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The effect of Ukrain on cancer of the urinary bladder

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SUMMARY

The aim of the present study was to evaluate therapeutic efficacy of Ukrain in patients with cancer of the urinary bladder and evaluate the influence of the drug on the pool of free amino acids (FAA) and their derivatives (AADS) in the blood plasma and tumor tissue. The study was carried out on 28 patients with T 1 NOM0 cancer of the urinary bladder.The application of Ukrain at a total dose of from 100mg to 300mg for treatment enabled to attain either complete or partial regresion of the tumor in 67.7 ± 9.1 % of the cases.
The study of FAA and AADS in patients treated with Ukraine disclosed that the drug may decrease an active transport of FAA into the tumour tissue inhibiting processes of protein biosynthesis, gluconeogenesis and production of energy, and in the same time, in the tumor bearer the drug may improve inbalanced FAA matabolism

INTRODUCTION

Ukrain is a semisynthetic compound prepared from Chelidonium majus L. alkaloids conjugated with Thio-Thepa. It has proven malignotoxic properties in vitro (1), and in vivo (2), induction of apoptosis (3), immunomodulatory and stimulatory properties in oncologic patients in the clinic (4). Partial and complete remision could be induced in a variety of different cancer types by the drug alone or in combination (5)

The aim of the study was to evaluate therapeutic efficacy of Ukrain, as neoadjuvant approach, in patients with carcinoma of the urinary bladder (CUB) as well as to evaluate the influence of the drug on the formation of free amino acids (FAA) and their derivatives (AADS) in the tumor tissue and blood plasma of patients treated with Ukrain

MATERIALS AND METHODS

The study was carried out on 28 patients with T1 N0M0 CUB divided into three groups. The first one was compoused of nine, the second one of ten, and the third one of nine patients.Ukrain was injected intravenously (i.v.) in a dose of 100 mg per injection daily. The first group of patients received a total dose for treatment 100 mg , the second and third group 200 mg nad 300 mg , respectively FAA and AADS were determined in homogenates of the tumor tissue, blood plasma and samples of unchanged UB in an amino acid analyzer according to the method of Benson modified by Nefyodov. The results were subjected to computed analysis according to Multi-Chroma programme. Statistic analysis was performed according to the computer programme BMODC 3d 7m.

RESULTS AND CONCLUSIONS

In the first group of patients treated with a dose of 100mg Ukrain a partial regresion of the tumor was observed in four cases, and stabilisation of the tumor progress in the remaining .In patients from the second group injected with 200mg of the drug,a complete regresion was observed in one case, a partial regression in four and stabilisation of the tumor growth in five patients.In the last group of patients injected with 300 mg of the drug, a complete regression of the tumor was seen in 2 cases, partial regression in six, and stabilisation of the tumor growth was noted in one patien (table 1)..

From the data presented above Ukrain used as neoadjuvant approach in patients with T1 N0M0 CUB was enable to attain either complete or partial regression of

Table 1. Results of application of Ukrain in patient with T1NOMO cancer of the urinary bladder

Namber of courses	Namber of patients	Total dose of the drug (mg)	Complette tumor regresion	Partial tumor regresion	Stabilization of tumor process
1 course	9	100	-	4	5
2 course	10	200	1	4	5
3 course	9	300	2	6	1
Total:	28	100-300	3	14	11

the tumor in 60,7 ± 9,2 % of the cases.The best results were obtained in patients treated with the highes dose.
As compared with healthy donors,the blood plasma of patients with CUB showed decreased concentration of thiol- containing FAA and glutamine (Gln) and reduced levels of non-essential (glutamine acid, proline, alanine) and aromatic (phenylalanine) FAA. Treatment with Ukrain eliminated the blood plasma FAA imbalance in patients with CUB, simultaneously enriching the pool of FAA and AADS in unchanged UB tissue, and decreased by 30 to 50 % in the tumor tissue concentration of Gln and Leucine (Leu),regulators of malignant cell proliferation and differentation (table 2 and 3).
Confirmatory for the data was computer analysis indicating that concentrations of Gln and Leu in the tumor tissue and the healthy tissue of UB after Ukrain treatment correlated highly significantly ,negatively (r = 0.95)
The here presented data indicated that Ukrain seems to be unique compound among cytostatics being simultaneously destructive for a malignat growth and anabolically active for the organism of a tumor - bearer.

