

INFLUENCE OF UKRAIN ON PATIENTS WITH SURGICALLY TREATED BREAST CANCER. PART II. HORMONAL PROFILE

UGLYANICA K.N.¹, FOMIN K.A.¹, NEFYODOV L.I.², VILKIEWICH T.W.³, NOWICKY J.W.⁴, BRZOSKO W.J.⁵, JANKOWSKI A.⁶

1) Medical Institute, Grodno, Belarus.

2) Institute of Biochemistry, Belarussian Academy of Sciences, Grodno, Belarus.

3) District Hospital, Grodno, Belarus.

4) Ukrainian Anti-Cancer Institute, Vienna, Austria.

5) Roch Brzosko Memorial Centre for Natural Medicine, Willowa 8/10, 00-790 Warsaw, Poland.

6) Clinic of Developmental Age Immunology, Medical Academy, Wroclaw, Poland.

Summary: *The present study was undertaken to evaluate the influence of Ukrain on the hormonal status of ten patients with breast cancer, treated in the preoperative phase by Ukrain. A control group consisted of eight patients of similar age and advancement of the disease, who did not receive the drug before mastectomy. The data were compared to those obtained in ten healthy women of similar age. The results indicate that Ukrain only slightly influences the hormonal dynamics and its destructive mode of action on neoplastic tissue does not significantly affect hormonal activities.*

Introduction

At least 15 hormones contribute to the development and functioning of the normal breast as well as of breast cancer cells. The most prominent role in influencing the tumour and its cells is played by prolactin, oestrogens, progesterone, androgens, glyccorticoids and medullary hormones of adrenal glands-(1-6). Specialized literature has devoted much space to these problems, particularly in relation to patients with breast cancer. The aim of the present study was to follow the influence of Ukrain, a new anticancer drug of plant origin, on

the profile of hormonal behaviour in breast cancer patients (7, 8).

Patients and methods

The investigations concerned 18 patients with breast cancer of stages T1-3NO-2MO. The age of the patients varied between 38 and 65 years.

Ten patients in the preoperative phase received treatment with Ukrain. The drug was administered intravenously in a dose of 5 mg every second day for 20 days. Each patient received a total of 50 mg. Seven or ten days after the end of this treatment the patients were subjected to a radical operation by the method of Patey or Halsted.

* Author to whom correspondence should be addressed.

The control group consisted of eight patients of similar age and advancement of the disease who did not receive Ukrain.

Hormone determinations were compared to those obtained in ten healthy women of ages similar to the patients. The hormone level was determined by the radioimmunological method with the use of sets and standards purchased at the Institute of Biochemistry of the Belarussian Academy of Sciences. Concentrations of cortisol, progesterone, oestradiol, prolactin, T_3 and T_4 were determined in blood serum taken before Ukrain treatment and after surgical intervention when the patients left the hospital. Determinations in the control group were made similarly.

Results were subjected to statistical analysis according to the computer programme prepared for biomedical studies.

Table I The level of T_3 (nmol/l) in blood serum in patients with breast cancer

Groups of patients	Samples taken at entry to hospital	Samples taken after treatment with Ukrain	Samples taken before discharge from hospital
Control	116 ± 9	116 ± 9	101 ± 7
Ukrain	131 ± 15	120 ± 9	103 ± 10

(The level of T_3 in healthy subjects: 105 ± 10, n = 10).

Table II The level of T_4 (nmol/l) in blood serum in patients with breast cancer

Groups of patients	Samples taken at entry to hospital	Samples taken after treatment with Ukrain	Samples taken before discharge from hospital
Control	1.6 ± 0.1	1.6 ± 0.1 ¹	1.4 ± 0.2 ¹
Ukrain	1.5 ± 0.1	1.5 ± 0.1 ¹	1.4 ± 0.1 ¹

(The level of T_4 in healthy subjects: 1.7 ± 0.1, n = 10).

$P < 0.05$ statistically significant to healthy subjects.

Results and discussion

In the initial examination no major differences were observed between the cancer patients and healthy women (Tables I-VI). There was only a slight

Table III The level of cortisol (nmol/l) in blood serum in patients with breast cancer

Groups of patients	Samples taken at entry to hospital	Samples taken after treatment with Ukrain	Samples taken before discharge from hospital
Control	610 ± 81	610 ± 81	681 ± 85
Ukrain	525 ± 87	615 ± 56	529 ± 47

(The level of cortisol in healthy subjects: 490 ± 53, n = 10).

Table IV The level of progesterone (nmol/l) in blood serum of patients with breast cancer

Groups of patients	Samples taken at entry to hospital	Samples taken after treatment with Ukrain	Samples taken before discharge from hospital
Control	1.5 ± 0.4	1.5 ± 0.4	2.9 ± 1.9
Ukrain	1.1 ± 0.6	0.9 ± 0.1	0.6 ± 0.1 ^{1,3}

(The level of progesterone in healthy subjects: 6.8 ± 3.8, n = 10).

$P < 0.05$ ¹ statistically significant to healthy subjects

³ statistically significant to patients after surgery

Table V The level of oestradiol (nmol/l) in blood serum of patients with breast cancer

Groups of patients	Samples taken at entry to hospital	Samples taken after treatment with Ukrain	Samples taken before discharge from hospital
Control	0.4 ± 0.1	0.4 ± 0.1	0.3 ± 0.1
Ukrain	0.2 ± 0.04	0.3 ± 0.03	0.2 ± 0.05

(The level of oestradiol in healthy subjects: 0.4 ± 0.1, n = 10).

