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Effect of Cyproterone/Acetate (SH-714) on Plasma Prolactin in Patients with Prostatic Cancer

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Summary. Plasma prolactin was measured in 10 patients with prostatic cancer during treatment with cyproterone acetate (300 mg/week i. m.) Prolactin was assayed during a six month period at weekly intervals during the first 4 weeks and then at monthly intervals. Orchiectomy was not carried out. After 6 months prolactin levels were elevated compared with pre-treatment levels. It is concluded from this study that cyproterone acetate interferes with prolactin secretion by the pituitary gland.

Key words: Prostatic cancer, Cyproterone acetate treatment, Prolactin levels.

INTRODUCTION

Animal experiments and clinical observations have shown that prolactin interferes with the biological activity of the normal and the neoplastic prostatic cell (11, 1, 5, 7). The mode of action is thought to involve stimulation of the uptake and metabolism of testosterone (5). Thus, the role of pituitary prolactin is of interest in patients with cancer of the prostate. The interactions of exogenous oestrogens and antiandrogens with plasma prolactin have been the subject of recent investigations, since stimulation of prolactin secretion by endocrine treatment might result in activation of cancer proliferation.

While the influence of oestrogens on pituitary prolactin release has been widely and intensively studied, little information exists about the effect of cyproternone acetate (SH-714) on prolactin levels. This study was designed to monitor prolactin levels in patients with prostatic cancer receiving cyproterone acetate, in order to clarify the effect of therapeutic concentrations on prolactin release.

MATERIALS AND METHODS

Ten patients, whose ages ranged from 50 to 78 years, with carcinoma of the prostate were studied. They were treated primarily with cyproterone acetate in a dose of 300 mg/week. Orchiectomy was not performed.

Before treatment was begun basal levels of plasma prolactin were determined on 3 consecutive days. During treatment plasma prolactin levels were monitored at weekly intervals up to 4 weeks and at monthly intervals up to 6 months after institution of treatment. Blood samples were taken between 1500 h and 1700 h. The patients did not receive any additional medication which is known to interfere with plasma prolactin levels (2).

The plasma levels of prolactin were determined by radioimmunoassay utilising a double antibody method (17). 125-labelled prolactin was used as tracer. The radioactivity was measured in an automatic Gamma Counter (PACKARD 5219). The endocrinological data were evaluated by means of a computer programme (17).

RESULTS

The result of this investigation are given in Table 1:

1. Pre-treatment levels of prolactin ranged from 2, 67 to 18, 84 ng/ml. There was no significant difference in the pre-treatment samples between the 1st, 2nd and 3rd day.
2. Plasma prolactin did not rise significantly during the first 5 months of treatment.
3. By the 6th month of treatment the elevation of prolactin was significant ($p < 0.05$).

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Table 1. Plasma concentrations of prolactin (ng/ml) in 10 patients with cancer of the prostate under cyproterone acetate (300 mg/week)

Time of investigation	Prolactin (ng/ml $\bar{X}$	s
Pre-treatment		
Day		
1	7.66	5.84
2	7.01	1.78
3	9.50	4.45
During treatment		
Week		
1	8.90	7.34
2	9.52	4.63
3	7.55	4.33
4	9.36	5.30
Month		
2	13.84	3.75
3	13.65	2.98
4	14.97	3.89
5	14.92	4.58
6	15.93	3.28

DISCUSSION

The physiological interaction of prolactin with the male reproductive system has been widely investigated. It is assumed from several experiments that prolactin interferes with Leydig cell function by synergistic action with LH (2). The role of prolactin in prostatic function has been investigated in several animal experiments which showed a stimulation of growth of prostatic epithelium. Prolactin is thought to induce uptake and metabolism of androgens (6).

Prolactin levels in healthy men show a wide intra- and inter-individual variation (14) probably due to stress factors at the time of investigation. There is also a diurnal variation of plasma prolactin levels (13, 15) which necessitates determination of prolactin at the same time of day. By comparison with the prolactin levels of healthy young men between age 20 and 40 years as determined in a previous study (14) there seemed to be no difference in the prolactin levels in men with prostatic cancer as demonstrated in this investigation.

