DRUGS EXPTL. CLIN. RES. XXII(Suppl.) 71-73 (1996)

INFLUENCE OF UKRAIN ON PATIENTS WITH SURGICALLY TREATED BREAST CANCER. PART III. THE IMMUNE SYSTEM

FOMIN K.A.[1], UGLYANICA K.N.[1], NEFYODOV L.I.[2], DJURD T.I..[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, Wrocław, Poland.

Summary: *The present study was undertaken to evaluate the influence of Ukrain on immune parameters in ten patients with breast cancer, treated with the drug in the preoperative phase. The control group consisted of eight patients of similar age and advancement of the disease, who did not receive Ukrain before mastectomy. The data were compared with the parameters obtained in 15 healthy blood donors. It was found that treatment with Ukrain distinctly regulates cellular and, slightly, humoral immunity, non-specific immunity and also complement activity.*

Introduction

The contribution of the immune system to the control of neoplastic processes seems undeniable and is confirmed by more and more physicians who endeavour to utilize it as an additional tool in the fight against cancer (1).

Breast cancer is one of the most frequently occurring neoplasms in women. Its treatment at the present moment is limited to surgery, supplemented by chemical medication and radiotherapy. This commonly applied and accepted procedure is directed against cancerous tissue, but at the same time it destroys not only the latter, but also the immune system, the system which is meant to protect the organism from neoplastic processes.

The aim of the present paper was the study of the behaviour of the immune system in the application of the new drug of plant origin with anticancer properties, Ukrain (2-4), in patients with breast cancer. Information collected to date indicates multiple effects of Ukrain on the immune system (3, 5-9).

Patients and methods

The investigations concerned 18 patients in

* *Author to whom correspondence should be addressed.*

0378-6501/96/0000071 + 3 $2.50/0

whom breast cancer of grade T1-3N0-2M0 was diagnosed. The age of the patients varied between 35-65 years. Ten patients received, before surgical intervention, Ukrain intravenously in a dose of 5 mg every second day for 20 days. Thus, each patient received a total of 50 mg. Seven to ten days after the end of medication the patients underwent mastectomy by the method of Patey or Halsted. Immunological examination was performed at admission to the hospital, after Ukrain administration and 7-10 days after the surgery.

The control group consisted of eight patients who did not receive the drug. Their ages and diagnoses corresponded to those of the medicated patients. The immunological parameters were compared to those in 15 healthy persons of ages corresponding to those of the patients.

T lymphocytes were determined by the rosette test with sheep erythrocytes. Subclasses of T lymphocytes were determined by means of monoclonal antibodies. Immunoglobulins G, M, A were determined by radial immunodiffusion according to the technique of G. Mancini. The complement level was evaluated on the basis of 50% haemolysis of sensitized sheep erythrocytes, and the phagocytic activity of leukocytes was confronted versus the Staphylococcal strain No 209.

Table I *Immune parameters in patients with breast cancer treated with Ukrain*

Investigated parameters		Control group	At entry to hospital	7 days before surgery	After surgery
T lymphocytes, %	U	61±2	63±3	74±4[1]	61±2[3]
	C		69±5	69±5	56±4
T lymphocytes, in total 10^9/l	U	0.8±0.1	0.9±0.1	1.1±0.2	0.8±0.2
	C		1.0±1.0	1.0±0.1	0.7±0.3
Active T lymphocytes, %	U	34±2	50±51	48±5[1]	36±2[2,3]
	C		43±6	43±6	41±4
Active T lymphocytes, in total 10^9/l	U	0.4±0.1	0.7±0.14[1]	0.7±0.1[1]	0.5±0.1
	C		0.6±0.1[1]	0.6±0.1	0.5±0.3
Suppressor T lymphocytes %	U	7.5±1.6	9.9±1.1	8.6±3.4	6.0±2
	C		3.0±0.6	3.0±0.6	12±5.8
Helper T lymphocytes, %	U	53±2.5	57.0±3.4	62.0±4.5	55±4.3
	C		67.0±4.7[1]	67.0±4.7	41±3.9[1,2]
Immunoglobulin G, g/l	U	12.5±0.9	12.0±1.1	10.0±1.2	10.6±1.0
	C		12.0±1.0	12.0±1.0	11.2±2.0
Immunoglobulin A, g/l	U	1.9±0.3	3.8±0.3[1]	2.8±0.4	3.0±0.6
	C		3.5±1.3	3.5±1.3	2.2±0.3
Immunoglobulin M, g/l	U	1.2±0.1	1.5±0.1	1.2±0.1	1.3±0.2
	C		0.9±0.2	0.9±0.2	0.8±0.1[1]
Complement titer (haemolytic activity)	U	58±4	58±5	60±7	54±9
	C		56±20	56±20	70±6
Phagocytic activity of leukocytes, %	U	63±4	52±7	55±5	58±6
	C		62±5	62±5	64±1

U - Ukrain group
C - Control group
P<0.05 [1] statistically significant to healthy subjects
[2] statistically significant to patients at entry
[3] statistically significant to patients after treatment with Ukrain

Results and discussion

As seen in Table I, both cellular and humoral immune parameters of patients with breast cancer differed from the norm observed in healthy people. The number of active T lymphocytes and T helpers was increased, both in relative and absolute figures. IgA concentration was also increased. The immune system is known to protect the human body from noxious factors, both external and internal. The same is true for malignant tissue. The growth of the latter depends on the efficiency of the immune system. It is, therefore, not astonishing that in patients with breast cancer changes in immune parameters may be expected. It is suggested in the literature that in patients with advanced neoplastic processes the immune phenomena are depressed (1).

