

## **LOW ENERGY SHOCK WAVE THERAPY INHIBITS INFLAMMATORY MOLECULARS AND SUPPRESSES PROSTATIC PAIN IN A CAPSAICIN INDUCED PROSTATITIS MODEL IN RAT**

### Hypothesis / aims of study

Low energy shock wave therapy (LESWT) has been suggested to attenuate inflammatory condition and reduce somatic pain [1]. Recently, several studies demonstrate that LESWT significantly improve pain, QoL, and voiding conditions in patients with nonbacterial prostatitis /CPPS comparison to the placebo treated group [2]. However, the mechanisms and molecular changes of LESWT on nonbacterial prostatitis /CPPS are still unclear. We hypothesize that LESWT can suppress inflammatory molecules, and reduce the inflammatory condition and prostatic pain in the nonbacterial prostatitis. To our knowledge, this is the first animal study to elucidate the effects and mechanisms of LESWT in a capsaicin induced nonbacterial prostatitis in rats.

### Study design, materials and methods

Adult male S.D. rats were injected with vehicle or capsaicin (10 mM, 0.1 cc) into the prostate. Right after injection, various numbers of shock wave (0, 100, 200 or 300 shocks; 0.12 mJ/mm<sup>2</sup>) were applied into the prostate. The nociceptive effects of capsaicin were evaluated for 90 min by using a behaviour approach. Behavioral changes following shockwave therapy were then scored every 30 minutes for 3 times 2 hours after recovery from anesthesia. We used a scoring scale of 1 to 5 as previous reported [3]. Blinded observers performed all experiments and each experimenter scored 2 rats in parallel. Three or seven days after LESWT, the prostate were removed for histology, COX-2, and TNF- $\alpha$  expression by using immunohistochemical staining.

### Results

Capsaicin injection into prostate induced marked behaviour changes: including closing of the eyes and hypolocomotion, which were significantly decreased by LESWT (Fig. 1). The eye open score increased in capsaicin group (3.25 $\pm$ 0.34 vs vehicle 1.37  $\pm$  0.08, p=0.0001) and significantly decreased after 100, 200 and 300 shockwave treatment (1.92 $\pm$ 0.37; 1.46 $\pm$ 0.14; 1.37 $\pm$ 0.12, respectively, p< 0.05 n=8 each group). Locomotion scores in all groups were lower after LESWT compared with capsaicin group but not significant in 100 shock wave group (3.46 $\pm$ 0.39; 3.00 $\pm$ 0.13; 2.13 $\pm$ 0.18; 1.75 $\pm$ 0.20, p<0.05, n=8 each group). Capsaicin induced inflammatory cells accumulation in prostate and significant higher COX-2, TNF-alpha positive stain cells compared with vehicle injection (Fig.2). The capsaicin-induced prostate inflammation was dose dependently ameliorated by LESWT. On day 3 LESWT decreased COX-2(+) cell accumulation in 100, 200 and 300 shockwave groups (4.5%, 63.5%, and 54.9% reductions, respectively) (Fig. 2b). The decrement was significant in 200, 300 shock wave group but not in 100 shock wave group ( p=0.002, 0.0046 and 0.757). The same result was observed at day 7 (Fig 2e) . The TNF-alpha cell(+) count increased with time (6.08 $\pm$ 1.00 for day 3 and 26.78 $\pm$ 8.36 for day 7, Fig 2c, 2f). L-ESWT also decreased the TNF-alpha(+) cells but was only significant at day 7 in both 200 and 300 shock wave group (p=0.028).

### Interpretation of results

LESWT decreased pain behaviour and reduce inflammatory conditions in capsaicin induced prostatitis. The effect of LESWT was dose and time dependent, which showed no significant effect at the dose of 100 shock waves, but the inflammatory conditions and pain behaviour were significantly reduced at the dose of 200 and 300 shock waves.

### Concluding message

Intraprostatic capsaicin injection activates COX2 and TNF- $\alpha$  expression in the prostate and induces prostatic pain. LESWT could inhibit the capsaicin induced COX-2 and TNF- $\alpha$  expression and inhibit prostatic pain and inflammation in a dose dependent fashion. This finding suggests a potential clinical benefit of LESWT at the optimal dose for the treatment of nonbacterial prostatitis.

