and actually increased about sixfold in the other (peptide 9). Thus, although the parent peptide (peptide G) was a rather selective V_2 antagonist, with a V_2/V_1 potency ratio of about 12, the 4-arginine-substituted analog (peptide 9) was much less specific, with a V_2/V_1 potency ratio of about 2.

When a 4-arginine was substituted in a potent linear V_1/V_2 antagonist (peptide H) this reduced V_2-antagonistic potency by about 3/4 while V_1-antagonistic potency remained unchanged (peptide 7). When one compares the properties of peptides 6, 7 and H (tables 1 and 2), which contain 4-glutamine, 4-arginine and 4-valine, respectively, it appears clear that the 4-valine moiety favored V_2-antagonistic potency while the 4-glutamine favored V_1-antagonistic potency. The 4-arginine analog (peptide 7) had intermediate properties, being about equally potent as a V_1 and V_2 antagonist.

These findings suggest that, from a limited number of comparisons, the substitution of 4-arginine for 4-glutamine or 4-valine in V_1 and V_1/V_2 antagonists is generally well-tolerated. Most antagonistic potencies are either preserved or somewhat decreased with no clear gains in antagonistic specificities. In general, it seems remarkable that substitution of arginine, an amino acid with a highly basic and hydrophilic side chain for amino acids with more neutral and hydrophobic side chains, glutamine or valine, has such relatively minor effects on agonistic[3,4] or antagonistic activities of these vasopressin analogs.

Since the peptides containing 4-arginine would be more highly charged than their 4-glutamine or 4-valine counterparts their distribution would be expected to be more limited by cellular membranes and the blood-brain barrier. Such highly charged peptides could be useful in those experimental circumstances in which one wishes to try to limit their distribution, to restrict their actions to the brain after intracerebral injection, for example. By exerting more localized actions they could become more incisive pharmacological tools.

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Adrenal corticosteroidogenesis after removal of ventral prostate gland

A. Chaudhuri, D. Ghosh, A. K. Chatterjee, N. M. Biswas and P. K. Ghosh*

*Department of Physiology, University Colleges of Science, 92 A.P.C. Road, Calcutta 700 009 (India), and * Department of Physiology, Southern Illinois University School of Medicine, Carbondale (Illinois 62901, USA)*
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Summary. Removal of the ventral prostate gland in adult male rats causes an increase in adrenal weight, and stimulation of adrenal Δ^5-3β-hydroxysteroid dehydrogenase activity along with elevation of serum levels of corticosterone and prolactin.
Key words. Prostatectomy; adrenal Δ^5-3β-HSD; serum corticosterone; serum prolactin.

The prostate gland, an important male accessory sex organ, is dependent upon several hormones for its physiological function of which androgens play a major role. It has been well established that the secretions of the prostate gland contribute a major constituent of seminal plasma. Little is known about the endocrine function of the prostate gland. Recently, several reports have been published regarding the existence of an adrenocorticotrophic hormone, inhibin and an insulin-like substance in the prostate gland[1-3]. However, the physiological role of these prostatic peptides in modulating endocrine functions remains unelucidated.

Adrenocortical activity is dependent mainly on circulating ACTH levels. In addition to ACTH, prolactin can stimulate adrenocortical functions[4]. Previous studies indicate that prostatectomy is associated with alteration of pituitary prolactin secretion. Unfortunately, there is an apparent paucity of information concerning the effects of removal of the prostate gland on adrenocortical functions. This is important for the evaluation of the side effects following prostatectomy, often used in the treatment of benign prostatic hypertrophy. The present experiments have been undertaken to demonstrate the activity of adrenal Δ^5-3β-hydroxysteroid dehydrogenase (Δ^5-3β-HSD) and serum levels of corticosterone and prolactin following the removal of the ventral prostate gland.