It has been shown that oestrogen causes a highly significant increase in prolactin levels in men. However, very little is known of the effect of cyproterone acetate on pituitary prolactin secretion. While Fonzo et al. (8), Bartsch et al. (3) and Gräf et al. (9) found an elevation of Prolactin with cyproterone acetate, Giusti et al. (10) did not observe any alteration of prolactin. Cyproterone acetate is an antiandrogen which blocks the effect of androgens at the receptor level (18, 4). Besides this action it has a gestagenic action resulting in a suppression of LH and testosterone concentrations (16). Because of the high cardiovascular risks with oestrogens, cyproterone acetate is used as an alternative to oestrogens in endocrine treatment of prostatic cancer. This study showed that prolactin levels are altered to some extent by cyproterone acetate but, compared to the effect of oestrogen treatment on prolactin levels in patients with prostatic cancer (12), the effect of cyproterone acetate seems to be less pronounced. The mean plasma levels of prolactin rise only two-fold on the average while under ethynyl oestradiol and stilboestrol in therapeutic dosages up to a ten-fold increase of prolactin can be observed.

As a result of this study it can be concluded that cyproterone acetate seems to interfere with pituitary prolactin release in the treatment of prostatic cancer. However, the degree of elevation of plasma prolactin levels is far less pronounced than under oestrogens.

REFERENCES

1. Asano, M.: Basic experimental studies of the pituitary prolactin-prostate interrelationships. Journal of Urology 93, 87 (1965)
2. Bartke, A.: Pituitary testis relationship: Role of prolactin in the regulation of testicular function. Sperm Action, Progress in Reproductive Biology 1, 136 (1977)
3. Bartsch, W., Horst, H.J., Becker, H., Nehse G.: Sex hormone binding globulin binding capacity, testosterone, 5-alpha-dihydrotestosterone, oestradiol and prolactin in plasma of patients with prostatic carcinoma under various types of hormonal treatment. Acta endocrinologica 85, 630 (1977)
4. Fang, S., Liao, S.: Antagonistic action of anti-androgens on the formation of a specific dihydrotestosterone receptor protein complex in rat ventral prostate. Molecular Pharmacology 5, 428 (1969)
5. Farnsworth, W.E.: Prolactin and androgen mobilisation. In: Normal and abnormal growths of the prostate. Goland, M. (ed.), p. 502. Springfield: Charles C. Thomas 1975
6. Farnsworth, W.E.: Role of lactogen in prostatic physiology. Urological Research 3, 129 (1975)
7. Farnsworth, W.E., Gonder M.J.: Prolactin and prostatic cancer. Urology 1, 10, 33 (1977)

8. Fonzo, D., Angeli A., Sivieri, R., Andriolo S., Frajria R., Ceresa F.: Hyperprolactinemia in girls with idiopathic precocious puberty under prolonged treatment with cyproterone acetate. Journal of Clinical Endocrinology and Metabolism 45, 164 (1977)
9. Gräf, K.J., Schmidt-Gollwitzer M., Koch U.J., Lorenz F., Hammerstein J.: Hyperprolactinemia induced by cyproterone acetate in human subjects. Acta Endocrinologica (Kobenhavn) Supplement 215, 87, 96 (1978)
10. Giusti M., Parazzi F., Reitano A., Bolognesi, F., Giordano G.: Longitudinal study of the behaviour of certain hormonal parameters in women undergoing treatment with cyproterone acetate. Acta Europaea Fertilitatis 8, 3, 211 (1977)
11. Grayhack, B.T.: Pituitary factors influencing growths of the prostate. National Cancer Institute Monographs 12, 189 (1963)
12. Harper, M.E.: Plasma steroid and proteine hormone concentrations in patients with prostatic cancer before and during oestrogen therapy. Acta Endocrinologica 81, 409 (1976)
13. Kapen, S., Weithmann, E.D.: The nocturnal rise of human prolactin independent on sleep. Journal of Clinical Endocrinology and Metabolism 37, 436 (1973)
14. Lunglmayr, G., Stackl W., Spona J.: Bedeutung des Prolaktins in Fällen von männlicher Subfertilität und Infertilität. Internationales Symposium über Parlodel, Vienna 1978
15. Nokin, L., Vekemans, M., Hermite M., Robyn, C.: Circadian periodicity of serum prolactin concentrations in man. British Medical Journal 561 (1972)
16. Schoones, R., Schalach, D.S., Murphy, G. P.: The hormonal effects of antiandrogen (SH-714) treatment in man. Investigative Urology 4, 635 (1971)
17. Spona, J.: Bestimmung und Bewertung der Prolactinspiegel und des Wachstumshormones. Internationales Symposium über Parlodel, Vienna, April 1978
18. Walsh, P.C., Korenman, S.G.: Mechanism of androgenic action: Effect of specific intracellular inhibitors. Journal of Urology 105, 850 (1971)

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