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Oxytocin produces contraction of human isolated prostate, an effect blocked by the novel and selective oxytocin receptor antagonist GSK557296: potential role in benign prostatic hyperplasia.

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INTRODUCTION AND OBJECTIVES: Oxytocin (OT) concentrations have been shown to be elevated in prostatic tissue from patients with benign prostatic hyperplasia (BPH) suggesting that OT may play a role in the disease. Not only has OT been shown to play a role in prostate cell proliferation it may also produce contraction of the prostate through its specific receptor, however this has not been definitively demonstrated. Therefore the aim of the present study was to evaluate whether OT produces contraction of human isolated hyperplastic prostate and determine whether this response is mediated by specific OT receptors using the selective oxytocin receptor antagonist GSK557296.

METHODS: Prostatic tissue was obtained from 9 patients (65 ± 3 years old) undergoing prostatic adenomectomy for BPH. Strips were mounted under 1 g of initial tension. After 60 min of equilibration, strips were exposed to 30 μ M norepinephrine (NE) to determine tissue viability. After wash-out and 60 min of re-equilibration, GSK557296 (0.1-1 μ M) or tamsulosin (10 nM) were incubated for 60 min followed by a single concentration of OT (1 μ M) or cumulative concentrations of NE (0.1-1000 μ M), respectively.

RESULTS: In preliminary experiments it was determined that cumulative concentration response curves to OT were not possible due to desensitization. In subsequent experiments, single applications of OT (0.1-1 μ M) produced contractions of isolated prostate with similar efficacy and potency to equivalent concentrations of NE. At 1 μ M, OT induced contractions equal to 12.5% of the maximal contraction to 30 μ M NE.

GSK557296 inhibited contractions induced by 1 μ M OT in a concentration-dependent manner. Responses to OT were reduced 33% in the presence of GSK557296 at 30 nM. At higher concentrations (100 nM and 1 μ M), GSK557296 inhibited OT-induced contractions by $\geq 60\%$.

NE (0.1 – 1000 μ M) induced concentration-dependent contractions with an EC50 value of approximately 10 μ M. Tamsulosin (10 nM) decreased the potency and efficacy of NE with an estimated pKB value of 9.19, similar to that previously reported.

CONCLUSIONS: This is the first definitive demonstration of a contractile effect of OT in human prostatic tissue through specific OT receptors. These effects of OT could contribute to symptoms of BPH.

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