THE BENEFITS OF LI-ESWT THERAPY IN ORGANIC ERECTILE DYSFUNCTION CASE WITH CHRONIC RENAL FAILURE: A CASE REPORT

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ABSTRACT

Erectile dysfunction (ED) is a common type of male sexual dysfunction that has a negative impact on the quality of life. Erectile dysfunction is common in men and the incidence increases with age. Erectile dysfunction can be caused by organic disorders, such as hormonal disorders and metabolic disorders. In this case report, the authors report the case of a man who developed chronic renal failure with multiple metabolic disorders and hypogonadism. This case report described the benefits of Li-ESWT therapy in patients who less responsive after receiving PDE-5 inhibitor therapy, tadalafil as first-line therapy for erectile dysfunction. This case report was evaluated using the IIEF-5 questionnaire and EHS score as a description of erection quality with PSV parameters from the results of penile CDUS during flaccid and VEGF parameters as angiogenesis factors. In this case report, the patient experienced improvements in erection quality, PSV parameters, and VEGF parameters after receiving Li-ESWT therapy.

Keywords: erectile dysfunction, chronic renal failure, Li-ESWT, tadalafil, PSV, VEGF.

ABSTRAK

Disfungsi ereksi (DE) adalah jenis disfungsi seksual pria yang berdampak negatif pada kualitas hidup. Disfungsi ereksi sering terjadi pada pria dan insidensinya meningkat seiring bertambahnya usia. Disfungsi ereksi dapat disebabkan oleh gangguan organik, seperti gangguan hormonal dan gangguan metabolisme. Dalam laporan kasus ini, penulis melaporkan kasus seorang pria yang mengembangkan gagal ginjal kronis dengan beberapa gangguan metabolisme dan hipogonadisme. Laporan kasus ini menggambarkan manfaat terapi Li-ESWT pada pasien yang kurang responsif setelah mendapat terapi penghambat PDE-5, tadalafil sebagai terapi lini pertama untuk disfungsi ereksi. Laporan kasus ini dievaluasi menggunakan kuesioner IIEF-5 dan skor EHS sebagai gambaran kualitas ereksi dengan parameter PSV dari hasil CDUS penis saat lembek dan parameter VEGF sebagai faktor angiogenesis. Dalam laporan kasus ini, pasien mengalami peningkatan kualitas ereksi, parameter PSV, dan parameter VEGF setelah menerima terapi Li-ESWT.

Kata kunci: disfungsi ereksi, gagal ginjal kronik, Li-ESWT, tadalafil, PSV, VEGF.

INTRODUCTION

Erectile dysfunction (ED) is the inability to achieve or sustain an erection sufficient for satisfactory sexual intercourse of at least three months. Erectile dysfunction is a common type of male sexual dysfunction that has a negative impact on the quality of life.[1] Erectile dysfunction affects about 15% to 50% of men and increases with age.[2] Erectile dysfunction is mostly caused by organic factors, especially in the vascular

system. Metabolic conditions can cause erectile dysfunction, such as hyperglycemia, hypercholesterolemia, and hypertension.[3–5] These conditions are commonly found in chronic renal failure (CRF). Chronic renal failure causes hypertension which interrupts blood flow to the microvascular system, which is known as hypertensive angiopathy. The process of hypertensive angiopathy can disrupt the penile tissue which causing disturbances in the quality of the erection. Chronic renal failure can also lead to decreased levels of androgens or hypogonadism.[6]

Erectile dysfunction with hypogonadism has the main treatment, namely androgen hormone substitution therapy for hypogonadism conditions. The first line of therapy for erectile dysfunction is *phosphodiesterase type 5 inhibitor (PDE-5 inhibitor).*[7,8] PDE-inhibitor therapy can be given in two ways when it is needed or given regularly every day. Regular administration of PDE-5 inhibitor therapy every day is known to have a better effect than the one taken when it is needed. PDE-5 inhibitor therapy has a mechanism of action by making vasodilation of blood vessels, so that blood flow is better and the quality of erection is improved.[9–11] This therapy only makes blood vessels vasodilated without repairing damaged blood vessel endothelium. Erectile dysfunction therapy has experienced many developments to date, one of which is developing regenerative therapy to repair damaged blood vessel endothelium due to metabolic conditions, including hypertensive angiopathy. Regenerative therapy that develops has two different mechanisms of action, namely stimulating the production of factors that will naturally stimulate the angiogenesis process or giving these factors externally, such as stem cell therapy, which is still experimental.[7] Low-intensity shock wave therapy or known as Low-Intensity Extracorporeal Shockwave Therapy (Li-ESWT) is a therapy that has a mechanism of action by causing microtrauma in the vascular and perivascular tissues of the penis which stimulating internal regeneration. Vascular Endothelial Growth Factor (VEGF) is one of the angiogenesis factors stimulated by this therapy.[12,13] Blood flow in the penile tissue can be seen from the Peak Systolic Velocity (PSV) parameters from the results of the penile Color Doppler Ultrasonography (CDUS) examination.[14–16] The penile CDUS examination can be performed in flaccid or erection conditions, penile CDUS examination in flaccid conditions has several advantages, namely that it is not invasive, which makes the patient is more comfortable during the examination.[17–19]

