must be chosen according to patient's medications and comorbidities, especially if there is cognitive impairment or polypharmacy. Indeed, antimuscarinics, known as the first-line treatment for OAB after lifestyle interventions, can lead to serious anticholinergic side effects that could be annoying (dry mouth, constipation) or severe in this population (confusion [5], acute urinary retention). Moreover, prescribing an antimuscarinic drug for a non-life-threatening condition as OAB can be troublesome, as it may lead to increase the overall anticholinergic burden. As potentially inappropriate medications and anticholinergic burden are known to be related to serious medical conditions such as falls, cognitive impairment [6] and pneumopathy [7], prescription of antimuscarinics should be carefully considered in older adults, especially in the frail ones. Transcutaneous posterior tibial nerve

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stimulation (TPTNS) is a non-drug alternative treatment, with no or little side effects, that could be considered in older patients. In addition, several studies in young adults have shown that TPTNS is as effective as antimuscarinics in the treatment of overactive bladder symptoms [8] without the side effects. Yet, there is a lack of evidence to assess efficacy of this device in this specific population (the older adults).

The primary aim of this study is to determine TPTNS efficacy in OAB in older adults. The secondary aim is to search for clinic or urodynamic predictive factors of treatment success.

Materials and methods

Patients

All patients over 65 consulting in two neurourology tertiary centers from 2010 to 2016, with overactive bladder symptoms and for whom a TPTNS had been introduced were included in this retrospective cohort. Patients for whom any of these data was not available were secondarily excluded. Age, gender, etiology of OAB (i.e., neurogenic, urologic or idiopathic), urinary tract symptoms and existence of detrusor overactivity on the last urodynamic study were retrospectively collected.

Intervention

TPTNS was realized with the device Urostim2® (Schwa-Medico, Germany). Two different programs were used: U01 in center 1 (20 min per day, frequency = 15 Hz, pulse duration = 150 μ s, intensity = according to the comfort level of the patient) and U02 in center 2 (20 min per day, frequency = 14 Hz, pulse duration = 210 μ s, intensity = according to the comfort level of the patient). These programs are both indicated in overactive bladder symptoms. The stimulation was realized at home by the patient with two self-adhesive surface electrodes. The position of electrodes was shown during a nurse consultation: the negative electrode was placed 2 cm behind the medial malleolus and the positive electrode 10 cm proximal to it (Fig. 1).

Outcome

The primary outcome was the global efficacy, assessed by the patient and defined by the purchase of the device between 3 and 6 months after the first utilization, which revealed patient's wish to continue this treatment, despite of the cost. Indeed, in our country, costs of TPTNS are totally supported by health authorities with reimbursement



Fig. 1 Urostim2® device, electrodes placement

of expenses, but only during 6 months. After that, the purchase of the stimulator is the responsibility of the patient. Thus, we can consider that the stimulator purchase is a strong argument for the efficacy of TPTNS and significant improvement of symptoms/quality of life.

Effect of clinical and urodynamic characteristics on efficacy was studied in secondary analysis.

Statistical analysis

Statistical tests were performed with the R software for Windows (Rx64 3.2.3). A Fisher's test was performed to compare the qualitative variables. A two-sample *t* test (Student) was used for mean comparisons after verifying normality and variance's equality. Statistical significance was set at the 95% level ($p < 0.05$). A logistic regression model was applied to search for predictive factors of efficacy in secondary analysis.

Results

Two hundred and sixty-four patients were included (mean age 74.1 ± 6.5 years, 63.8% of women), 201 in center 1, 63 in center 2 (Table 1). Urinary incontinence was related by 83.7% of patients, which could be pure urgency (54.5%), or mixed (26%) incontinence.

