

The expression of androgen receptors in the epithelial cells of the rat prostate lateral lobe in experimental hyperprolactinaemia: a morphological and immunohistochemical study

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The effect of hyperprolactinaemia on the prostate has still not been fully elucidated. The aim of the study was to estimate the influence of hyperprolactinaemia on expression of the androgen receptor (AR) in rat epithelial cells of the prostate lateral lobe and on the morphology of these cells. Studies were performed on sexually mature male Wistar rats. To provoke hyperprolactinaemia rats received i.p. metoclopramid (MCP). For light and electron microscopy the lateral lobes were obtained routinely. The intensity of the immunohistochemical reaction of AR (expression of AR) in the epithelial cells of the prostate lateral lobe was assessed by optical density measurements with the help of computer image analysis. Ultrastructural observations of the epithelial cells of the lateral lobe were carried out by means of transmission and scanning electron microscopes. The results showed a more than twofold increase in prolactin (PRL) concentration in the serum, but a twofold decrease in testosterone (T). The intensity of the immunohistochemical reaction of AR in the epithelial cells of the lateral lobe in the experimental group was higher than in the control group. We noted changes in the morphology of the epithelial cells of the prostate lateral lobe in the experimental group.

key words: androgen, androgen receptor, hyperprolactinaemia, prostate, TEM, SEM

INTRODUCTION

Androgens play an important role in prostate development, growth and function. These hormones originate from two comparable sources, the testis and the adrenal precursors (DHEA and DHEA-S) [2]. Androgen receptors have been detected in epithelial and stromal cells throughout the prostatic ducts of the ventral, dorsal and lateral lobes [1]. Prolactin

(PRL) promotes the growth and function of the prostate in synergism with androgens or without androgens [4, 5]. Our goal was to estimate the effect of hyperprolactinaemia after administration of MCP on the expression of AR in epithelial cells of lateral lobe of rat prostate. We examined expression of AR in the lateral rat lobe, as this lobe is most homologous to the human [3] and the most sensitive to PRL [4].

MATERIAL AND METHODS

Studies were performed on 20 sexually mature male rats of Wistar strain. The animals were divided into 2 groups, the control and the experimental. To provoke hyperprolactinaemia the experimental group received *i.p.* metoclopramid (MCP, Polfa Starogard, Poland) in a dose of 2.2 mg/kg body mass for 14 days (time of rat seminiferous epithelium cycle). The rats of the control group were given saline. Prolactin concentration was measured in the serum using a rat prolactin enzyme immunoassay kit (ELISA, Spi-Bio, France). Testosterone concentration was measured in the serum using a radioimmunoassay kit (Farnos Diagnostika, Finland). For light and electron microscopy (TEM and SEM) the prostate lateral lobes were obtained routinely. The ultrathin sections were assessed under a JEM-1200 EX transmission electron microscope and under a JEOL JSM-6100 scanning electron microscope. For immunohistochemical detection of AR in the prostate lateral lobe Avidin-Biotin Horseradish Peroxidase Complex (ABC/HRP; Dako/AS, Denmark) was used. Tissue sections were incubated with primary antibody: the polyclonal antibody against androgen receptor (NCL-ARp, Novocastra Lab., Ltd. Newcastle, UK) and subsequently with secondary antibody, biotinylated goat anti-rabbit IgG (Vector Lab., Burlingame, CA, USA). Diaminobenzidine (DAB) was used to visualise the immunochemical reaction. The intensity of the immunohistochemical reaction was assessed by optical density measurements of its product in by means of a computer image analyser (Quantimet 600 S, Leica, UK). The optical den-

sity of the immunohistochemical reaction product was related to the density of AR.

RESULTS AND DISCUSSION

In rats of the experimental group, the mean PRL concentration was more than twice as high (28.6 ± 5.2), whereas the mean T concentration was approximately twice as low (1.35 ± 0.8), as compared to the respective control groups (13.7 ± 3.4 and 3.42 ± 1.9). The immunohistochemical study showed the presence of AR in the epithelial and stromal cells of the lateral lobe of the prostate in the experimental and control groups. The epithelial cells of the lateral lobe of rats with hyperprolactinaemia revealed a higher optical density of immunocytochemical reaction product for AR (Fig. 1B) as compared to the control rats (Fig. 1A). A significant increase in ($p < 0.001$) the mean values of the Integrated Optical Density (IOD) (626 ± 288) and the Mean Optical Density (MOD) (0.75 ± 0.11) immunohistochemical reaction product of AR was noted in the experimental animals as compared to IOD (563 ± 289) and MOD (0.67 ± 0.21) in the control rats. As compared to the control rats (Fig. 2A, 3A), transmission and scanning electron microscopes showed the following changes in rats with hyperprolactinaemia: widened cisternae of the rough endoplasmic reticulum (Fig. 2B), dictyosomes of the Golgi apparatus with widened cisternae and reductioned number of dense granules; small number of microvilli on the apical brush border small amount of secretory material at surface of the epithelial cells (Fig. 3B).

