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Cyproterone-acetate in the treatment of breast cancer - clinical and experimental results

The anti-androgen cyproterone-acetate (CPA) was used in the palliative treatment of breast cancer. 41 patients with progressive disease received 200 mg CPA orally per day. This treatment was able to induce remission or a status of no change in 34 % of these patients, who were all pretreated with different endocrine and/or chemotherapeutic regimen.
To evaluate the way of action of CPA in breast cancer, we studied on one hand the serum levels of different hormones representing the function of the adrenals, pituitary and the gonades. The androgens dehydroepiandrosterone, androstendione, dihydrotestosterone and testosterone decreased by 30 - 50 %. FSH and LH showed a marked decrease from their high postmenopausal levels. Cortisole, estrone, estradiol and prolactin were not altered significantly.
On the other hand the direct influence of CPA on human breast cancer cells was investigated in vitro. Permanent cell lines, recently established in our own laboratory, and MCF-7 cells were incubated with CPA in a dose range of 1 - 1000 ng/ml. An inhibition of proliferation was observed at doses higher than 100 ng/ml. This value is in the range of serum peak levels (100-1000 ng/ml) after oral administration of 100 mg CPA orally. Therefore we suppose that the benefit of CPA may result from both indirect and direct effects.

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Effect of Cyproterone Acetate (CPA) on Testosterone Concentration in the Initial Phase of Administration of an LH-RH-Agonist (LH-RH-A)

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After LH-RH-A treatment had been introduced as a new approach to advanced prostatic cancer it became evident that the initial rise of serum testosterone which occurs as a rule might be disadvantageous. Therefore the idea of simultaneously administering antiandrogens is widely discussed. Particularly those with antigonadotropic activity may be favourable. Our study was performed to verify the beneficial role CPA, an antiandrogen with antigonadotropic properties, could play as a supplement of LH-RH-A treatment. For this purpose an LH-RH-A alone and in combination with CPA was administered each regimen for seven days to male volunteers (n = 9) for intraindividual comparison. Testosterone serum levels were determined by RIA daily during the trial. The rise of testosterone induced by the LH-RH-A was blunted when the agonist was given in combination with CPA. The area under the concentration-time curve during combination was significantly reduced when compared to the corresponding area during agonist administration alone ($p < 0.05$). We conclude from the results of this study that CPA exhibits apart from its antiandrogenic action at the target organ level an additional favourable effect due to its antigonadotropic potency when administered in the initial phase of LH-RH-A treatment. CPA therefore appears to be a reasonable supplementation of medical castration with LH-RH-A in prostatic cancer patients.