

## THE EFFECTS OF TAMOXIFEN ON THE NUMBER OF OVARIAN FOLLICLES IN TUMOR-BEARING RATS TREATED WITH CYCLOPHOSPHAMIDE

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### Abstract Body

Breast cancer therapy includes cyclophosphamide (CPA), a treatment that can decrease the number of ovarian follicles and reduce ovarian steroidogenesis. Tamoxifen (TAM) was recently suggested to prevent follicle loss in cancer-free rats exposed to ovotoxic cancer drugs. The aim of the present study was to determine the effects of TAM on the follicle number and serum steroid hormone levels in tumor-bearing rats treated with CPA. Female Wistar rats were treated with a single dose of N-methyl-N-nitrosourea (50 mg/kg b.w.) to induce mammary tumors. Then, the tumor-bearing rats were randomly assigned to four groups (n=25 per group): 1/ control untreated, 2/ TAM-treated, 3/ CPA-treated and 4/ CPA+TAM-treated group. On day 1, the TAM-treated group received implants gradually releasing TAM (1 mg/kg b.w./d). On day 3, the CPA-treated group received 50 mg/kg b.w. CPA and weekly thereafter 10 mg/kg b.w. CPA for four weeks. The fourth group received both TAM and CPA as described above. At the end of the experiment, the ovaries and serum were collected (n=4-5). The ovaries were fixed, sectioned and stained with H&E. The follicles at each developmental stage were counted (8-10 sections per ovary). Progesterone (P4) and estradiol (E2) serum levels were analyzed by radioimmunoassay. One-way ANOVA was used to determine significant differences in the follicle number and steroid hormone level between the groups (p<0.05). We found that CPA decreased the number of primordial as well as primordial plus primary follicles and that TAM abolished this effect. The concentration of P4 was significantly higher in CPA-treated rats than in CPA+TAM-treated rats. E2 was not affected by CPA and CPA+TAM, but it was decreased by TAM alone. Our results indicate that TAM abrogated the adverse effects of CPA on the ovarian follicle reserve.

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