Table 2. Concentrations of free amino acids and their derivatives in blood plasma (μM) of patients with the T1N0M0 urinary bladder cancer before and after Ukrain treatment (i.v., 10 mg in a day, 10 times, for 20 days)

Compound	Donors (n=28)	before Ukrain (n=28)	after Ukrain (n=28)
Cysteic acid	15,197 ± 0,778	8,225 ± 0,979*	8,00 ± 1,20*
Taurine	104,77 ± 3,96	136,4 ± 35,5	199,8 ± 29,3*
Aspartic acid	15,70 ± 1,73	31,45 ± 4,14*	93,9 ± 43,1*
Serine	163,23 ± 7,77	160,0 ± 12,1	198,39 ± 7,11*#
Glutamic acid	34,02 ± 4,95	159,6 ± 28,2*	212,1 ± 21,0*
Glutamine	1399,0 ± 49,3	1024 ± 170*	1047 ± 110*
Proline	218,4 ± 22,6	305,9 ± 14,3*	303,2 ± 13,8*
Glycine	232,8 ± 12,6	278,2 ± 21,4	348,0 ± 15,5*#
Alanine	393,5 ± 12,7	567,5 ± 34,5*	576,3 ± 43,6*
α-aminobutyrate	35,12 ± 3,08	15,15 ± 2,87*	46,0 ± 15,7
Valine	252,6 ± 10,3	304,2 ± 12,1*	325,6 ± 15,2*
Cystine	110,54 ± 8,24	23,40 ± 4,56*	29,75 ± 5,15*
Ethanolamine	74,18 ± 2,58	229,8 ± 12,8*	250,04 ± 8,59*
Ornithine	104,01 ± 6,10	128,7 ± 11,3	181,6 ± 13,0*#

Table 3. Concentrations of free amino acids and their derivatives in normal and tumor tissue (mmol/g) of patients with the T1N0M0 urinary bladder cancer before and after Ukrain treatment (i.v., 10 mg in a day, 10 times, for 20 days)

	normal tissue		tumor tissue	
Compound	before Ukrain (n=28)	after Ukrain (n=28)	before Ukrain t (n=28)	after Ukrain (n=28)
Cysteic acid	0,0924 ± 0,0127	0,253 ± 0,049*	0,0911 ± 0,0160	0,1628 ± 0,0494
Taurine	3,989 ± 0,264	7,95 ± 1,31*	5,187 ± 0,861	3,969 ± 0,755
P-ethanolamine	0,6129 ± 0,0458	1,468 ± 0,260*	1,717 ± 0,398	1,227 ± 0,324
Aspartic acid	0,8430 ± 0,0635	1,394 ± 0,149*	2,835 ± 0,517	1,941 ± 0,457
Glutamic acid	3,502 ± 0,205	5,922 ± 0,817*	6,703 ± 0,938	5,34 ± 1,38
Glutamine	1,656 ± 0,110	1,883 ± 0,156	3,648 ± 0,746	1,05 ± 0,119*
Methionine	0,2058 ± 0,0332	0,2727 ± 0,0514	0,3019 ± 0,0297	0,135 ± 0,0296*#
Leucine	0,4867 ± 0,0698	0,5790 ± 0,0974	1,242 ± 0,104	0,705 ± 0,204*
Tyrosine	0,3205 ± 0,0473	0,535 ± 0,0263*	0,819 ± 0,104	0,368 ± 0,0428*
Phenylalanine	0,2207 ± 0,0390	0,3297 ± 0,0414	0,6768 ± 0,0656	0,231 ± 0,0594*

* - p<0,05 compared to donors
# -p<0,05 p<0,05 compared to group before treatment of Ukrain

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