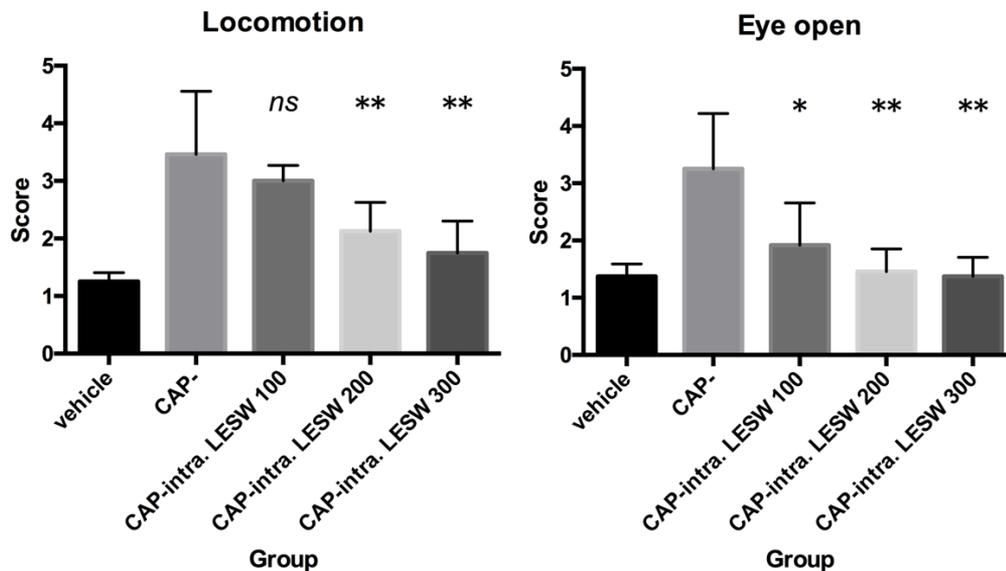


Figure 1. Behavior Score (\*  $p < 0.05$ , \*\*  $P < 0.01$ , *ns*: non-significant)

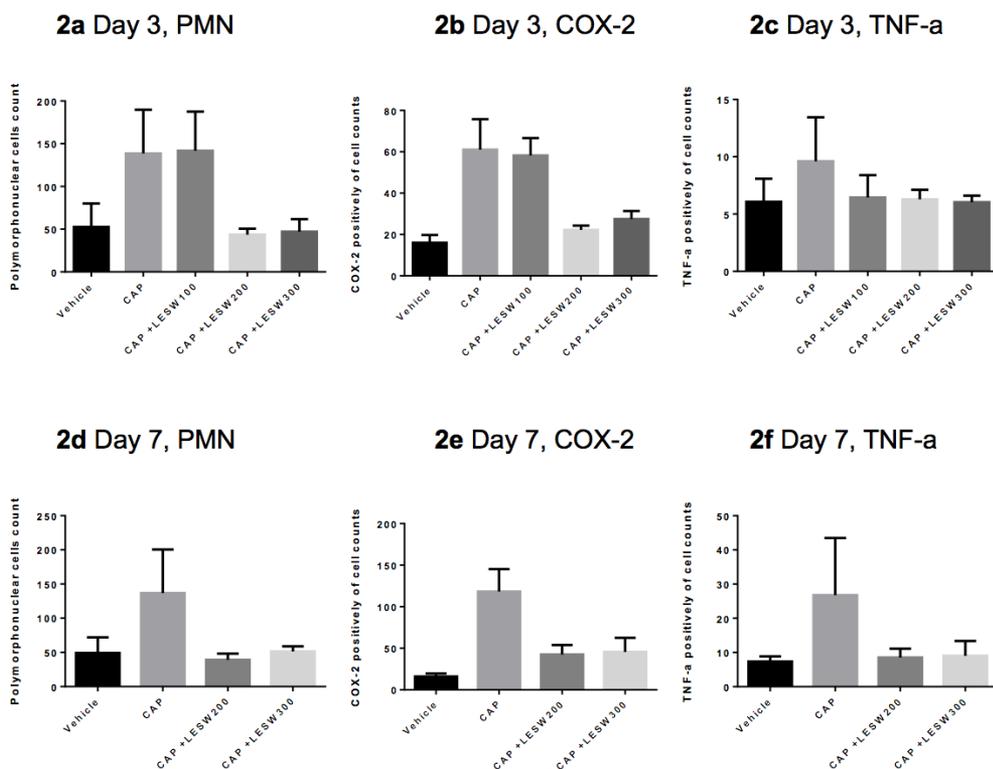


Figure 2. Average cell count in 200x visual field. (\*  $p < 0.05$ )

#### References

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3. Wang HJ, Lee WC, Tyagi P, Huang CC, Chuang YC. Effects of low energy shock wave therapy on inflammatory moleculars, bladder pain, and bladder function in a rat cystitis model. *NeuroUrol Urodyn.* 2016 doi:10.1002/nau.23141.

#### Disclosures

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