Abstract #15-6311 Low Intensity Extracorporeal Shockwaves Therapy Improves Erectile Function in Diabetic Type II Rats Independently of NO/cGMP Pathway

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OBJECTIVES

- Urological functional complications such as erectile dysfunction (ED) significantly impact the quality of life of diabetic patients who are poor responders to PDE5 inhibitors.
- Low intensity extracorporeal shock waves therapy (LI-ESWT) has been reported to significantly improve erectile function in ED patients.
- The mechanism of action of LI-ESWT is still unknown.

Aim of the study:

- Assess the effects of LI-ESWT.
- In vivo on erectile function in the Goto-Kakizaki rats (GK), a validated model for type 2 diabetes-associated ED [1].
- Ex vivo on endothelium-dependent, -independent and nitricergic relaxations of cavernosal strips from GK rats.

MATERIALS & METHODS

- LI-ESWT treatment protocol (based on parameters described by Vardi et al.[1,14] in clinical studies).
- Male GK and age-matched Wistar rats received 2 sessions of LI-ESWT per week for 3 weeks, repeated after a 3-week no-treatment interval. Shockwaves were delivered by a calibrated probe yielding a controlled energy flux density of 0.80 ± 0.02 mJ/mm² at a compact hydrocatheterized unit with a focused ultrasound source (Chopette Ed 1000, Multipuls Ltd, Germantown, MD, USA).
- To facilitate coverage and transmission of the shockwaves, the penis of each anesthetized rat was manually stretched and dipped into a specifically designed water-filled tank. Following a 4-week wash-out period, erectile function was assessed by electrical stimulation of the cavernosal nerves in rats under anesthesia.

RESULTS

- Erectile function evaluation: electrical stimulation of the cavernous nerve (CN) in GK rats.

Effect of LI-ESWT on erectile function in GK rats

- The erectile responses elicited by cavernosal nerve stimulation at increasing stimulation frequencies in anesthetized Wister and GK rats.
- Both acute sildenafil or LI-ESWT significantly improved erectile responses in GK rats.
- Neither treatment restored normal erectile responses.

Effect of LI-ESWT on endothelium-dependent, -independent and nitricergic relaxations of cavernosal strips from GK rats

- The combination of LI-ESWT with sildenafil significantly potentiated the effect of LI-ESWT alone and tended to potentiate the effect of acute sildenafil.

- The present study describes a relevant preclinical paradigm to investigate LI-ESWT in the rat by adapting the machine and treatment modalities to adequately mimic what has been performed in men [2,3,5].
- Furthermore, this study reports, in an experimental model of ED associated to diabetes type II,:
  - the beneficial disease-modifying effect of LI-ESWT;
  - the beneficial effect of LI-ESWT combined to an acute administration of PDE5-I compared to standard-of-care PDE5-I therapy alone.
- To our knowledge, this is the first study to investigate the effect of LI-ESWT on endothelial and nitricergic relaxations of cavernosal strips from diabetic GK and age-matched Wistar rats. Interestingly, this study clearly demonstrates that the effect of LI-ESWT is not modulated by the NO/cGMP pathway.
- Thus, there is a need to search for alternative mechanisms of action to explain the beneficial effects of LI-ESWT i.e., possible angiogenesis and neovascularization to improve cavernosal blood supply? Anti-inflammatory effect? Anti-oxidative effect?...