TREATMENT

Neuromodulative treatment of overactive bladder – noninvasive tibial nerve stimulation

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Abstract

Background: **Conservative treatment of overactive bladder employes behavioral or invasive neuromodulatory inhibition of miction reflex and administration of anticholinergic drugs.**
Main purpose: **The aim of this study was to use non-invasive stimulation of the tibial nerve with the intention to achieve desired therapeutic effects without iatrogenic nerve damage using a superficial electrostimulation.**
Methods: **All patients suffered from overactive bladder (OAB) without bladder outlet obstruction. OAB was examined by the Behavioral urge score BUS (0.0 – the best and 1.0 – the worst score), the International prostate symptom score IPSS (0 – the best and 35 – the worst score) and the Incontinence quality of life questionnaire IQOL (0.0 – the worst and 1.0 – the best index). The patients were divided into 3 groups: Group I – patients with electrode attached behind the medial ankle of the left lower extremity. The intensity of stimulation corresponded to 70 % of the maximum amplitude of response from musculus abductor hallucis. Frequency of stimulation was 1 Hz and duration of the square impulse was 0.1 ms. Surface stimulation lasted 30 minutes and was repeated once a week. Group II – patients were treated by oral oxybutynin 5 mg t.i.d. Group III – patients without treatment. The BUS, IPSS, and IQOL were repeated after the treatment.**
Results: **The study included 28 females of average age 54 year (range 45 to 63). Mean IPSS was 17 (range 12 to 21), mean index of quality of life IQOL was 30 (range 12 to 78) and mean BUS score was 0.68 (range 0.50 to 0.86). Group I with stimulation did achieve statistically significant changes following the treatment: decrease of mean IPSS from 17±3 points to 6±4 points after the treatment, increase in mean IQOL from 36±10 to 68±20 and decrease of mean BUS from 0.65±0.12 to 0.43±0.16. Group II had similar statistically significant differences after the treatment of OAB. Group III noted no changes in the complaints.**
Conclusion: **Noninvasive stimulation had improved subjective symptom related to overactive bladder, had no adverse events and was well tolerated.** ***(Fig. 1, Tab. 1, Ref. 18.)***
Key words: overactive bladder, electric nerve stimulation, tibial nerve, anticholinergics.

Symptoms of the lower urinary tract belong to the set of symptoms that greatly affect the patient's quality of life. Overactive bladder (OAB) includes urgency, frequent voiding, nocturia, and urge urinary incontinence (Abrams and Wein, 2000). In most cases, the etiology and exact etiopathogenesis of the disease is unknown. Conservative treatment includes behavioral inhibition of miction reflex and administration of anticholinergic drugs.

In the couple of years, the interest in regulatory mechanisms of lower urinary tract has significantly increased. Invasive treatment by neuromodulation has made new possibilities in regulation of the nerve tracts available, as well as, made the pathophysiology of overactive bladder more clear. The fact, that neuromodulation is one of invasive and financially demanding method, gave rise to the development of minimally invasive peripheral stimulation SANS (Stoller, 1999).

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Stoller's stimulation belongs to minimally invasive therapeutic methods because the stimulatory electrode is placed close to the tibial nerve in the region of medial ankle. The aim of this research was to produce non-invasive stimulation and achieve comparable effect by superficial electrode without iatrogenic damage to the tibial nerve.

In 2001, it was for the first time in Slovak Republic at the Jessenius Faculty of Medicine in Martin, that the superficial stimulation of tibial nerve was used, which tested the effectiveness of modified superficial Stoller's afferent nerve stimulation (SANS).