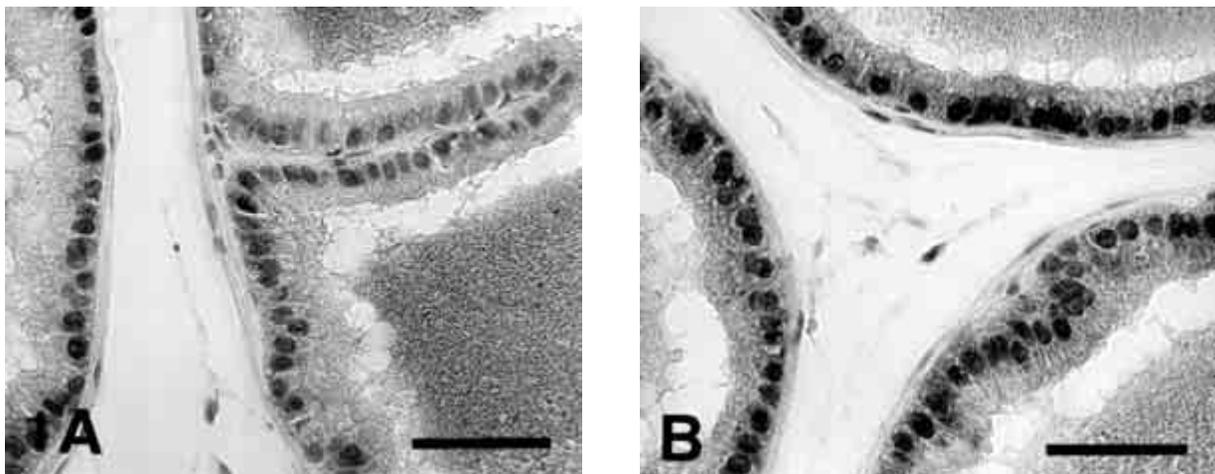


Figure 1. Immunohistochemical reaction of ARs in the epithelial cells of the lateral lobe of a control rat (A) and a MCP rat (B). Bar: 50 μ m.

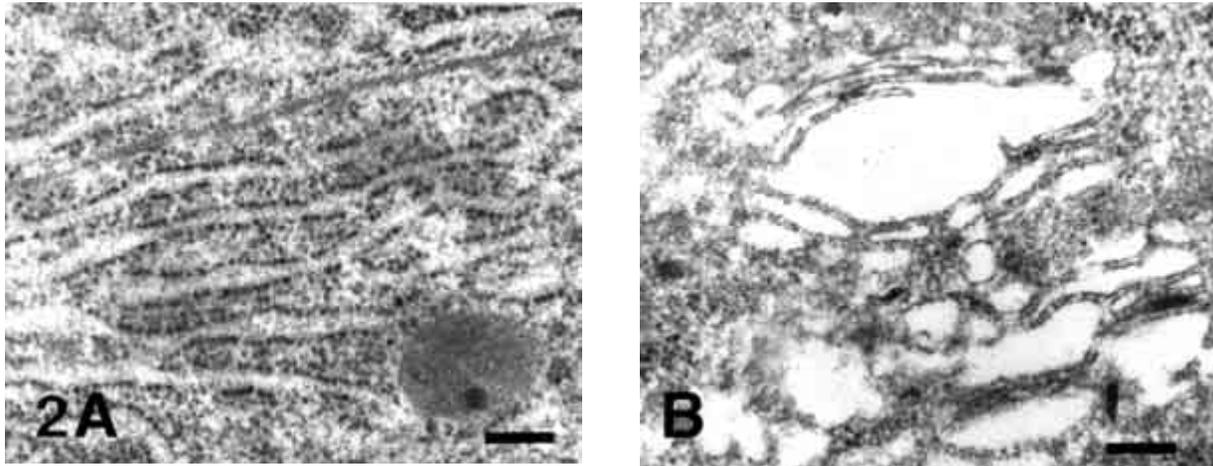


Figure 2. Cistern of rough endoplasmic reticulum in the epithelial cells of the lateral lobe of a control rat (A) and a MCP rat (B). TEM. Bar: 200 nm.