In the patients under study numerous immune parameters were slightly imbalanced, thus indicating that the cancerous process with which they were admitted was not very extensive. Changes

during Ukrain treatment: the relative and absolute T lymphocyte counts and the percent of helpers were increased, with consequent improvement of the CD4/CD8 index. The IgA level was slightly increased, as well as phagocytic activity of leukocytes towards bacteria and complement activity. On the basis of the foregoing observations it may be affirmed that Ukrain had a positive effect on the immunological processes, both cellular and humoral. These observations are in line with the data of other authors (3, 8, 9) that the drug has a normalizing effect on the immune system.

Among new observations of the mechanism of action of Ukrain, its normalizing influence on the immune system as regards immunoglobulin A synthesis should be stressed, although its positive effect on nonspecific immunity expressed in higher phagocytic activity was moderate, as was the influence on the rise of the lytic efficiency of the complement.

The above-described positive effects of Ukrain were not observed in patients of the control group (Table I). Reverse phenomena were observed, mainly in the sphere of cellular immunity. The relative and absolute T lymphocyte counts diminished, while the number of suppressor T lymphocytes rose and T helper lymphocytes decreased.

With regard to humoral immunity measured by the immunoglobulin level, an increase was noted, this being explained by the deepening cellular resistance deficit and lack of phenomena of cellular control over the immunoglobulin synthesis.

To conclude, from the immune point of view Ukrain application before surgical intervention in patients with breast cancer is highly recommended.

As demonstrated by the investigations, patients with breast cancer, even in early stages, exhibit immune parameters indicating immune deficiency as regards both cellular and humoral resistance. This state is aggravated by surgery. Ukrain administered before surgical intervention compensates this immune deficit and protects the patient from its worsening as a result of the operation. In view of this, administration of Ukrain to breast cancer patients before the operation is highly recommended, if only for immune reasons.

It should be borne in mind that Ukrain is also a drug with anticancer properties. These two actions of Ukrain make it, at the present time, a unique drug in the oncological clinic.

References

(1) Jarygin L.M., Malyshev V.S., Denisov L.E., Zimin Y.I. *Immune parameters in patients with breast cancer after mastectomy.* Chirurgia, **11**, 42-45, 1988.

(2) Hohenwarter O., Strutzenberger K., Katinger H., Liepins A. Nowicky J.W. *Selective inhibition of* in vitro *cell growth by the antitumour drug Ukrain.* Drugs Exptl. Clin. Res., **XVIII** (Suppl.), 1-4, 1992.

(3) Musianowycz J., Judmajer F., Manfreda D., Spängler P., Albrecht H., Hoffmann J., Meijer D. *Clinical studies of Ukrain in terminal cancer patients (Phase II).* Drugs Exptl. Clin. Res., **XVIII** (Suppl.), 45-50, 1992..

(4) Sotomayor E.M., Rao K., Lopez D.M., Liepins A. *Enhancement of macrophage tumoricidal activity by the alkaloid derivative Ukrain.* In vitro *and* in vivo *studies.* Drugs Exptl. Clin. Res., **XVIII** (Suppl.), 5-11, 1992.

(5) Danilos J., Zbroja-Sontag W., Baran E., Kurylcio L., Kondratowicz L., Jusiak L. *Preliminary studies on the effect of Ukrain on the immunological response in patients with malignant tumours.* Drugs Exptl. Clin. Res., **XVIII** (Suppl.), 55-62, 1992.

(6) Danysz A., Kokoschinegg M., Hamler F. *Clinical studies of Ukrain in healthy volunteers (Phase I).* Drugs Exptl. Clin. Res., **XVIII** (Suppl.), 39-43, 1992..

(7) Nowicky J.W., Manolakis G., Meijer D., Vatanasapt V., Brzosko W.J. *Ukrain both as an anticancer and immunoregulatory agent.* Drugs Exptl. Clin. Res., **XVIII** (Suppl.), 51-54, 1992.

(8) Slesak B., Nowicky J.W., Harlozinska A. In vitro *effects of* Chelidonium majus L. *alkaloid thiophosphoric acid (Ukrain) conjugates on the phenotype of normal human lymphocytes.* Drugs Exptl. Clin. Res., **XVIII** (Suppl.), 17-22, 1992.

(9) Staniszewski A., Slesak B., Kolodziej J., Harlozinska-Szmyrka A., Nowicky J.W. *Lymphocyte subsets in patients with lung cancer treated with thiophosphoric acid alkaloid derivatives from* Chelidonium majus L. (*Ukrain*). Drugs Exptl. Clin. Res., **XVIII** (Suppl.), 63-67, 1992.