

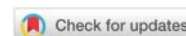
LOW-INTENSITY SHOCKWAVE TREATMENT FOR NEUROGENIC BLADDER WITH CHRONIC URINE RETENTION - CASE REPORT

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Abstract: We present a case of neurogenic bladder accompanied by chronic urine retention in a patient diagnosed with multiple sclerosis (MS). This condition was effectively managed by low-intensity shockwave therapy (Li-ESWT).

Low-intensity focused shockwave therapy (Li-ESWT) is becoming increasingly important in the treatment of urological problems. This case study investigates the feasibility and efficacy of using Li-ESWT to reduce post-void residual volume in persons with neurogenic bladder, representing the first examination of its sort.

Bladder dysfunction (BD) frequently occurs in patients who have been diagnosed with multiple sclerosis (MS). Bladder dysfunction (BD) can occur due to the impairment of nerve impulses in the central nervous system regions involved for regulating bladder function and managing the contractions of the urinary sphincters, which is caused by the lesions associated with multiple sclerosis (MS). Urinary retention can cause various symptoms, including insufficient bladder emptying, urinary incontinence, frequent urinary tract infections, urosepsis resulting in the development of kidney abscesses due to localised kidney infection, and reduced kidney function.

Optimal bladder function is essential for individuals with MS, as it plays a critical role in preserving kidney health, preventing urinary tract infections and incontinence, reducing the frequency of MS episodes, and improving their overall well-being.

A 31-year-old woman was referred to our urology office with a chronic urinary tract infection caused by a neurogenic bladder with a significant volume of residual urine. A kidney abscess formation was identified as a complication. Li-ESWT, which stands for low-intensity extracorporeal shockwave therapy, was used as a part of a multimodal strategy to treat the urinary bladder. This treatment was delivered off-label. The therapy was given on a weekly basis for a period of 6 weeks. The procedure included administering 2500 shocks at a rate of four pulses per second, with an energy flux density (EFD) of 0.25 millijoules per square millimetre. The EFD (Energy Flux Density) used in our study exceeded 0.32 mJmm², the fR (frequency rate) was set at 8 Hz (pulses per second), the treatment sessions consisted of 12 cycles of Li-ESWT (Low-Intensity Extracorporeal Shockwave Therapy), and a total of 3000 shocks were administered. At the intervals of one week, three months, six months, nine months, and twelve months following the administration of Li-ESWT and tadalafil 2.5 mg, the post-void residual (PVR) volume was consistently below 50 ml. The Li-ESWT treatment effectively reduced the post-void residual urine volume.

Low-intensity extracorporeal shockwave therapy (Li-ESWT) can safely and efficiently decrease the amount of urine left in the bladder after voiding in individuals with neurogenic bladder caused by multiple sclerosis (MS). We have effectively demonstrated that Li-ESWT is a feasible and safe treatment for chronic urine retention, resulting in a decrease of post-void residual (PVR) volume from 200 ml to 50 ml. In the future, Li-ESWT has the potential to be advanced as a more efficacious alternative therapy for individuals experiencing chronic urinary retention. Further investigation is necessary to confirm the effectiveness of ESWT in addressing the neurogenic bladder.

Keywords: neurogenic bladder, multiple sclerosis, low intensity shockwave therapy, post-void residual volume, detrusor underactivity.

Field: Medical sciences and Health

1. INTRODUCTION

Low-intensity focused shockwave therapy (Li-ESWT) is gaining significance in the management of urological disorders. This case study examines the feasibility and efficacy of utilising Li-ESWT to decrease post-void residual volume in individuals with neurogenic bladder, marking the first investigation of its kind.

Bladder dysfunction (BD) commonly manifests in individuals diagnosed with multiple sclerosis (MS). Bladder dysfunction (BD) can arise when the lesions associated with multiple sclerosis (MS) impair the nerve impulses in the central nervous system regions responsible for regulating bladder function and

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controlling the contractions of the urine sphincters. Urinary retention can lead to many symptoms, such as incomplete bladder emptying, urinary incontinence, frequent urinary tract infections, urosepsis with the formation of kidney abscesses as a result of localised kidney infection, and decreased kidney function.

2. CASE DESCRIPTION

A 31-year-old female patient diagnosed with Multiple Sclerosis (MS) has been receiving frequent urological check-ups at our urology clinic since April 2020. The patient was consistently taking dimethyl fumarate as part of their treatment for multiple sclerosis. Neurological evaluations, including MRI scans of the head and spine conducted in March 2020 and March 2022, revealed that the condition remained stable, with no signs of abnormal growths in the specific area of the brain responsible for controlling urination. During the initial presentation, the patient was diagnosed with pyelonephritis affecting the right kidney. The patient's ability to empty their bladder was normal, with a post-void residual volume (PVR) of 50 ml. Hematuria was identified during routine urological evaluation. A cystoscopy was conducted in June 2021. No anomalies were detected. The examination of the upper urinary tract using magnetic resonance urography (MRU) did not reveal any significant findings. Based on the patient's age and absence of other medical conditions, we maintain a strong belief that multiple sclerosis is the underlying cause of the urinary impairment.

