

THE EFFECT OF RESINIFERATOXIN ON THE SENSORY NERVE OF THE RAT PROSTATE

Hypothesis / aims of study

Resiniferatoxin (RTX) is an ultrapotent capsaicin analog that gives long-term desensitization of sensory neurons and depletes the sensory neuropeptide calcitonin gene-related peptide (CGRP) due to a combination of neuron loss and decreased synthesis in the surviving cells. It has been reported that the majority of the afferent innervation to the ventral prostate in the rat is localized to sensory nerves from the L5 and L6 segments which overlaps with input from the bladder. It has also been shown that non-selective denervation of the prostate results in a loss of functional and structural integrity of the gland. This study aimed to determine the feasibility and effect of sensory blockade to the prostate by investigating the changes in CGRP expression and structure of the rat prostate after direct application of RTX.

Study design, materials and methods

Fifteen Sprague-Dawley rats (250-300g) were divided into four groups: normal controls (n=3); RTX treated rats (100nM) (n=6); vehicle (30% ethanol) treated rats (n=3); denervation rats (n=3). Resiniferatoxin or vehicle 0.02cc was injected into the left ventral prostate using a 30G needle. Bilateral hypogastric nerve was cut near the major pelvic ganglion in the denervation group. Rats were subsequently sacrificed after 4 and 8 weeks. The prostate glands were harvested, weighed, and histologically studied for morphologic changes and immunostained for CGRP expression.

Results

The weight of the prostate increased at 4 and 8 weeks, however, there were no differences in weight of the prostate between the groups. Histologically, a generalized atrophy of the stromal component and subsequent increase in size of the glandular portion was observed in the RTX injected group at 4 and 8 weeks where the changes were most prominent at 8 weeks (figure). The average glandular thickness of the control, RTX, vehicle, and denervated groups were 7.8, 5.9, 6.8, and 7.3µm, respectively, at 4 week and 8.3, 4.5, 7, and 9.2µm, respectively, at 8 weeks. The number glands observed under x100 power field for control, RTX, vehicle, and denervated groups were 32.5, 29.5, 34, 40.5, respectively, at 4 weeks and 31, 20.25, 29, 33, respectively, at 8 weeks. Immunoreactivity to CGRP was completely blocked in the RTX injection group only at 8 weeks.

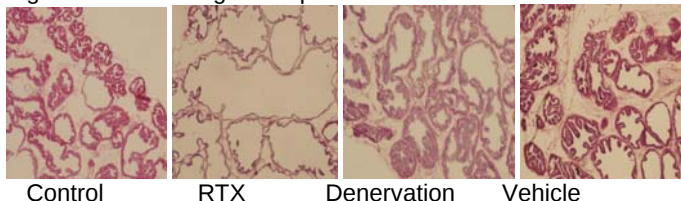
Interpretation of results

Selective blockade of the sensory nerve in the prostate is feasible by injection of RTX into the prostate gland. Injection of RTX in the prostate also results in changes of stromal:glandular ratio where the stromal component is reduced.

Concluding message

It may be possible that in the future, the long-acting neurotoxin RTX may be used for the treatment of common pathologies of the human prostate such as perineal pain syndrome and/or benign prostatic hyperplasia.

Figure. H&E staining of the prostate at 8 weeks



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ANIMAL SUBJECTS: This study followed the guidelines for care and use of laboratory animals and was approved by Yonsei University animal ethics committee