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Control of Hormonal Treatment of Carcinoma of the Prostate

J. Frick

Department of Urology, University Medical School, Innsbruck, Austria

Summary. Hormone therapy still has a central role in the treatment of carcinoma of the prostate. The present study is concerned with the possibility of controlling the administration of hormones by estimation of plasma testosterone and LH levels. Plasma testosterone levels were determined by a new modification of competitive protein binding method, and LH by a conventional radioimmunoassay.

Key words. Carcinoma of prostate, plasma testosterone levels, plasma LH levels, Silastic implants of ethinyl estradiol.

Introduction

With certain restrictions hormonal therapy is still the basis of the treatment of carcinoma of the prostate. The administration of estrogens and progestogens produces a favourable alteration in the hormonal milieu and these compounds may also have direct effect on the neoplasm itself. About 80% of cases of carcinoma of the prostate are hormone sensitive.

In the healthy male about 85% of all the biologically active testosterone circulating in peripheral plasma is produced by Leydig cells in the testis; the second most important site of its production is the adrenal cortex. There is evidence, too, that the cells of the prostate can produce testosterone from nonandrogenic precursors. Together the adrenal cortex and the so-called peripheral testosterone synthesis account for the 15% of plasma testosterone not produced by Leydig cells.

The response of prostatic carcinoma to hormonal treatment is unpredictable sometimes and there may be severe side effects, including gynaecomastia, loss of hair and psychiatric disturbances. Accordingly, an attempt has been made to find parameters of the effects of administered steroids that could easily be measured and so could be used to control the doses given. Serum acid phosphatase activity has not proved to be as reliable a criterion as was hoped.

Circulating plasma levels of testosterone, 17 ß-estradiol and such pituitary hormones as the gonadotrophins are a good guide to the moment hormonal situation. As it is now possible to measure these hormones by methods sufficiently simple and reliable to permit their use in routine clinical practice, it seemed probable that they would afford a suitable means of evaluating the efficacy of hormonal therapy. The present study is a preliminary account of the plasma levels of testosterone and LH in patients with carcinoma of the prostate receiving various hormone treatments.

Material and Methods

1. In 8 men more than 60 years of age an attempt was made to find the lowest dose of estrogen required to produce marked suppression of Leydig cell function.
2. In 34 patients with cancer of the prostate plasma testosterone levels were measured during treatment.
3. LH (luteinizing hormone) determinations were done in 11 men who had cancer of the prostate; 10 had been orchiectomized for more than 1 year and were receiving regular doses of estrogen, and one man had had no treatment at all.

Plasma testosterone levels were assayed by the author's own method which was based on competitive protein binding, (5). By modifying the original technique it was possible to measure very low plasma testosterone concentrations in children, women, or men after orchiectomy and long-term estrogen therapy.

LH estimations were done by the radioimmunoassay of Crosignani et al. (3).

Results

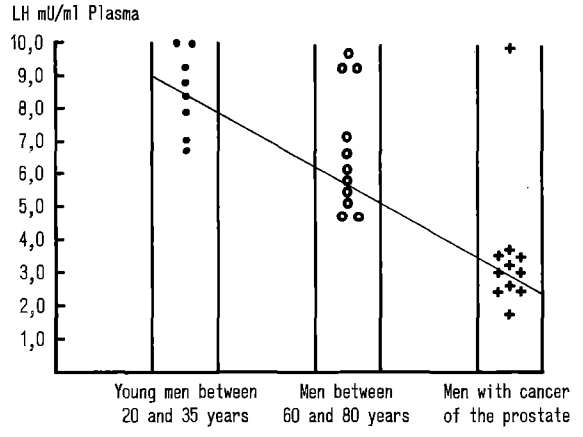
The mean plasma testosterone level in 58 healthy young male volunteers 20 to 38 years of age, was 0.52 ± 0.11 (S. D.) ug/100 ml plasma.

50 mg ethinylestradiol/per patient given as 2 silastic capsules implanted subcutaneously released about 45 ug of hormone/capsule/24 h. This produced distinct suppression of Leydig cell function within 6 months.

Of the patients who had been orchiectomized more than one year previously, 80% received Retalon 100 mg every 3 months, and 20% had two implanted silastic capsules containing ethinylestradiol. The mean plasma testosterone level in this group was 0.089 ± 0.052 (S. D.) ug/100 ml plasma; with a range of 0.014-0.145 ug/100 ml plasma.

The LH levels of 11 patients with prostatic carcinoma are shown in Table 1, column III. The plasma LH levels of young men are listed separately in column I, and of men over 60 years in column II.

Table 1



Discussion

Administration of a very potent estrogen, such as ethinyl-estradiol, in a form that permits constant absorption should mean that only a very low dose would be required to produce marked supression of Leydig cell activity.

In the second group of patients a mean plasma testosterone level of 0.089 ± 0.052 (S. D.) ug/100 ml plasma was found, a result that clearly demonstrates incomplete suppression of androgen production. The small amount of testosterone in these subjects must have been produced by the adrenal cortex and other peripheral mechanisms.

In some cases the plasma testosterone level remained high despite orchiectomy and long-term estrogen therapy. These patients had almost always shown exacerbation of the disease at about the same time as the appearance of metastases. Apparently the adrenal cortex and peripheral routes of testosterone synthesis in these cases were stimulated to produce excessive amounts of androgens and estrogens lost their inhibitory effect becoming therapeutically valueless. Suppression of the adrenal cortex by the administration of corticosteroids should be attempted under these circumstances.

Measurement of plasma LH levels is another possible means of determining the effect of hormonal therapy. As the method has been in use for only a few months, the number of cases investigated is still small. However, of the 11 patients studied, 10 had low plasma LH-levels (1 - 3.5 mU/ml plasma); in all of them orchiectomy had been performed more than 6 months previously and they were receiving regular hormone therapy, as noted above. The one case of prostatic carcinoma who had a plasma LH level comparable to that of healthy young men had refused both orchiectomy and hormone treatment. This technique appears very promising because an experienced technician should be able to perform 180 - 200 plasma LH assays a week.

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References

1. Alder, A., Burger, H., Davis, J., Dulmanis, A., Hudson, B., Sarfaty, G., Straffon, W.: Carcinoma of the prostate: response of plasma luteinizing hormone and testosterone to oestrogen therapy. Brit. med. J. 1, 28-30 (1968).
2. Baulieu, E. E., Lasnitzki, L., Robel, P.: Testosterone metabolism in rat prostate grown in organ culture and hormone action. Advances in the Biosciences 3, Oxford, Braunschweig: Pergamon Press - Vieweg, 1968.
3. Crosignani, P. G., Nakamura, R. M., Hovland, D. N., Mishell, D. J., Jr.: A method of solid phase radioimmunoassay utilizing polyprophylene discs. J. clin. Endocr. 30, 153 (1970).
4. Frick, J., Kincl, F. A.: The measurement of plasma testosterone by competitive protein binding assay. Steroids 13, 495 (1969).
5. Frick, J.: Improved plasma testosterone assay by competitive protein binding. (in press).
6. Hotchkiss, J., Atkinson, L. E., Knobil, E.: Time course of serum estrogen and Luteinizing hormone concentrations during the Menstrual cycle of the Rhesus monkey. Endocrinology 89, 177 (1971).
7. Kullander, S.: On the adrenocortical production of sex hormones in gonadectomized rats. Acta med. scand. Suppl. 445, 389 (1966).

Dr. J. Frick
Department of Urology
University Medical School
Anichstraße 35
A-6020 Innsbruck
Austria