In September 2021, the female patient experienced repeated episodes of inflammation in her right kidney, known as recurrent pyelonephritis. A worsening of micturition was reported. The sonography of the urine bladder detected a post-void residual (PVR) volume over 100 ml. After administering suitable antibiotic therapy, the patient's laboratory findings and physical state returned to normal.

In October 2021, the patient experienced a novel urinary tract infection and a fever. The patient had inpatient therapy involving the intravenous infusion of antibiotics and the installation of a bladder catheter. The MRI and urography detected a renal abscess in the right kidney measuring 1.7 cm in diameter, although there was no blockage in the upper urinary system. The abscess could not be punctured due to its inaccessible placement. Consequently, the abscess was managed conservatively by using extended intravenous antibiotics.

Following her release from the hospital, sonography revealed the presence of residual urine over 200 ml on many occasions. As an additional treatment option, the patient began intermittent self-catheterization along with intravesical bladder instillation of chondroitin sulphate. This active ingredient helps temporarily replace the protective layer of sulfated glycosaminoglycan in the bladder. Additionally, the patient started pelvic floor muscle training. The patient declined to have a urodynamic study, which was subsequently not conducted.

Four cycles of single-dose intravesical treatment with chondroitin sulphate were given within a period of four weeks. The post-void residual (PVR) was assessed using disposable catheters during intravesical therapy, producing approximately 200 to 250 ml volume. The administration of distigmine (5 mg) orally twice a day was started as the initial treatment option (Bougas DA, 2004), but it was discontinued after 4 weeks due to its lack of effectiveness.

Subsequently, the patient underwent 12 cycles of low intensity shockwave therapy (Li-ESWT) administered on a weekly or biweekly basis to the urinary bladder as an off-label treatment from January 2022 to April 2022. We employed the PiezoWave (Lee Y-C, 2020) shockwave apparatus, manufactured by Richard Wolf GmbH and ELvation Medical in Germany. Similar to a previous investigation on the treatment of an overactive bladder utilising Li-ESWT (Lee Y-C, 2020), the number of delivered pulses, the F10G10 applicator, the region of administration, and the shockwave penetration were utilised. The energy distribution at energy level 20 yielded a peak energy flux density (EFD) of 0.32 mJ/mm² at a frequency (fR) of 8 Hz (pulses per second). A total of 36,000 shockwaves were administered throughout the whole 12-week therapy duration. Tadalafil 2.5 mg was prescribed as an off-label application and used once a day as an adjuvant till the completion of Li-ESWT. At the intervals of one week, three months, six months, nine months, and twelve months following the administration of Li-ESWT and tadalafil 2.5 mg, the post-void residual (PVR) volume was consistently below 50 ml.

3. RESULTS AND DISCUSSION

Optimal bladder function is crucial for individuals with MS, specifically in maintaining their kidney health, preventing urine infections and incontinence, minimising the frequency of MS episodes, and enhancing their overall well-being. Based on the neurological follow-up, which involved conducting MR scans of the head and spine, it was determined that the urinary dysfunction in this patient was not caused

by an acute attack of multiple sclerosis (MS).

An in vivo study has investigated the impact of Li-ESWT on bladder function. (Wang HS, 2018). The study demonstrated that Li-ESWT improved the condition of underactive bladder (UAB) and urine incontinence in a rat model of diabetic underactive bladder. This study proposes that the enhancement may be attributed to the repair of the bladder and urethral structure and function, which is facilitated by the preservation of neuronal integrity and innervation through Li-ESWT.

The initial clinical investigation of Li-ESWT demonstrated a statistically significant reduction in symptoms of Detrusor underactivity (DU)/UAB, as well as a tendency to lower post-void residual (PVR) volume compared to the placebo group (Shen YC, 2023). The treatment was administered weekly for a duration of 6 weeks. It involved the delivery of 2500 shocks, with a frequency rate of four pulses per second and an energy flux density (EFD) of 0.25 millijoules per square millimetre. In our situation, the EFD (Energy Flux Density) employed was higher than 0.32 mJmm², the fR (frequency rate) was 8 Hz (pulses per second), the treatment sessions consisted of 12 cycles of Li-ESWT (Low-Intensity Extracorporeal Shockwave Therapy), and a total of 3000 shocks were administered. The study conducted by Shen et al. suggests that Extracorporeal Shock Wave Therapy (ESWT) may have a positive impact on enhancing bladder sensation (Shen YC, 2023).

Another investigation discovered that Li-ESWT alleviated symptoms of overactive bladder and enhanced bladder voiding function in female patients (Lee Y-C, 2020).

Temporary ischemia and flow return to basal levels after drainage in male Sprague Dawley rats, as a result of acute urine retention (Shimizu S, 2009). Transient bladder ischemia is believed to cause a temporary reduction in detrusor compliance (Tracey AT, 2019). In this particular instance, the patient is experiencing chronic urine retention as a result of multiple sclerosis (MS). Prior research has linked persistent ischemia to the pathological advancement towards detrusor overactivity, ultimately resulting in DU (Andersson K-E, 2017).

