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INFLUENCE OF UKRAIN ON PATIENTS WITH SURGICALLY TREATED BREAST CANCER. PART I. CLINICAL AND LABORATORY PARAMETERS

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Summary: *Studies were undertaken to evaluate the influence of Ukrain on clinical and laboratory parameters in ten patients with breast cancer treated with the drug in the preoperative phase. The control group was composed of eight patients of similar age and advancement of the disease who did not receive Ukrain before mastectomy. Data from the present studies indicate that the drug is distinctly helpful from the surgical viewpoint by increasing tumour hardness and enlargement of metastatic lymph nodes. Furthermore, treatment with it is fully safe, with no side effects or allergic reactions.*

Introduction

In recent years the interest in Ukrain has increased, as seen by the numerous clinical and experimental papers appearing in the medical literature (1).

The aim of the present study was to follow-up the influence of Ukrain on clinical and laboratory parameters in patients with breast cancer subjected to surgery. In the available literature no such investigations appear to have been reported..

Patients and methods

Investigations were performed on 18 patients with primary breast cancer. Their mean age was 52 years. Clinical diagnosis was confirmed by histological examination of the biopsy material. The patients were divided according to age into groups, and the degree of advancement of the tumour was evaluated according to the Classification of Malignant Tumours (Tumour/Node Metastasis) (TNM) classification recommeded by the Union Internationale de Combat de Cancer (UICC) (Table I).

A group of eight patients served as control. All patients were clinically classified for radical surgical treatment. In the preoperative period they received only supportive treatment.

A group of ten patients with breast cancer received Ukrain before surgery. The drug was applied intravenously in a dose of 5 mg every

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Table I *Classification of patients according to age and disease stage*

Groups of patients	Mean age, years	Stage of cancerous process			
		T1N0M0 or T2N0M0	T1N1M0 or T2N1M0	T3N0M0 or T3N1..M0	Total
Control	53	2	4	2	8
Ukrain	52	4	4	2	10

second day for a period of 20 days. Each patient received 10 ampoules, i.e., 50 mg of the drug. Seven to ten days after the last injection the patients were operated. Mastectomy was performed according to Patey's or Halsted's method.

The influence of Ukrain on the body as a whole was evaluated according to haematological, immunological, hormonal, blood serum and amino acid parameters. The influence of Ukrain on the cancer was evaluated by clinical examination, mammography (MA), ultrasonography (USG) and morphological criteria. Control procedures were performed before and after surgery in both groups of patients, i.e., in the control group and that treated with Ukrain. Tumour tissue and lymph nodes obtained at operation were subjected to morphological macroscopic examinations by light and electron microscopy. The cancerous tissue was additionally compared with the tissue of the normal breast in regard to amino acid content. Material for examination was taken from all patients and evaluated by the same examining team. Surgical interventions were executed by the same team of surgeons. The patients were anaesthetised by inhalation.

Results

In eight patients there were no side effects of Ukrain, although two after application of the drug felt pain in the breast at the site of the tumour. In all patients a hardening of the tumour was noted by palpation, with slight increase in tumour size after administration of the drug. There were no allergic reactions associated with Ukrain. In USG examination the influence of Ukrain was also noticeable. The structure of the tumour was more pronounced and its size increased, on an average 2.1 to 2.3 cm.

The influence of Ukrain was more noticeable, however, in radiological examination, particularly in four patients in whom, before application of the drug, MA had not demonstrated any cancerous changes. In two of these patients the characteristic neoplastic shadows now appeared and in the remaining two, besides the shadows, a distinct vascular outline additionally appeared around the tumour. In the remaining six patients the neoplasms visible at MA became more pronounced after treatment with Ukrain, with well-outlined contours. The appearance of the tumour at MA or USG, and its slight increase in size confirmed by hardening at palpation after Ukrain therapy, may be attributed to sclerosing processes. In view of the foregoing observations it may be affirmed that Ukrain is a safe drug, well tolerated by patients; it helps clinical visualisation of the tumour by USG and MA and thus facilitates diagnosis.

From the surgical point of view, the action of Ukrain is particularly noteworthy not only on cancerous tissue of the breast but also on metastases to the lymph nodes. The latter also enlarged and sclerosed. This is very helpful in localizing the nodes involved in the cancerous process. However, it was also observed that, after Ukrain treatment, lymph nodes without metastases also became enlarged. The number of lymph nodes detected after treatment with the drug reached 23-25, whereas in the control group only 11-13 could be found.