Materials and methods

For the present investigation, 40 adult male albino rats of the Wistar strain were used. They were kept in animal houses with controlled temperatures ranging from 26 °C to 30 °C and exposed to 12 h illumination daily. Standard laboratory food and water were provided ad libitum. The animals were divided into 2 groups. In each group, 10 animals were prostatectomized and the remaining 10 animals were sham-operated. The first group of prostatectomized animals along with the sham-operated control animals were killed on the 15th day while the other group along with sham-operated control rats were sacrificed on the 22nd day. The experiment was so adjusted that all the animals were killed on the same day. Blood was obtained from all animals by decapitation and serum was collected by centrifugation. The adrenal glands were dissected out and weighed. For assay of adrenal Δ^5-3β-HSD activity, the adrenal gland was immersed into ice-cold homogenizing medium consisting of equal parts of 0.9 % sodium chloride and 0.1 M sodium phosphate buffer, pH 7.4, to give a tissue concentration of 5 mg/ml. The enzyme was assayed by spectrophotometric measurement of the production of Δ^4-androstenedione from dehydroepiandrosterone[5]. Serum level of corticosterone was measured by spectrofluorometry[6,7]. The fluorescence was measured in a spectrofluorometer at 462 nm (excitation) and 518 nm (emission) by setting the instrumental sensitivity to an arbitrary point at 80 with high standard (0.8 µg of corticosterone per 0.5 ml of distilled water). Serum level of prolactin was measured by radioimmunoassay using kit supplied by the NIADDK Rat Pituitary Distribution Program[8]. The intra-assay coefficient of variation was 6.8 %. All serum samples were assayed in duplicate at two levels in order to eliminate interassay variation.

Results and discussion

Removal of the ventral prostate gland caused a significant increase in adrenal weight and Δ^5-3β-HSD activity following 14 days and 21 days of surgery (figs 1 and 2). Serum levels of corticosterone and prolactin appeared to increase significantly following 14 days and 21 days of prostatectomy (figs 3 and 4).

The results of these experiments on the effects of prostatectomy on adrenal corticosteroidogenesis provide a number of new conclusions. The study reported here demonstrates that removal of the ventral prostate gland

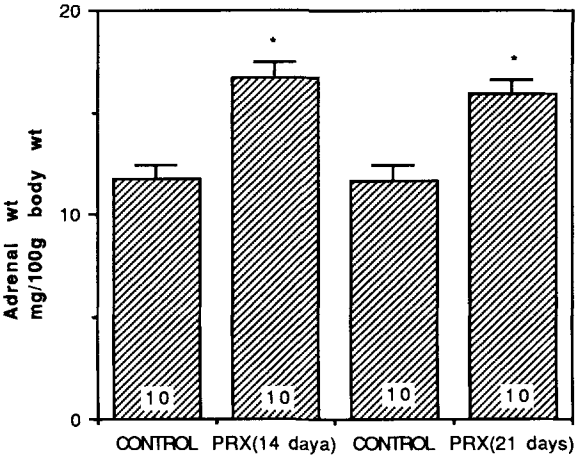

Figure 1. Adrenal weight in sham-operated and prostatectomized rats. Values represent the mean ± SEM of 10 rats per group. Values marked with an asterisk are significantly different from the corresponding control values ($p < 0.05$).

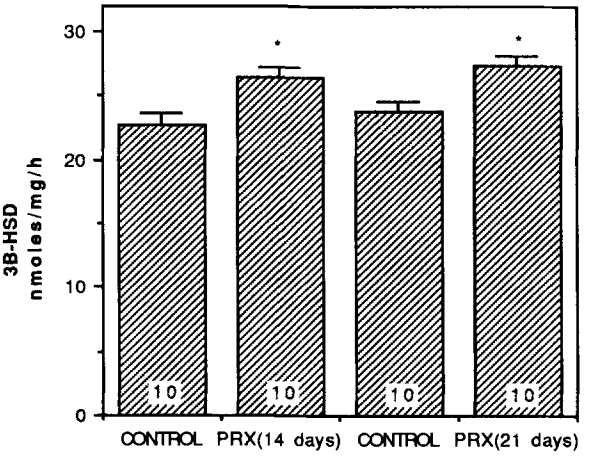

Figure 2. Adrenal Δ^5-3β-HSD activity in prostatectomized and sham-operated rats. Values represent mean ± SEM of 10 rats per group. Values marked with an asterisk are significantly different from the corresponding control values ($p < 0.05$).

