Oxytocin as a pharmacological target for benign prostatic hyperplasia

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Background

The pathogenesis of Benign Prostatic Hyperplasia (BPH) is associated with both the non-malignant growth of the prostate (static component), and increased smooth muscle tone (dynamic component) which can lead to irritative and obstructive lower urinary tract symptoms, affecting the quality of life of patients. A recent study has shown that the levels of circulating oxytocin is significantly upregulated in men with (BPH), and exogenous oxytocin significantly increased the proliferation of prostatic fibroblasts [1]. In this study, we investigated whether oxytocin regulates the smooth muscle tone of the human prostate gland.

Methods

Samples of human prostate were collected from the transition (TZ) and peripheral zone (PZ) of men undergoing radical prostatectomy. Immunohistochemistry was used to confirm the presence and localization of the oxytocin receptor (OXTR). Tension recordings were obtained using organ bath techniques, with specimens incubated with increasing concentrations of oxytocin (0.1nM to 10 μ M). The basal tension (mN), amplitude (N/g) and frequency of spontaneous contractions were quantified.

Results

Using Immunohistochemistry, OXTR was found to be widely expressed in both the epithelial and stromal compartment of TZ and PZ specimens of human prostate (n =10). Application of exogenous oxytocin to TZ specimens significantly augmented the frequency of spontaneous contractions at 10 μ M by $70 \pm 21\%$ when normalized to baseline frequency ($p < 0.05$, n = 8). The half-maximal increase in frequency (EC₅₀) occurred at 300nM. A similar efficacy was observed in patient matched PZ specimens (n=4).

Conclusion

We have established that oxytocin is able to induce contractility of the human prostate in both the TZ and PZ of the human prostate. Given that patients with BPH have elevated levels of oxytocin and that oxytocin has previously been shown to induce proliferation of prostate fibroblasts, is widely expressed in both the prostate stroma and epithelium, and is able to induce muscle contractility, targeting of the OXTR and associated downstream signalling is an attractive prospect in designing new and novel BPH pharmacotherapies.

1. Xu, H., et al., Oxytocin: its role in benign prostatic hyperplasia via the ERK pathway. Clin Sci (Lond), 2017. 131(7): p. 595-607.