CASE REPORT

A 52-year-old man from Sidoarjo came to the Andrology Clinic of Dr. Soetomo Regional General Hospital with complaints of decreased erection quality. The patient complained that he experienced erectile problems since he was diagnosed with chronic renal disease and undergoing hemodialysis for five months before visiting the Andrology clinic. The decline in erection quality occurs slowly. The erection quality assessment using the Erection Hardness Score (EHS) at the initial visit was found to be consistent with the EHS score of 1 indicates that the penis is larger than normal, but not hard. Nocturnal Penile Tumescence (NPT) is still felt, but the frequency is quite rare and the quality is not good. The International Index of Erectile Function (IIEF) questionnaire could not be assessed because the patient had not have sex for the last three months. Furthermore, the

patient also complained about a decrease in sex drive. The patient has clinical manifestations of a Partial Androgen Deficiency in Aging Men (PADAM) score. Apart from suffering from chronic renal disease, the patient also had a history of hypertension, heart failure, hyperuricemia, and dyslipidemia. The patient is also a light smoker, but this smoking habit has been stopped since five years ago. Regular treatment is carried out from the internal medicine department, the patient receives several routine medications such as Bisoprolol, Candesartan, Allopurinol, and Atorvastatin. Patients also undergo regular hemodialysis twice a week.

In general, the results of the physical examination found that the patient was a grade 2 obese male with a Body Mass Index (BMI) score of 32.2 kg/m^2. Physical examination of other organs showed no abnormalities. The results of the genital examination showed that the size of the right and left testicles were 15cc and 15cc with the consistency of testicles being elastic. The results of laboratory tests showed hemoglobin 10.3 g/dL, hematocrit 31.1%, urea 203 mg/dL, serum creatinine levels reached 14.31 mg/dL, testosterone levels 181.8 ng/dL, and levels of Prostate Specific Antigen (PSA) 0.402 ng/mL.

The patient received short-acting Testosterone (Sustanon®) injection 250 mg using IM procedure every two weeks and Phosphodiesterase type 5 inhibitor (PDE-5 inhibitor) drug in the form of Tadalafil (Cialis®) 1 x 5 mg. Hemodialysis is still carried out according to the schedule determined by the internal medicine department. The results from the evaluation of therapy for 10 weeks showed an increase in the quality of erection and improvement in patient's self-confidence, the EHS score increased to 2, with laboratory results of hemoglobin 11.7 g/dL, hematocrit 36.5%, urea 131 mg/dL, serum creatinine 12.37 mg/dL, testosterone 1174 ng/dL, and PSA 0.49 ng/mL. The patient admits that he has tried to have sex with his partner again.

Based on the results, adjustments were made to the therapy given to the patient in the form of adjusting the duration of the injection of Short-acting Testosterone (Sustanon®) 250 mg to every three weeks, the PDE-5 inhibitor drug, Tadalafil (Cialis®) to 1 x 2.5 mg, and Li-ESWT therapy was added. Li-ESWT therapy uses tools from the BTL-6000 Topline SWT with an energy density of 0.09 mJ/mm^2, a frequency of 5Hz, 600 shock waves per point, with a total of five points (the distal, medial, and proximal penile corpus, and in the crux dextra, and sinistra), with a duration of three minutes per point. Li-ESWT therapy was carried out twice per week for four weeks. The patient did not experience any side effects from Li-ESWT therapy. VEGF examination of the patient's blood and penis Color Doppler Ultrasonography (CDUS) to determine the peak systolic velocity (PSV) in the cavernous arteries during the flaccid condition was performed before and after undergoing the Li-ESWT therapy program. The quality of the patient's erection according to the EHS score was 2, and the IIEF-5 questionnaire had a result of 13 before receiving the Li-ESWT therapy program. The patient experienced an improvement in erectile quality after four weeks of Li-ESWT therapy with an EHS score of 4, IIEF-5 to 25, and a positive NPT. Penile CDUS examination with the results of the PSV parameter increased from 10.8 cm/second before Li-ESWT therapy to 13.95 cm/second after therapy. This is also supported by the increase in VEGF parameters from the results of blood plasma tests from 30.18 pg/mL to 67.56 pg/mL after receiving therapy