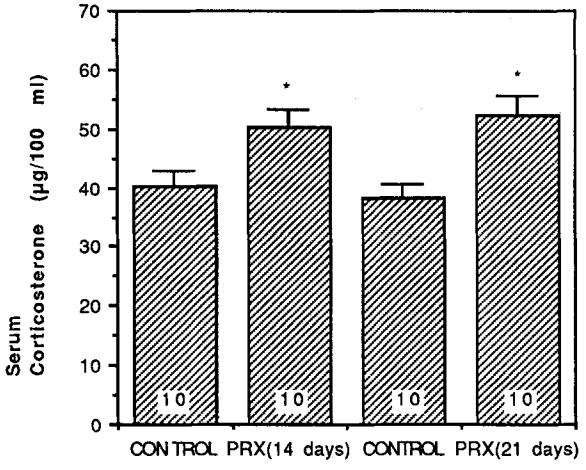

Figure 3. Serum levels of corticosterone after removal of the ventral prostate gland. Values represent the mean ± SEM of 10 rats per group. Values marked with an asterisk are significantly different from the corresponding control values ($p < 0.05$).

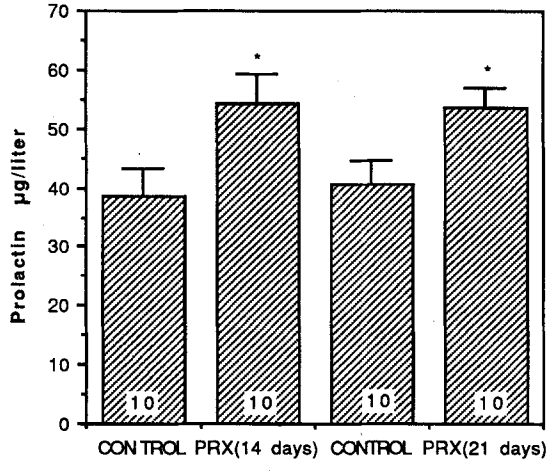

Figure 4. Serum levels of prolactin in sham-operated and prostatectomized rats. Values represent mean ± SEM of 10 rats per group. Values marked with an asterisk are significantly different from the corresponding control values ($p < 0.05$).

increases adrenal weight and stimulates Δ^5-3β-HSD activity in the adrenal gland after 14 and 21 days. Serum levels of corticosterone and prolactin are also increased following removal of the prostate gland.

Since the enzyme Δ^5-3β-HSD plays an important role in corticosteroid synthesis, the present observations indicate that adrenal corticosteroidogenesis is stimulated after 14 days of removal of the ventral prostate gland. The elevation of serum level of corticosterone is the effect of increased adrenal corticosteroidogenesis following prostatectomy. The elevation of the serum level of prolactin in our present experiments subsequent to 14 and 21 days of prostatectomy may be due to the absence of a prolactin-regulating factor secreted by the prostate gland[9]. Moreover, the increase in serum prolactin level in prostatectomized rats is in agreement with our previous findings where we showed that prostatectomy in rats resulted in the stimulation of testicular androgenesis in association with elevation of prolactin level in the serum[10].

Prolactin is known to be involved in stimulating the adrenocortical functions[4]. The adrenal hypertrophy and stimulation of Δ^5-3β-HSD activity following 14 and 21 days of prostatectomy are possibly due to the hypersecretion of prolactin. The mechanism of hypersecretion of prolactin following prostatectomy is not clear from these experiments. Our recent observations indicate that prostatectomy is associated with the inhibition of dopamine turnover in median eminence and medial basal hypothalamus (unpubl. obser.). So the stimulation of prolactin secretion in our experiment may be due to the inhibition of the hypothalamic dopaminergic system as dopamine is known to inhibit prolactin secretion[11]. In 1972, Witorsch and Kitay[12] observed that there is a definite increase in corticosterone secretion after prolactin treatment in rats, which partly supports the consequences of the elevation of serum corticosterone following prostatectomy.

The possibility remains, therefore, that prostatectomy stimulates adrenal corticosteroidogenesis in rats indirectly by increasing the serum prolactin level.

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