Materials and methods

The original invasive SANS uses the region of medial ankle for percutaneous tibial nerve stimulation using a needle electrode inserted in the vicinity of the nerve. The intensity of stimulation reaches 10 mA, the frequency from 1 to 10 Hz and application time is 30 minutes. It uses standard square impulses. When using the modified non-invasive stimulation SANS it is necessary to use surface electrodes for the area of medial ankle and stimulation of tibial nerve with different values, which cannot be set by the original SANS stimulator. We have used an electromyographic device Nicolet Viking II E. The patient stayed in a horizontal position on her back and the electrodes were placed behind the medial ankle of the left lower extremity. Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimalization of the electrode position and set intensity of stimulation we had proceeded on with a therapeutic stimulation of tibial nerve. Intensity of the surface SANS was equal to 70 % of intensity, at which the maximal amplitude of response was registered from the abductor hallucis muscle (stimulation by a constant voltage and regulated intensity of direct current). Frequency of stimulation was 1 Hz and duration of square impulse was 0.1 ms. Surface stimulation of 30 minutes duration was repeated once a week for a period of 5 weeks.

The group included patients with overactive bladder (OAB) without bladder outlet obstruction. Urodynamic examination confirmed the diagnosis and was completed by the Behavioral urge score (BUS) according to the Frequency volume chart (0.0 – without OAB, 1.0 – the highest stage of OAB; Van Waalwijk van Doorn et al., 1997; Svihra et al., 1998). Subjective complaints were assessed according to the International prostate symptom score – IPSS (0 – without symptoms, 35 – the most severe) (Cockett et al, 1993) and the quality of life according to the Incontinence quality of life questionnaire – IQOL (0 – the worst quality of life, 100 – the best quality of life (Patrick et al, 1999; Svihra et al, 2002). All scales were verified in a population of Slovak patients.

To check the effectiveness of surface SANS we had formed a therapy group with oxybutynine given in standard peroral therapeutic dose of 5 mg three times a day and a group of patients without treatment. Statistical software SPSS 10.1 was used for different types of analyses. In all groups Mann–Whitney U test and Wilcoxon non-parametric test were assessed, with a statistically significant difference of value of $p<0.05$.

Results

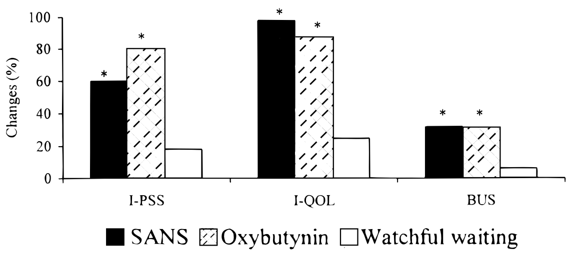
Study includes 28 females with average age of 54 years (range: 45–63). Nine randomly chosen females formed the group with SANS stimulation, ten females formed the oxybutynine group and nine females the group without treatment. According to IPSS, the lower urinary tract symptoms reached the average value of 17 points (range: 12–21), mean index of quality of life IQOL reached the value of 30 (range: 12–78) and mean BUS score equaled to 0.68 (range: 0.50–0.86). Urodynamic examination confirmed OAB without bladder outlet obstruction. Noninvasive SANS stimulation was performed in 9 cases, total of 45 stimulations. According to regulation we used standard intensity of 25 mA, which was sufficient to evoke dorsal flection of a thumb of left foot. All stimulations were performed on left side and no adverse events were recorded; the patients tolerated well the duration and periods of stimulation. In one case it was necessary to prematurely terminate the stimulation.

The group with SANS stimulation achieved statistically significant differencies after the treatment. Mean IPSS value changed from 17 ± 3 points before treatment to 6 ± 4 points after treatment, mean IQOL index from 36 ± 10 to 68 ± 20 and mean BUS score from 0.65 ± 0.12 to 0.43 ± 0.16 (Tab. 1).

Decrease in IPSS, increase in IQOL and decrease in BUS by more than 50 % were evaluated as a clinical success of SANS

Tab. 1. Characteristics of patients with non-invasive SANS.