Table 1. Condition of the erection quality and initial laboratory results and after 10 weeks of therapy

	Initial Condition	**After 10 week of Therapy**
EHS	1	2
IIEF-5	-	13
NPT	rare	rare
Hemoglobin	10.3 g/dL	11.7 g/dL
Hematocrit	31.1 %	36.5 %
Ureum	203 mg/dL	131 mg/dL
Creatinine	14.31 mg/dL	12.37 mg/dL
Testosterone	181.8 ng/dL	1174 ng/dL
PSA	0.402 ng/mL	0.49 ng/mL

Table 2. Evaluation results of erection quality, PSV parameters, and VEGF parameters before and after combination therapy with Li-ESWT for four weeks

	Before Li-ESWT	**Before Li-ESWT**
EHS	2	4
IIEF-5	13	25
NPT	Rare	Always
PSV*	10.8 cm/second	13.95 cm/second
VEGF	30.18 pg/mL	67.56 pg/mL

DISCUSSION

In this case, there are many other conditions that comorbid to chronic renal failure including hypertension, heart failure, hyperuricemia, dyslipidemia, anemia, obesity grade 2, hypogonadism, and smoking habits. In the initial condition, the patient came to the andrology clinic and had received routine hemodialysis therapy twice a week with medical therapy in the form of bisoprolol, candesartan, allopurinol, and atorvastatin.

The conditions that occur in this case have a great influence on worsening the quality of the patient's erection. Uncontrolled hypertension can damage the microvascular system in the penis.[20] The condition of dyslipidemia can lead to plaque or atherosclerosis which interferes with the elasticity of blood vessels.[21] Conditions of anemia and heart failure can cause a decrease in oxygen supply to the tissues.[22,23] Hypogonadism will cause a decrease in sexual desire or libido, along with impaired erection quality.[24,25] Obesity can worsen the hypogonadism condition.[26–28] Smoking habits can also increase Reactive Oxygen Species (ROS) levels which can damage the endothelium of blood vessels and impairs the elasticity.[29] Medical therapy that is taken regularly also has a role in worsening erection quality, such as bisoprolol.[30]

The patient is given androgen hormone substitution therapy in the form of a short-acting Testosterone (Sustanon®) injection every two weeks and a PDE-5 inhibitor drug in the form of Tadalafil (Cialis®) 5 mg daily after a complete assessment. The patient experienced an improvement in the erection quality, but not hard enough for penetration after receiving therapy for 10 weeks. This indicates that the damage that occurs to the erectile tissue of the penis is severe enough that it does not respond to androgen substitution therapy and PDE-5 inhibitors that have been given.

Based on the results after 10 weeks of therapy, the patient was given an adjustment to

the therapy given including the duration of androgen substitution therapy to three weeks due to supraphysiological testosterone levels, and administration of additional regenerative therapy, namely Li-ESWT. PDE-5 inhibitor (Cialis®) therapy was also reduced to 2.5 mg daily. Combination therapy was carried out for four weeks and re-evaluated. The results of the combined post-therapy evaluation showed that the patient experienced an improvement in erection quality. The improvement in erection quality occurred at the end of the second week after therapy. This occurs according to theory, namely an increase in the levels of angiogenesis VEGF factor after undergoing two weeks of therapy. Angiogenesis factors will stimulate neovascularization, resulting in improved blood flow. This can be evaluated by an increase in the PSV parameters. According to the theory, this can be detected after four weeks of therapy. The patient had a significant increase in PSV parameters from the penile CDUS examination of the cavernous arteries at the end of the fourth week.

CONCLUSION

Li-ESWT therapy improves the quality of erection in the patient who is less responsive after receiving first-line therapy, namely the PDE-5 inhibitor. Li-ESWT therapy is one of the combination therapy that can be given to the patient with erectile dysfunction.

CONFLICT OF INTEREST

There is no conflict of interest from all parties in this case report case.

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