VEGF is a signal protein that stimulates angiogenesis and reestablishes oxygen delivery to tissues in cases of insufficient blood flow, such as in hypoxic circumstances (Shen Y-C, 2021). Interleukin 9 (IL-9) is a cytokine produced by CD4⁺ helper cells that controls various hematopoietic cell types, increasing cell proliferation and preventing apoptosis (Perumal NB, 2011). Sugaya et al. found that approximately 35% of the individuals in their study who had interstitial cystitis also had an allergy or autoimmune condition linked to the excessive production of IL-4. The IL-4 and its receptor genes are robustly associated with immunological diseases (Sugaya K, 2002).

Under pathological hydrostatic pressure, the β -Adrenoceptor regulates the expression of inflammatory cytokines and contraction in human bladder smooth muscle cells through autophagy1 (Chen G, 2020). Shen et al. conducted a study where they found that patients with refractory interstitial cystitis and bladder pain syndrome who were randomly assigned to receive Li-ESWT had improved symptoms and urine biomarkers compared to those who received a placebo. At 4 weeks, the group that received Extracorporeal Shock Wave Therapy (ESWT) exhibited a decrease in the expressions of Vascular Endothelial Growth Factor (VEGF) and Interleukin-4 (IL-4), whereas the expression of Interleukin-9 (IL-9) increased. These authors proposed that Extracorporeal Shock Wave Therapy (ESWT) may exert an influence on immunological regulation by affecting mast cells and their IL4 reaction (Shen Y-C, 2021).

Adjuvant daily therapy with tadalafil 5 mg (PDE5i) effectively enhanced the effectiveness and duration of the advantages of Li-ESWT in patients with erectile dysfunction by preventing the breakdown of cGMP (Gallo L, 2022). The NO/cGMP/G Kinase pathway appears to have a significant impact on the regulation of bladder myocyte tone (Deka DK, 2004). Additionally, treatment with PDE5i may help reduce the progression of ischemia-related functional and structural changes in the bladder (Andersson K-E, 2017).

This case report aims to investigate the possible advantages of Li-ESWT, taking into account its anti-inflammatory and anti-apoptotic properties, as well as its capacity to stimulate stem cells. Therefore, Li-ESWT may be efficacious for urinary bladder conditions that are characterised by reduced inflammatory reactions, heightened innervation of bladder nerves, tissue regeneration, and enhanced blood vessel formation via angiogenesis. Furthermore, Li-ESWT can result in improved contractile activity of the bladder and urethra muscles and improved composition of the bladder wall. The bladder experienced ischemia and a decline in innervation, resulting in impaired transmission of nerve impulses due to multiple sclerosis (Shen Y-C, 2021) (Jin Y, 2017).

The main processes underlying the action of Li-ESWT on the bladder include modulated local immune responses, increased bladder nerve innervation, enhanced vascularization and angiogenesis, regulation of β -Adrenoceptors response, activation of stem cells, reduction of bladder ischemia, and inhibition of urothelial cell apoptosis.

Our case demonstrated a substantial enhancement of post-void residual volume (PVR) from over 200 ml to less than 50 ml after undergoing treatment with low-intensity extracorporeal shockwave therapy (Li-ESWT) in combination with adjuvant therapy involving the administration of tadalafil 2.5 mg. This improvement has been sustained for a duration of 9 months thus far.

The patient has reported the absence of any negative consequences experienced during the treatment, as well as a notable enhancement in voiding function following Li-ESWT. There was no observed enhancement following the initial pharmacological intervention.

Prior to the multimodal Li-ESWT therapy, the administration of distigmine and chondroitin sulphate was carried out. Nevertheless, we cannot simply attribute the outcome in this case to the initial treatment, as there was no immediate observation of clinical improvement. Observable progress in the patient's condition was apparent with the implementation of a comprehensive treatment strategy that included Lithotripsy-Enhanced Extracorporeal Shock Wave Therapy (Li-ESWT) and Tadalafil medication.

In the present case, PVR served as the primary diagnostic instrument for assessing treatment efficacy, and it was not possible to conduct a urodynamic examination prior to and following the treatment. This is because of the rapid alleviation of symptoms and the patient's failure to comply with additional intrusive procedures. Hence, the alleviation of symptoms and the notable enhancement in clinical presentation provide robust evidence in favour of the positive result of PVR following Li-ESWT, thereby minimising the likelihood of alternative factors contributing to better PVR.

4. CONCLUSION

This case report is the initial documentation of the application of Li-ESWT in the treatment of a patient presenting with neurogenic bladder and chronic urine retention. We have successfully shown that Li-ESWT is a viable and secure therapy for persistent urine retention, reducing post-void residual (PVR) volume from 200 ml to 50 ml. In the future, Li-ESWT could be developed as a more effective alternative treatment for people suffering from chronic urine retention. Additional research is required to validate the efficacy of ESWT in treating the neurogenic bladder.

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