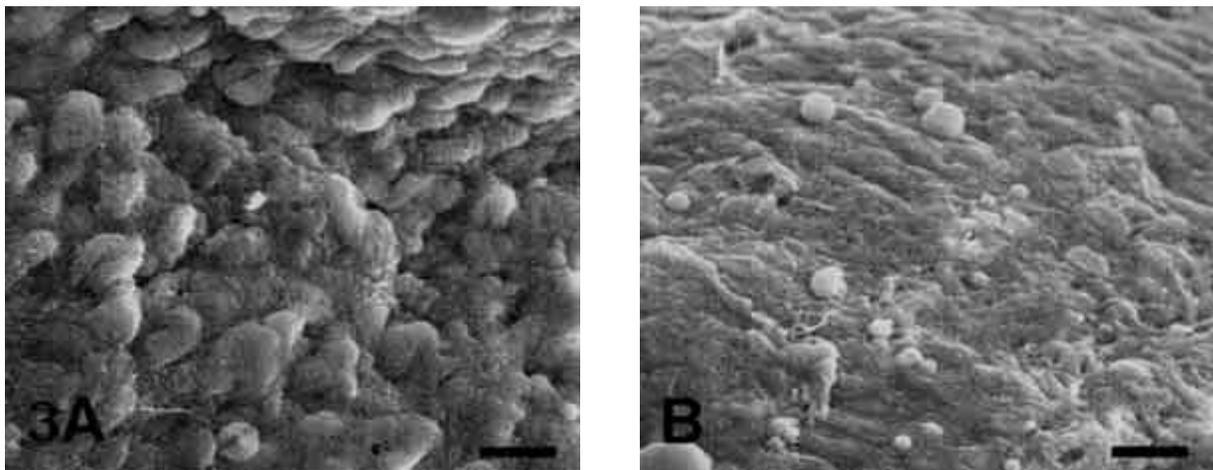


Figure 3. Surface of the epithelial cells of the lateral lobe of a control rat (A) and a MCP rat (B). SEM. Bar: 10 μ m.

Previous studies showed that chronic hyperprolactinaemia after administration of Sulpirid-induced enlargement and inflammation of the lateral lobe. The ventral and dorsal lobes were without any histological change in this case [6]. Prins [4] demonstrated that higher PRL levels in pituitary grafts increased the weight and content of protein and DNA in the lateral lobe without changes in these parameters in the ventral and dorsal lobes. Prins [4] also showed that higher PRL levels increased expression of AR exclusively in the lateral prostate. Our present study demonstrated that hyperprolactinaemia after administration of MCP in male rats significantly increased the quantity of AR in the epithelial cells of the prostate lateral lobe, in spite of a decreased T level. Ultrastructural changes in the epithelial cells of the lateral prostate in rats with hyperprolactinaemia were connected with higher levels of PRL and decreased levels of T.

REFERENCES

1. Banerjee PP, Banerjee S, Brown TR (2001) Increased androgen receptor expression correlates with development of age dependent, lobe-specific spontaneous hyperplasia of Brown Norway rat prostate. *Endocrinology*, 142: 4066–4075.
2. Labrie F (1991) Intracrinology. *Mol Cell Endocrinol*, 78: C113–C118.
3. Price D (1963) Comparative aspects of development and structure in the prostate. *Natl Cancer Inst Monogr*, 12: 1–27.
4. Prins GS (1987) Prolactin influence on cytosol and nuclear androgen receptors in the ventral, dorsal, and lateral lobes of the rat prostate. *Endocrinology*, 120: 1457–1464.
5. Reiter E, Hennuy B, Bruyninx M, Cornet A, Klug A, McNamara M, Closset J, Hennen G (1999) Effect of pituitary hormones on the prostate. *Prostate*, 38: 159–165.
6. Van Coppenolle F, Slomianny Ch, Carpentier F, Le Bourhis X, Ahidouch A, Croix D, Legrand G, Dewailly E, Fournier S, Cousse H, Authie D, Raynaud J-P, Beauvillain J-C, Dupouy J-P, Prevarskaya N (2001) Effect of hyperprolactinemia on rat prostate growth: evidence of androgen-dependence. *Am J Physiol Endocrinol Metab*, 280: E120–E129.