



Low Intensity Shockwaves to Treat the Neurogenic Bladder with Chronic Urinary Retention - A Case Report

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Abstract

We report a case of neurogenic bladder with chronic urinary retention in patient with Multiple Sclerosis (MS) successfully treated with Low Intensity Shockwaves (Li-ESWT).

A 31-year-old female was referred to our urological office with chronic urinary tract infection due to neurogenic bladder with high residual urine volume. As complication a renal abscess formation was detected. As part of a multimodal approach Li-ESWT of the urinary bladder (off-label use) was administered and effectively reduced post-void residual urine volume.

Li-ESWT can safely and effectively reduce post-void residual volume in patients with neurogenic bladder due to MS.

Keywords: Neurogenic bladder; Multiple sclerosis; Low intensity shockwaves; Post-void residual volume; Detrusor underactivity

Key Findings

Li-ESWT can be an effective and safe treatment for chronic urinary retention and reduced PVR in patient with neurogenic bladder.

What is known and what is new?

The Li-ESWT is used in different urological conditions like nephrolithiasis, erectile dysfunction, chronic prostatitis, urinary incontinence, interstitial cystitis.

Clinical improvement became evident after the multimodal approach involving Li-ESWT with significant reducing of the PVR due to restoration of the bladder, the urethral structure and function after improving neuronal integrity and innervation.

What is the implication, and what should change now?

Further studies are necessary to confirm the effectiveness of ESWT for treatment of the neurogenic bladder as it appears to be a promising therapy approach for this indication.

Introduction

Low-Intensity Focused Shockwaves (Li-ESWT) are becoming increasingly important for the treatment of urological conditions. In this case report, we investigated for first time if post-void residual volume can safely and effectively be reduced using Li-ESWT in patients with neurogenic bladder.

Bladder Dysfunction (BD) is present in many people with Multiple Sclerosis (MS). BD may occur when MS-associated lesions deteriorate the nerve signals in the central nervous system areas that control bladder function and contractions of the urinary sphincters. A bladder that does not empty properly can cause symptoms, including an inability to empty the bladder completely, urinary incontinence, recurrent urinary tract infection, urosepsis with renal abscesses developing as a complication of focal pyelonephritis, and deterioration of kidney function.

Case Presentation

A 31-year-old female patient with a history of MS had been having regular urological follow-ups in our urological practice since April 2020. The patient was on regular medication with dimethyl

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fumarate for MS. Neurological examinations including MRI of the head and spine in March 2020 and March 2022 showed stable disease without evidence of suspicious lesions in the brain region responsible for micturition. At her first presentation, the patient had pyelonephritis of the right kidney; voiding was normal with a Post-Void Residual volume (PVR) of 50 ml. Hematuria was detected during regular urological examination. A cystoscopy was performed in June 2021. This did not reveal any abnormalities. Investigation of the upper urinary tract with Magnetic Resonance Urography (MRU) was also unremarkable. Given the age of the patient and the lack of comorbidities we still strongly assume multiple sclerosis to be the origin of the voiding dysfunction.

The female patient developed recurrent pyelonephritis of the right kidney in September 2021. Subjectively, a worsening of micturition was reported. Sonography of the urinary bladder revealed a PVR of more than 100 ml. After appropriate antibiotic treatment, the laboratory results and physical condition of the patient were normal.

In October 2021 the patient developed a new urinary tract infection with fever. Inpatient treatment with intravenous administration of antibiotics and placement of a bladder catheter were performed. Magnetic Resonance Imaging (MRI) of the abdomen and urography revealed evidence of renal abscess formation in the right kidney with a diameter of 1.7 cm but without obstruction of the upper urinary tract. Abscess puncture was not possible due to the location of the abscess. Due to this fact, the abscess was treated conservatively with prolonged i.v. -antibiotics.

After being discharged from hospital, sonography showed residual urine formation of more than 200 ml on a few occasions. As further therapy was considered, intermittent self-catheterization in combination with intravesical bladder instillation with chondroitin sulfate (Active principle: Temporary replacement of the sulfated glycosaminoglycan protective layer in the bladder) and pelvic floor muscle training was initiated. Further investigation consisting of a urodynamic study was proposed but was rejected by the patient and not performed.

Four cycles of single-shot intravesical therapy with chondroitin sulfate were administered over four weeks. PVR was measured with single-use catheters during intravesical treatment and was approximately 200 ml to 250 ml. Oral therapy with Distigmine (5 mg) twice daily was initiated as first-line treatment attempt [1] but ceased after 4 weeks due to inefficacy.