Patient's number	IPSS before SANS	IPSS after SANS	IQOL before SANS	IQOL after SANS	BUS before SANS	BUS after SANS
1	14	7	48	64	0.53	0.42
2	20	13	22	58	0.67	0.57
3	18	5	34	81	0.62	0.27
4	13	2	52	87	0.50	0.23
5	12	10	43	45	0.58	0.46
6	21	4	28	79	0.86	0.41
7	18	3	31	85	0.79	0.39
8	15	10	40	28	0.60	0.77
9	19	2	30	82	0.71	0.35



* p < 0.05

Fig. 1. Changes after SANS and oxybutynin treatments and watchful waiting.

treatment. According to these criteria, five patients (56 %) had significant improvement of OAB symptoms. Two patients (22 %) had non-significant improvement and in two patient no therapeutic response to SANS occurred.

Oxybutynine group achieved comparable therapeutic results, however, two patients (20 %) refused further treatment due to adverse effects – dry mouth. In two patients (20 %), the oxybutynine dose was reduced to 2 times 5 mg a day. Control group without treatment recorded no statistically significant changes of values of assessed markers (Fig. 1).

Discussion

The standard first line treatment of overactive bladder is administration of anticholinergic and spasmolytic drugs (Andersson et al, 1998). Since drug therapy failed, new conservative methods were searched. Recently, several new methods employing the actual knowledge from neurophysiologic regulations of the lower urinary tract arised. These are based on a fact that increased instability of urinary bladder can be inhibited by direct or indirect stimulation of sacral miction reflex. The root S3 is stimulated and reflexes are neuromodulated by intravesical, anal, vaginal, penile, perineal, sacral or tibial approach (Fall et Lindstron, 1994; Janez et al, 1979; Lindstrom et all, 1983; Madersbacher, 1990; McGuire et al, 1983; Nakamura et Sakurai, 1984; Schmidt, 1988; Vodusek et al, 1986; Walsh et al, 1999). Several methods were unsuccessful due to low efficacy of surface stimulation. Sacral neuromodulation reaches effectiveness of 60 %, however, it represents significant invasiveness for a patient. Conversely, tibial stimulation is minimally invasive and can be used repeatedly (Balken et al, 2001).

The original method of tibial nerve stimulation was described by McGuire (1983). The method was further improved by Stoller (1999), who used the knowledge of classic Chinese acupuncture. The method is considered minimally invasive, since it is based on using very fine puncture electrode G26.

In Slovakia, the SANS stimulation is not in use. Our literature sources lack the knowledge about neurophysiologic therapy of the lower urinary tract dysfunction associated with overactive bladder. This study is the first one to evaluate the possibilities of its therapeutic utilization, especially in farmacologically refractory disease. As a reference criterium of a successful treatment we use the results achieved after anticholinergic treatment. The efficacy of drug treatment approaches 70 to 80 % in multicentre placebo controlled double-blind randomized studies. The occurrence of adverse events is within the range of 20 to 60 % according to chosen effective substance and its farmacokinetics in human body (Andersson et al, 1998).

When evaluating the tolerance of drug treatment significant anticholinergic adverse event could be accounted, since it offen becomes the main reason for refusal of further treatment. In our study the adverse events were observed, and two out of ten patients refused further treatment of drug treatment due to significant occurence of dry mouth. On the other hand, patients with non-invasive SANS tolerated the treatment very well, and we had not observed adverse events. We assume, that non-invasive SANS is acceptable and safe conservative treatment in case of overactive bladder.

When evaluating the clinical efficacy we have used changes of subjective and objective markers by more than 50 % as the marker of success. We have achieved therapeutic response of 60 % versus 80 % of therapeutic response in drug treatment. Balken et al (2001) achieved similar therapeutic response when using the original invasive needle SANS. Our results document good tolerance of non-invasive SANS and comparable efficacy with invasive SANS. Non-invasive SANS achieved statistically significant improvement of overactive bladder symptoms in contrast to patients with watchful waiting.

Confirmation of the results requires a more complex randomized clinical studies according to the specific disorders of the lower urinary tract. The classic invasive SANS method does not allow application of intensity greater than 10 mA, because the stimulator that is used does not allow it. Our non-invasive SANS method uses intensities reaching the value of 40 mA. We used a prototype of a portable stimulator, which provides such values. It enables a wider application of non-invasive SANS method also in other indications in functional disorders of the lower urinary tract.