The global efficacy of TPTNS on OAB syndrome was 45.1% (41.8% in center 1, 55.6% in center 2, $p = 0.06$). Patients with neurogenic bladder had 47.1% of efficacy versus 42.7% for which with non-neurogenic bladder ($p = 0.54$). None of the tested factors was found significant

Table 1 Characteristics of study participants

| | <i>N</i> = 264 |
|------------------------------------|----------------|
| Female gender | 167 (63.3%) |
| Age (mean ± SD) | 74.1 ± 6.5 |
| Age over 75 | 103 (39%) |
| Etiology of OAB | |
| Neurogenic bladder | 140 (53%) |
| Stroke | 18 (6.8%) |
| Spinal cord lesion | 14 (5.3%) |
| Multiple sclerosis | 22 (8.3%) |
| Extrapyramidal syndrome | 62 (23.5%) |
| Peripheral nerve damage | 10 (3.8%) |
| Other encephalic pathology | 12 (4.5%) |
| Urological/gynecological pathology | 42 (15.9%) |
| Idiopathic | 61 (23.1%) |
| Other non-neurological pathology | 9 (3.4%) |
| Symptoms | |
| Urge incontinence (pure) | 144 (54.5%) |
| Stress incontinence (pure) | 8 (3%) |
| Mixed incontinence | 69 (26%) |
| Nocturia | 189 (71.6%) |
| Voiding dysfunction | 114 (43.2%) |
| Urodynamic study | |
| Detrusor overactivity | 154 (58.3%) |

to predict success of the treatment, especially for older age (various age range were tested), stress urinary incontinence or DO, whether neurogenic or not (Table 2). There was no influence of prior therapy failure for OAB on the main outcome. In multivariate analysis, including factors with a

trend toward significance, none of the factors was significantly associated with success of the treatment.

Discussion

TPTNS is an effective treatment of OAB in older adults, whether neurogenic or not, with a success rate (complete or partial) of 45.1%. No clinical or urodynamic factors may predict its efficacy. These findings confirm results of prospective randomized studies, on a small number of subjects. Thus, Booth et al. [9] have shown a significant improvement on IPSS score at 6 weeks, in 11 patients on 13 enrolled, after 2 PTNS sessions by week in a geriatric population. Schreiner et al. [10] have found a significant efficacy in 51 women over 60, treated by PTNS once a week, in addition to pelvic muscle floor training versus pelvic muscle floor training alone (76 vs. 26.9%). Other specific trials in older population have been conducted but with a questionable statistical reliability of the results [11, 12].

Due to retrospective design, we could not assess efficacy with number of leakages or differences in urinary symptoms before and after treatment. Our primary outcome is based on subjective improvement reported by the patients. Efficacy was assessed later in follow-up (6 months for 76.1% of the study population vs. 6–12 weeks in trials), which confirmed feasibility and adherence of patients at middle term, for a daily treatment at home, that is not supervised. In comparison, adherence to antimuscarinic drugs in OAB is around 30–43% in older adults [13]. If feasibility of this treatment could be limited by orthopedic or cognitive disorders, compliance to oral drug could also

Table 2 Univariate analysis of factors associated with success of transcutaneous posterior tibial nerve stimulation in overactive bladder

| | Success = 119 | Failure = 145 | <i>p</i> |
|---|---------------|---------------|----------|
| Female gender | 76 (63.9%) | 91 (62.7%) | 0.9 |
| Age over 75 | 44 (37%) | 59 (40.7%) | 0.62 |
| Age (mean ± SD) | 73.8 ± 6.1 | 74.3 ± 6.8 | 0.55 |
| Neurogenic OAB | 66 (55.5%) | 74 (51%) | 0.54 |
| Detrusor overactivity | 64 (53.7%) | 90 (62.1%) | 0.6 |
| Detrusor overactivity in neurogenic bladder | 40 (70.2%) | 51 (71.8%) | 0.85 |
| Detrusor overactivity in non-neurogenic bladder | 24 (50%) | 39 (57.4%) | 0.46 |
| Urge incontinence | 99 (83.2%) | 113 (77.9%) | 0.36 |
| Pure urge incontinence | 66 (55.5%) | 78 (53.8%) | 0.81 |
| Stress incontinence | 36 (30.3%) | 40 (27.6%) | 0.69 |
| Pure stress incontinence | 3 (2.5%) | 5 (3.4%) | 0.74 |
| Mixed incontinence | 34 (28.6%) | 35 (24.1%) | 0.49 |
| Nocturia | 80 (67.2%) | 109 (75.2%) | 0.05 |
| Voiding dysfunction | 47 (39.5%) | 67 (46.2%) | 0.38 |
| Center (1) | 84 (70.6%) | 117 (80.7%) | 0.06 |
| TPTNS as first-line treatment | 37 (31.1%) | 37 (25.5%) | 0.34 |

be difficult for older adults with cognitive or motor impairment because of trouble taking drugs, or difficult schedule.