In the breasts inspected after surgery from which material was taken for morphological studies, localisation of the tumour was characteristic and easy. On cross section, minute dispersed yellowish foci could be seen, and around the tumour a connective tissue capsule. In histopathological study in all patients adenocarcinoma was diagnosed, in four cases poorly differentiated. In this group metastases to lymph nodes were found in four patients. The postoperative course in both groups did not differ. The sutures were removed on postoperative day 11-12. Lymphorrhoea cea-

sed towards the end of the third postoperative week.

As demonstrated by the haematological parameters, both groups of cancer patients did not differ significantly from normal before surgery. Slight lymphopenia and monocytosis were noted and a raised sedimentation rate characteristic of patients with neoplasms. Postoperatively, in the control group changes were observed in the haematological parameter usually noted in patients after moderately severe surgical interventions, i.e., a fall of erythrocyte count and haemoglobin, a rise of multinuclear leukocyte count with generally unchanged numerical values for leukocytes and a decrease in lymphocytes. This was accompanied by a raised sedimentation rate.

Analysis of haematological parameters in patients treated with Ukrain demonstrated that the drug does not prevent anaemia. In regard to leukocytes, after Ukrain a shift to the left was not observed, and the lymphocyte count as compared with the preoperative state was not depressed. Monocyte count was slightly increased (Table II). Other authors using Ukrain in experimental investigations noted a similar influence on haematological parameters (1). The positive reaction of haematological parameters to the drug may be attributed to its action on haematopoetic processes. It is interesting to note that after Ukrain treatment, a rise in sedimentation rate was not noted, whereas the thrombocyte count markedly decreased.

As regards biochemical parameters, no significant differences in relation to controls were found (Table III). No influence was found on electrolyte concentration, glucose, total protein and serum enzymes, and no change in blood coagulation was noted.

Table IV presents the coagulation time in patients of both groups; in both it was markedly higher. This is characteristic of patients with neo-

Table II *Haematological parameters in breast cancer patients treated with Ukrain (50 mg/treatment)*

Investigated parameters		Control group	At entry to hospital	After treatment with Ukrain	8-10 weeks after surgery
Erythrocytes, $10^{12}/l$	U	4.4 ± 0.1	4.2 ± 0.1	4.2 ± 0.1	$3.5 \pm 0.1^{1,2,3}$
	C		4.2 ± 0.1	4.2 ± 0.1	$3.5 \pm 0.1^{1,2}$
Haemoglobin, g/l	U	144 ± 3	139 ± 4	140 ± 4	$117 \pm 5^{1,2,3}$
	C		138 ± 3	138 ± 3	$114 \pm 4^{1,2}$
Thrombocytes, $10^9/l$	U	244 ± 15	223 ± 12	203 ± 11	227 ± 8
	C		218 ± 16	218 ± 16	215 ± 17
Leukocytes, $10^9/l$	U	4.6 ± 0.2	5.1 ± 0.3	4.6 ± 0.3	5.5 ± 0.6
	C		5.0 ± 0.4	5.0 ± 0.4	6.0 ± 1.6
Eosinophils, %	U	1.82 ± 0.26	1.2 ± 0.39	1.5 ± 0.58	2.1 ± 0.67
	C		1.14 ± 0.29	1.14 ± 0.29	2.6 ± 1.12
Band cells; %	U	1.73 ± 0.2	2.2 ± 0.61	1.0 ± 0.36	3.1 ± 0.71^{3}
	C		2.0 ± 0.47	2.0 ± 0.47	$8.0 \pm 2.2^{1,2}$
Polymorphonuclears, %	U	58.1 ± 1.6	60.8 ± 2.6	62.7 ± 2.4	61.3 ± 1.8
	C		61.7 ± 1.9	61.7 ± 1.9	68.8 ± 1.2^{1}
Basophils, %	U	0.14 ± 0.09	0.3 ± 0.21	0.3 ± 0.15	0.3 ± 0.15
	C		0.29 ± 0.16	0.29 ± 0.16	0.4 ± 0.24
Lymphocytes, %	U	34.1 ± 1.4	28.2 ± 2.2^{1}	27.3 ± 1.9^{1}	25.7 ± 2.2^{1}
	C		28.5 ± 1.7^{1}	28.5 ± 1.7	$13.6 \pm 2.2^{1,2}$
Monocytes, %	U	4 ± 0.5	7.3 ± 0.5^{1}	5.9 ± 0.5^{1}	7.3 ± 0.8^{1}
	C		6.4 ± 0.6^{1}	6.4 ± 0.6	6.6 ± 0.9^{1}
Sedimentation rate, mm/h	U	6.1 ± 1.5	10.2 ± 1.2	11.2 ± 2.8	$28.6 \pm 3.8^{1,2,3}$
	C		10.7 ± 0.9^{1}	10.7 ± 0.9	$48.2 \pm 6.7^{1,2}$