Thereafter, the patient received 12 cycles of Low Intensity Shockwave Therapy (Li-ESWT) administered weekly or biweekly to the urinary bladder as an off-label use from January 2022 to April 2022. We used the PiezoWave [2] shockwave unit (Richard Wolf GmbH and ELvation Medical, Germany). The number of pulses administered, the F10G10 applicator, the area of application and the shockwave penetration were used in analogy to a previous study on treatment of an overactive bladder by using Li-ESWT [2]. The energy distribution at energy level 20 resulted in a maximum Energy Flux Density (EFD) of 0.32 mJ/mm² with a frequency (fR) of 8 Hz (pulses/second). In total, 36,000 shockwaves were delivered over the entire treatment period of 12 weeks. Adjuvant Tadalafil 2.5 mg once daily as an off-label use was prescribed and continued until the Li-ESWT was completed. At one week, 3-, 6-, 9- and 12-months after treatment with Li-ESWT and tadalafil 2.5 mg PVR was under 50 ml.

Discussion

A healthy bladder function is essential for patients with MS, particularly their long-term kidney function, preventing urinary infections and urinary incontinence, reducing the number of MS attacks and improving their quality of life. According to the neurological follow-up which included MR scans of the head and spine, the voiding dysfunction in this case was not related to an acute MS attack.

The effects of Li-ESWT on bladder function has been the subject of an *in vivo* study [3]. In that study, Li-ESWT ameliorated Underactive Bladder (UAB) and urinary incontinence in a diabetic underactive bladder rat model. This work suggests that the improvement could be a result of a restoration of the bladder, the urethral structure and function due to neuronal integrity and innervations by Li-ESWT.

In the first clinical study Li-ESWT observed a statistically significant decrease of Detrusor Underactivity (DU)/UAB symptoms, but also, a trend to decrease PVR versus placebo [4]. The treatment was performed once a week for 6 weeks, with 2500 shocks, fR of four pulses per second, and EFD of 0.25 mJ/mm² [4]. In our case, the used EFD, fR, treatment sessions and shocks were higher 0.32 mJ/mm² EFD, fR 8 Hz pulses per second, 12 cycles of Li-ESWT and 3,000 shocks. The study by Shen et al. implies that ESWT might have effects on the improvement of bladder sensation [4].

In another study, Li-ESWT was found to ameliorate overactive bladder symptoms, but also improved bladder voiding function in female patients [2].

Acute urinary retention may lead to temporary ischemia and flow returns to basal levels following drainage in male Sprague Dawley rats [5]. The transient bladder ischemia is suggested to lead to a reversible decrease in detrusor compliance [6]. In our case, the patient has chronic urinary retention due to MS. Previous studies have associated chronic ischemia with pathologic progression to detrusor overactivity, and eventually DU [7]. VEGF is a signal protein that promotes blood vessel formation and restores oxygen supply to tissues in inadequate blood circulation, like in hypoxic conditions [8]. Interleukin 9 (IL-9) is a cytokine secreted by CD4+ helper cells that controls various hematopoietic cell types, increasing cell proliferation and preventing apoptosis [9]. Sugaya et al. reported that about 35% of their study participants with interstitial cystitis had some allergic or autoimmune disease associated with the overproduction of IL-4. The IL-4 gene and its receptor gene are strongly linked to immune diseases [10]. The β -Adrenoceptor controls inflammatory cytokine expression and contraction in human bladder smooth muscle cells through autophagy under pathological hydrostatic pressure [11]. Shen et al. have reported improved symptoms and urinary biomarkers in refractory interstitial cystitis and bladder pain syndrome patients randomized to Li-ESWT versus placebo. The ESWT group showed a reduction of VEGF and IL-4 expressions, increased IL-9 expression at 4 weeks. These authors suggested that ESWT could have effects on immune modulation through mast cells IL4 reaction [8].

The combination of adjuvant daily therapy with tadalafil 5 mg (PDE5i) was effective in increasing the efficacy and duration of the benefits of Li-ESWT in patients with erectile dysfunction by inhibiting the degradation of cGMP [12]. The NO/cGMP/G Kinase pathway seems to play an important role in regulating bladder myocytes tone [13] and treatment with PDE5i may prevent the advancement of ischemia-related functional and structural bladder alterations [7].

This case report aims to explore the potential benefits of Li-ESWT, considering its anti-inflammatory and anti-apoptotic effects and its ability to activate stem cells. Thus, Li-ESWT may be effective for UB that is known to be associated with decrease of inflammatory responses, increased bladder nerve innervation, regeneration, and vascularization through angiogenesis. In addition, Li-ESWT may lead to enhanced bladder and urethra muscle contractile function and ameliorated bladder wall composition. The bladder ischemia and deteriorated innervation of the bladder deteriorated the transmission of nerve signals because of MS [3,8,14].

The pathophysiology suggested previously such as modulated local immune responses in the bladder, increased bladder nerve innervation, enhanced vascularization and angiogenesis, regulation of β -Adrenoceptors response, activation of stem cells, reducing bladder ischemia, and inhibited urothelial cell apoptosis are considered to be the main process of the action of Li-ESWT of the bladder.

In our case, a significant improvement of PVR from over 200 ml to less than 50 ml after treatment with Li-ESWT combined with adjuvant therapy consisting of tadalafil 2.5 mg was achieved for 9 months so far.

