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JOURNAL ARTICLE

Effects of triptorelin, a gonadotropin-releasing hormone agonist, on the human prostatic cell lines PC3 and LNCaP

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Some analogues of gonadotropin-releasing hormone (GnRH) influence the in vitro proliferation of cultured human cells by complex interactions that are only partially understood. This study explored the effect of Triptorelin, a GnRH agonist, on the LNCaP and PC3 prostatic cell lines, which are, respectively, responsive and unresponsive to androgen stimulation. The toxicity and cell cycle modifications induced by the drug were investigated by FACScan analysis; the effect on cell proliferation in different culture conditions was determined by counting in a Burkler chamber; and the expression of binding sites for ¹²⁵I-Triptorelin was revealed by displacement experiments. PC3 cell growth was completely unaffected by Triptorelin. The drug caused a double stimulatory-inhibitory action on the growth of actively proliferating LNCaP cells, depending upon the dose and environment. A significant inhibitory effect on proliferation, ranging from 25% to 65% compared with controls, was observed at a high dose (10⁻⁴ M) according to the culture conditions; and a proliferative effect (42% compared with controls) was observed at a lower dose (10⁻⁷ M) only in fetal bovine serum-supplemented medium. Displacement experiments revealed the expression of moderately high affinity and low affinity binding sites in LNCaP cells (K_d = 2.6 x 10⁻⁸ and 7.7 x 10⁻⁶ M) but only low affinity binding sites in PC3 cells (K_d = 2.7 x 10⁻⁶ M), which suggests that the expression of binding sites with different affinity could be associated with a biological response to the drug. Proliferation studies in the presence of Cetrorelix, a GnRH antagonist, confirmed the different sensitivity of the 2 cell lines to GnRH analogues and showed that the proliferative effect of Triptorelin on LNCaP cells can be inhibited by the antagonist. Data confirm the cell specificity of Triptorelin's action and the peculiarity of its effects on prostatic cell proliferation in our experimental conditions.

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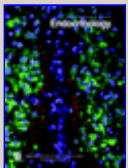
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