



Low intensity-Shockwave Therapy (Li-ESWT) delivered by Aries® improves erectile function and decreases cavernosal fibrosis of spontaneously hypertensive rats (SHR)

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Objectives: Li-ESWT has been reported to improve erectile function in patients with vasculogenic ED, and convert PDE5i non-responders into responders. Erectile function of SHR, a validated rat model of hypertension associated ED, is partially improved by PDE5is. Here, we investigated whether Li-ESWT could affect erectile function with and without acute sildenafil in SHR. A pronounced accumulation of collagen in erectile tissue of SHR has been described, thus we also investigated the histological features of SHR erectile tissue after ESWT.

Methods: 2 groups of male SHR (CTRL and ESWT; n=14/group) were treated twice/week for 6 weeks. Only in the ESWT group, shockwaves were delivered to the penis at the mid-shaft and base (Aries®, Dornier MedTech, Germany). Each session comprised 1000 shocks per site (total: 2000 shocks, EFD: 0.06 mJ/mm²). 4 weeks after the final session, erectile function was assessed by recording intracavernosal pressure (ICP) and mean arterial pressure (MAP) under electrical stimulation of the cavernous nerve (ES CN), first in absence then in presence of sildenafil (0.3mg/kg *iv*). Then rats were sacrificed, the corpora cavernosa were harvested and prepared for histological analysis. Cavernosal smooth muscle (SM)/collagen ratio was assessed by trichrome staining. Cavernosal microvasculature and nitrergic nerves were assessed by immunohistology against CD31 and nNOS.

Results: ESWT increased erectile responses of SHRs (at 10 Hz, Δ ICP/MAP: +17%; AUC_{tot}/MAP: +17%, p<0.001 vs. CTRL). Combining ESWT with sildenafil improved erectile response of SHRs (at 10Hz, AUC_{tot}/MAP: +40%, p<0.001 vs. CTRL) and further enhanced the effect of either therapy alone (+20%, p<0.01 vs. SHRs treated with ESWT, +16%, p<0.001 vs. SHRs treated with sildenafil). Histological analysis showed a 2.5 fold increase in the SM/collagen ratio following ESWT.

Conclusion: ESWT using Aries® improved erectile function in SHR and potentiated responses to sildenafil. This improvement was accompanied by an increase in the SM/collagen ratio. These results suggest ED is effective for vasculogenic ED as mono-therapy, and in combination with PDE5i. This study is the first to report that ESWT increases cavernosal smooth muscle proportion in the SHR.