The patient has reported no adverse effects occurred during treatment and significant improvement of the voiding function after Li-ESWT. No improvement had been reported after the initial medication-based treatment.

Distigmine and chondroitin sulfate treatments preceded the described multimodal Li-ESWT therapy. However, we do not attribute the success in this case solely to this initial approach, as clinical improvement was not initially observed. Clinical improvement became evident after the multimodal approach involving Li-ESWT and Tadalafil therapy.

In this case, PVR was the leading diagnostic tool to measure treatment outcome and no urodynamic study before and after the treatment could be carried out. This is due to the quick symptom relieve and patient noncompliance concerning further invasive measurements. Thus, symptom relief and the significantly improved clinical presentation strongly support the PVR outcome after Li-ESWT making confounding causes of the improved PVR less possible.

Conclusion

To the best of our knowledge, this is the first case report on the use of Li-ESWT to treat a patient with neurogenic bladder and chronic urinary retention. We demonstrated that Li-ESWT can be an effective and safe treatment for chronic urinary retention and reduced PVR from 200 ml to 50 ml. Li-ESWT could become a better alternative therapy for patients with chronic urinary retention in the future. Further studies are necessary to confirm the effectiveness of ESWT for treatment of the neurogenic bladder.

References

1. Bougas DA, Mitsogiannis IC, Mitropoulos DN, Kollaitis GC, Serafetinides EN, Giannopoulos AM. Clinical efficacy of distigmine bromide in the treatment of patients with underactive detrusor. *Int Urol Nephrol*. 2004;36:507-12.

2. Lee Y-C, Chuang S-M, Lin K-L, Chen WC, Lu JH, Chueh KS, et al. Low-intensity extracorporeal shock wave therapy ameliorates the overactive bladder: A prospective pilot study. *Biomed Res Int*. 2020;2020:9175676.
3. Wang HS, Oh BS, Wang B, Ruan Y, Zhou J, Banie L, et al. Low-intensity extracorporeal shockwave therapy ameliorates diabetic underactive bladder in streptozotocin-induced diabetic rats. *BJU Int*. 2018;122:490-500.
4. Shen YC, Chen CH, Chancellor MB, Chuang YC. Prospective, randomized, double-blind, placebo-controlled, pilot study of extracorporeal shock wave therapy for detrusor underactivity/underactive bladder. *Eur Urol Focus*. 2023;9:524-30.
5. Shimizu S, Saito M, Kinoshita Y, Kazuyama E, Tamamura M, Satoh I, et al. Acute urinary retention and subsequent catheterization cause lipid peroxidation and oxidative DNA damage in the bladder: Preventive effect of edaravone, a free-radical scavenger. *BJU Int*. 2009;104:713-7.
6. Tracey AT, Anele UA, Vince RA, Speich JE, Klausner AP, Ratz PH. Bladder attack: Transient bladder ischemia leads to a reversible decrease in detrusor compliance. *Transl Androl Urol*. 2019;8:703-11.
7. Andersson K-E, Boedtker DB, Forman A. The link between vascular dysfunction, bladder ischemia, and aging bladder dysfunction. *Ther Adv Urol*. 2017;9:11-27.
8. Shen Y-C, Tyagi P, Lee W-C, Chancellor M, Chuang YC. Improves symptoms and urinary biomarkers in refractory interstitial cystitis/bladder pain syndrome patients randomized to extracorporeal shock wave therapy versus placebo. *Sci Rep*. 2021;11:7558.
9. Perumal NB, Kaplan MH. Regulating Il9 transcription in T helper cells. *Trends Immunol*. 2011;32:146-50.
10. Sugaya K, Nishijima S, Yamada T, Miyazato M, Hatano T, Ogawa Y. Molecular analysis of adrenergic receptor genes and interleukin-4/interleukin-4 receptor genes in patients with interstitial cystitis. *J Urol*. 2002;168:2668-71.
11. Chen G, Jin X, Luo D, Ai J, Xiao K, Lai J, et al. β -Adrenoceptor regulates contraction and inflammatory cytokine expression of human bladder smooth muscle cells *via* autophagy under pathological hydrostatic pressure. *NeuroUrol Urodyn*. 2020;39:2128-38.
12. Gallo L, Pecoraro S, Sarnacchiaro P. Adjuvant daily therapy with L-arginine 2,500 mg and tadalafil 5 mg increases efficacy and duration of benefits of low-intensity extracorporeal shock wave therapy for erectile dysfunction: A prospective, randomized, single-blinded study with 1-year follow-up. *Investig Clin Urol*. 2022;63:83-91.
13. Deka DK, Brading AF. Nitric oxide activates glibenclamide-sensitive K⁺ channels in urinary bladder myocytes through a c-GMP-dependent mechanism. *Eur J Pharmacol*. 2004;492:13-9.
14. Jin Y, Xu L, Zhao Y, Wang M, Jin X, Zhang H. Endogenous stem cells were recruited by defocused low-energy shock wave in treating diabetic bladder dysfunction. *Stem Cell Rev Rep*. 2017;13:287-98.