Table VI The level of prolactin (nmol/l) in blood serum in patients with breast cancer

Groups of patients	Samples taken at entry to hospital	Samples taken after treatment with Ukrain	Samples taken before discharge from hospital
Control	263 ± 73	263 ± 73	716 ± 182 ³
Ukrain	264 ± 104	211 ± 65	751 ± 212 ¹

(The level of prolactin in healthy subjects: 105 ± 10, n = 10).

$P < 0.05$: ¹ statistically significant to healthy subjects

³ statistically significant to patients after surgery

depression of progesterone concentration in the cancer patients, and a slight rise in the cortisol level. The same observation has been reported

ted by other authors. This phenomenon seems understandable in view of the stress which may be evoked in patients by the consciousness of neoplastic disease.

As regards oestrogens and prolactin in breast cancer patients, some authors reported a rise (1, 9) and others a normal level (10-12). According to Hertz (11), the rise in serum oestradiol concentration in cancerous patients is of no pathogenetic significance.

As shown in Tables I-VI, Ukrain in a dose of 50 mg did not distinctively affect the level of the analysed hormones as compared to the control group. The absence of other reports in the literature does not allow comparison of our observations. One study relative to this problem (13) was performed in rats. Ukrain given for three months in a dose of 28 mg/kg body weight daily produced a significant rise of the prolactin level. Of course this result cannot be transferred to humans, particularly when doses of Ukrain applied to our patients were much lower and the period of medication shorter.

Hormonal analysis seven to ten days after radical mastectomy demonstrated the following parameters. Concentrations of T_3 and T_4 , cortisol and oestradiol in the control group of patients did not differ from those found preoperatively, whereas progesterone and prolactin concentrations were significantly increased. The considerable rise in prolactin occurring 10-14 days after surgical intervention in patients not treated with Ukrain has been described by other authors (14). It could only be explained by the complex mechanisms of neurohormonal regulation intervening under the influence of stress and operative trauma, reflected in prolactin synthesis. As shown in Tables I-VI, Ukrain did not affect the T_3 , cortisol and oestradiol levels. A slight depression of T_4 level and progesterone was observed, with prolactin concentration distinctly increased.

Comparison of the results before operation with those at the time of discharge from hospital indicates that the application of Ukrain and the operation did not influence T_3 , T_4 and oestradiol concentrations. The cortisol level showed a tendency to decrease, whereas the progesterone level fell

markedly and the prolactin concentration rose (Tables I-VI).

The present observations indicate a slight influence of Ukrain on the hormone dynamics, noticeable as a depression of the cortisol and progesterone levels in blood serum. The small effect of Ukrain noted after its application to cancerous patients does not allow the assumption that hormones play a significant role in the action of the drug.

References

- (1) Tepperman J., Tepperman H.M. "Metabolic and endocrine physiology". Year Book Publications, Chicago, London, 1985, p. 653.
- (2) Hedley A. et al. *Breast cancer in thyroid disease: fact or fallacy?* Lancet, I, 131-133, 1981.
- (3) Harris A. et al. *Sex hormone binding globulin levels and prognosis in early breast cancer.* Lancet, I, 279-280, 1981.
- (4) Bulbrook K. et al. *Plasma prolactin levels and age in female population: relation to breast cancer.* Int. J. Cancer, 28, 43-45, 1981.
- (5) Shin R. "Hormones and breast cancer". Cold Spring Harbor, New York, 1981, pp. 185-196.
- (6) Kung W., Ross W., Eppenberger U. *Growth stimulation of human breast cancer MCF-t cells by dibutyl cyclic AMP.* Cell. Biol. Int. Rep., 7, 345-351, 1983.
- (7) Musianowycz J. et al. *Clinical studies of Ukrain in terminal cancer patients (Phase II).* Drugs Exptl. Clin. Res., XVIII (Suppl.), 45-50, 1992.
- (8) Sotomayor E.M., Rao K., Lopez D.M., Liepins A. *Enhancement of macrophage tumouricidal activity by the alkaloid derivative Ukrain: In vitro and in vivo studies.* Drugs Exptl. Clin. Res., XVIII (Suppl.), 5-11, 1992.
- (9) Rolandi E. et al. *Plasma prolactin in breast cancer.* Lancet, II, 845-846, 1974.
- (10) Mitra J., Hayward J., Mcneilly A. *Hypothalamic-pituitary-prolactin axis in breast cancer.* Lancet, I, 889-891, 1974.
- (11) Hertz R. *Steroid-induced, steroid-producing and steroid-responsive tumors.* In: "Steroid hormone action and cancer". Raven Press, New York and London, 1976, pp. 1-14.
- (12) Hoff J., Hoff-Bardier M., Bayard F. *La prolactine. Son rôle dans l'hormonodépendance des cancers du sein.* J. Gynec. Obstet. Biol. Reprod. (Paris), 7, 18-30, 1978.
- (13) Jaietto-Wojtowicz E. et al. *Effect of single and prolonged administration of Ukrain on prolactin concentration in rats.* Drugs Exptl. Clin. Res., XVIII (Suppl.), 89-91, 1992.
- (14) Zilva J.F., Pannall P.R. "Clinical chemistry in diagnosis and treatment". Lloyd-Luke, London, 1984, p. 527.