

Expression of human type-I LHRH receptors and type-I LHRH in human benign prostatic hyperplasia

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Summary

The majority of men will develop symptoms of benign prostatic hyperplasia (BPH) after 70 years of age. Various studies indicate that antagonists of LHRH, such as cetrorelix, exert direct inhibitory effects on BPH mediated by specific LHRH receptors. The presence of four different isoforms of luteinizing hormone-releasing hormones (LHRH) and one LHRH receptor (LHRH-R) has been reported in vertebrates. In the human genome only LHRH-I and LHRH-II genes have been identified. The human LHRH-I gene is composed of four exons separated by three introns. Three LHRH receptor or receptor-like genes have been demonstrated. The well-established type-I LHRH receptor (LHRH-R-I) gene is composed of three exons separated by two introns.

Our aim was to investigate the mRNA for LHRH and LHRH receptors with reverse transcriptase-polymerase chain reaction (RT-PCR) using gene specific primers and the expression of LHRH receptors in specimens of human BPH. Fifty-five human BPH specimens were obtained at surgery. Normal human pituitaries collected at autopsy served as control. RNA extraction and RT-PCR with gene-specific primers for LHRH-R-I forward (F1)/reverse (R1), LHRH-R-I F2/R3, LHRH-R-I F1'/R2' were carried out to determine the mRNA expression for LHRH-R-I transcript forms. The expected PCR products amplified with gene specific primers were LHRH-R-I F1/R1 with 319 bp, LHRH-R-I F2/R3 with 309 bp, LHRH-R-I F1'/R2' with 219 bp and LHRH-I with 230 bp. The characteristics of binding sites for LHRH on 20 samples were determined by ligand competition assays. The LHRH receptor expression was also examined in 64 BPH specimens by immunohistochemistry.

PCR products for LHRH-R-I F1/R1 were detected in 39 (71%) and for LHRH-R-I F2/R3 in 5 of 35 (14%) and for LHRH-I in 18 of 35 (51%) BPH samples. No PCR products for LHRH-R-I F1'/R2' were found. Eighteen of 20 (90%) samples showed a single class of high affinity binding sites for [D-Trp⁶]LHRH with a mean K_d of 4.04 nM and a mean B_{max} of 527.6 fmol/mg membrane protein. LHRH antagonist cetrorelix showed high affinity binding to LHRH receptors in BPH. Positive immunohistochemical reaction for LHRH receptors was present in 42 of 64 (67%) BPH specimens.

In conclusion, we detected mRNA for LHRH-R-I in human BPH specimens. Our results suggest that LHRH-R-I gene may have more than two splice variants or uncharacterised transcript forms of LHRH-R-I. Our findings support the merit of further investigation of the expression of LHRH-R-I and its transcript forms in human BPH. A high incidence of LHRH receptors in BPH supports the use of LHRH antagonists such as cetrorelix, for treatment of patients with lower urinary tract symptoms from BPH.

Key words: receptors for LHRH, transcript forms, human benign prostatic hyperplasia

Kulcsszavak: LHRH-I, LHRH receptor transzkript variánsok, benignus prosztata hiperplázia (BPH)