Superiority of TPTNS or antimuscarinics against the other treatments could not be demonstrated [14]. Of course, patients that could not be included because of “lack of follow-up” represent an important bias, but uncontrollable in a retrospective study. However, most of our patients have previously tried without success (or with too important side effects), anticholinergic drugs, before TPTNS. TPTNS could be also prescribed in fecal incontinence [15]. If some patients in our study presented fecal incontinence associated to OAB, we were not able to quantify how many patients also improved their anorectal disorders. This secondary therapeutic indication is interesting in older adults, with an increased prevalence of fecal incontinence in this population, allowing to use TPTNS for both urinary and anorectal disorders.

Best scheme of treatment is still not determined. Many different protocols have been used in trials. If van der Pal et al. [16] have shown symptom recurrence for 7/11 patients after TPTNS 6-week interruption, Monteiro et al. [17] have found in all their 12 patients, a persistent subjective efficacy at 12 months (after 45-day treatment). Frequency is also variable: once, twice, three times a week, or daily are described. Yet, Finazzi et al. [18] have not found any difference between PTNS applied once a week and three times a week. In the SUmIT trial [19], patient-adapted rhythm of transcutaneous stimulation after a primary 12-week phase: 17 days was the median time between two stimulations to maintain a moderate to marked efficacy at 36 months.

Despite the retrospective character of this study, large recruitment allows to improve power of secondary analysis. Neither clinical symptoms nor urodynamic data can predict success, which is consistent with precedent results [20, 21]. If cystometric response has been demonstrated [22], it was not correlated with clinical efficacy at 30 or 90 days [23].

A trend toward significance of the center exists ($p = 0.06$) probably due to differences in patient characteristics between the two centers (over 75-year-old patient proportion, detrusor overactivity). If program device influence can be evoked (U01 vs. U02), this trend disappears after multivariate adjustment.

Failure of a first-line treatment like bladder antimuscarinics is not a predictive factor of failure in our study, which is consistent with van Balken et al. study [20]. TPTNS is effective for 43.4% of our study population as a second-line treatment, 53% in Ammi et al. cohort [21], so non-responders to antimuscarinics may benefit from this treatment.

Other methods, based on stimulation of sacral nerves have been evaluated in older adults. Daily transcutaneous stimulation of the sacral region has demonstrated his efficacy on OABSS score in post-stroke incontinence [24]. Placement of electrode may be more difficult in sacral region than on the ankle, and patient depends on a third person to realize his treatment. Implanted sacral nerve stimulation efficacy have also been established in older adults (> 80% of implantation after first stage procedure success), but at long term, older adults seems more likely to undergo device removal compared with patients under 70 [25].

Conclusions

TPTNS is an effective treatment for OAB in older adults, whatever etiology or associated symptoms are. Absence of side effects and impact on anticholinergic burden makes it a treatment of choice in this population, potentially as a first-line therapy. It should be appropriate to assess efficacy, compliance, adherence and side-effect incidence in prospective randomized trials, specifically in older adults, to determine the most suitable treatment in overactive bladder in this particular population.

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Compliance with ethical standards

Conflict of interest The authors have no financial or any other kind of personal conflicts with this paper. GRAPPPA (Clinical research Group of perineal dysfunctions in older adults) was funded in 2013 by Pr G. Amarenco.

Ethical approval This retrospective study was accepted by the local ethics committee. The study protocol and data collection were conducted in accordance with the ethical standards of the national research committee and with the Declaration of Helsinki.

Informed consent All patients were advised of the research and not opposed to the use of their anonymized data.

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