Noninvasive SANS method is very perspective therapeutic practice in dysfunctional diseases of lower urinary tract. Slovak modification of non-invasive SANS uses triple intensity values while preserving the same therapeutic efficacy and good tolerance in patients. Application in refractive drug treatment of overactive bladder enables modification of the miction reflex inhibition and improvement of the quality of life in patients.

References

Andersson KE, Appell R, Cardozo L, Chapple C, Drutz H, Finkbeiner A, Haab F, Vela Navarrete R. Committee 11. Pharmacological treatment of urinary incontinence. In: Abrams P, Khoury S, Wein A. The 1st International Consultation on Incontinence. Monaco, Plymouth, Health Publication Ltd., 1998, 447—486.

Abrams P, Wein A. Introduction: Overactive bladder and its treatment. Urology 2000; 55: 12.

Balken RM, Vandoninck V, Gisolf KWH, Vergunst H, Kiemeney LALM, Debruyne FMJ, Bemelmans BLH. Posterior tibial nerve stimulation as neuromodulative treatment of lower urinary tract dysfunction. J Urol 2001; 166: 914—918.

Cockett ATK, Khoury S, Aso Y, Chatelain C, Denis L, Griffiths K, Murphy G. Recommendations of the International Consensus Committee. In: Proccedings of the 2nd International Consultation on Benign Prostatic Hyperplasia (BPH). Paris, 1993, p. 553—564.

Fall M, Lindstrom S. Transcutaneous electrical nerve stimulation in classic and nonulcer interstitial cystitis. Urol Clin North Amer 1994; 21: 131—139.

Janez J, Plevnik S, Suhel P. Urethral and bladder responses to anal electrical stimulation. J Urol 1979; 122: 192—194.

Lindstrom S, Fall M, Carlsson CA. The neurophysiological basis of bladder inhibition in response to intravaginal electrical stimulation. J Urol 1982; 129: 405—410.

Madersbacher H. Intravesical electrical stimulation for the rehabilitation of the neuropathic bladder. Paraplegia 1990; 28: 349—352.

McGuire EJ, Zhang SC, Horwinski ER. Treatment of motor and sensory detrusor instability by electrical stimulation. J Urol 1983; 129: 78—79.

Nakamura M, Sakurai T. Bladder inhibition by penile electrical stimulation. Brit J Urol 1984; 56: 413—415.

Patrick DL, Martin ML, Bushnell DM, Marquis P, Andrejasich CM, Buesching DP. Cultural adaptation of a quality-of-life measure for urinary incontinence. Europ Urol 1999; 36: 427—435.

Schmidt RA. Applications of neurostimulation in urology. Neurourol Urodyn 1988; 7: 585—590.

Stoller ML. Afferent nerve stimulation for pelvic floor dysfunction. Europ Urol 1999; 35 (Suppl): 16—20.

Švihra J, Javorka Jr K, Ľupták J, Kliment J. Non-invasive evaluation of urge incontinence in women. Abctracts, 1st International Consultation on Incontinence, WHO, Monaco, 1998, 51.

Švihra J, Baška T, Martin M, Bushnell D, Kliment J, Ľupták J, Sopilko I, Dusenka M. Prevalence of female overactive bladder with urinary incontinence in Slovakia. Europ Urol 2002; 1 (Suppl): 85.

Van Waalwijk van Doorn ES, Ambergen AW, Janknegt RA. Detrusor activity index: quantification of detrusor overactivity by ambulatory monitoring. J Urol 1997; 157: 596—599.

Vodušek DB, Light JK, Libby JM. Detrusor inhibition induced by stimulation of pudendal nerve afferents. Neurourol Urodyn 1986; 5: 381—385.

Walsh IK, Johnston RS, Keane PF. Transcutaneous sacral neurostimulation for irritative voiding dysfunction. Europ Urol 1999; 35: 192—196.

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