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 surgery

Table III *Biochemical parameters of blood plasma in patients treated with Ukrain (50 mg/treatment)*

Investigated parameters		Control group	At entry to hospital	After treatment with Ukrain	8-10 weeks after surgery
Total protein, g/l	U	78 ± 1	75 ± 2	71 ± 1^{1}	$66 \pm 2^{1,2,3}$
	C		73 ± 21	73 ± 2	72 ± 11
Urea, µmol/l	U	6.0 ± 0.2	6.0 ± 0.6	6.4 ± 0.4	5.6 ± 0.3
	C		6.2 ± 0.7	6.2 ± 0.7	4.8 ± 0.7
Bilirubin, µmol/l	U	13.1 ± 1.2	10.0 ± 0.7	10.0 ± 0.5	$8.4 \pm 0.4^{1,2,3}$
	C		11.1 ± 0.7	11.1 ± 0.7	14.5 ± 2.4
ALAT, µmol/l	U	0.41 ± 0.1	0.79 ± 0.36	0.71 ± 0.08^{1}	0.57 ± 0.14
	C		0.71 ± 0.26	0.71 ± 0.26	0.59 ± 0.12
ASPAT, µmol/l	U	0.31 ± 0.05	0.44 ± 0.12	0.48 ± 0.1	0.42 ± 0.09
	C		0.46 ± 0.09	0.46 ± 0.09	0.52 ± 0.09
K, µmol/l	U	3.96 ± 0.1	4.39 ± 0.14^{1}	4.33 ± 0.07^{1}	4.46 ± 0.15^{1}
	C		4.29 ± 0.14	4.29 ± 0.14	4.44 ± 0.07^{1}
Na, µmol/l	U	142 ± 1	143 ± 2	144 ± 1	140 ± 1
	C		142 ± 1	142 ± 1	144 ± 1
Cl, µmol/l	U	102 ± 1	103 ± 1	107 ± 2^{2}	106 ± 1^{1}
	C		104 ± 1	104 ± 1	101 ± 1
Glucose, µmol/l	U	4.7 ± 0.1	5.1 ± 0.6	5.2 ± 0.4	4.7 ± 0.2
	C		5.2 ± 0.4	5.2 ± 0.4	7.3 ± 1.2

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 surgery

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Table III *Coagulation parameters in patients with breast cancer treated with Ukrain (50 mg/treatment)*

Investigated parameters		Control group	At entry to hospital	After treatment with Ukrain	8-10 weeks after surgery
Prothrombin index, %	U	0.93 ± 0.02	0.92 ± 0.02	0.94 ± 0.02	0.94 ± 0.02
	C		0.95 ± 0.03	0.95 ± 0.03	0.91 ± 0.04
Fibrinogen, g/l	U	1.86 ± 0.11	2.33 ± 0.2	1.89 ± 0.13	3.02 ± 0.29[1,3]
	C		2.4 ± 0.17	2.40 ± 0.17	4.61 ± 0.39[1,3]
Thrombin time, s	U	13.7 ± 0.3	15.9 ± 0.4[1]	15.8 ± 0.9[1]	15.2 ± 0.8
	C		15.9 ± 0.4[1]	15.9 ± 0.4	13.6 ± 0.2[2]
Bleeding time, s	U	34.7 ± 1.3	41.9 ± 2.3[1]	41.2 ± 1.9[1]	44.9 ± 2.4[1]
	C		42.8 ± 1.9[1]	42.8 ± 1.9	42.6 ± 2.6[1]

U = Ukrain group
C = Control group
P<0.05
[1] statistically significant to healthy subjects
[2] statistically significant to patients on admission
[3] statistically significant to patients after surgery

plasms. As shown in Table IV, after intervention the fibrinogen value increased, other coagulation parameters remaining unchanged. This was true for both groups. Observations indicate that Ukrain does not affect blood coagulation.

On the basis of the present clinical observations and laboratory analyses, it may be concluded that Ukrain is well tolerated by patients, does not evoke allergic reactions and exerts no toxic influence on the organism. Clinical behaviour and biochemical investigations indicate that the drug does not affect homeostasis. Local changes in tumour and in lymph nodes occurring under the influence of the drug leads to the conclusion that Ukrain has anticancer properties.

References

(1) Jagiełło-Wójtowicz E., Kleinrok Z., Matuszek B., Surmaczyńska B., Baran E., Nowicky J.W., Nowicky W. *Effect of three months treatment with Ukrain on peripherial blood morphology in rodents.* Drugs Exptl. Clin. Res., **XVIII** (Suppl.). 79-83, 1992.