Боли в животе наблюдались обычно в конце лихорадочного периода, интенсивность их варьировала от ноющих в эпигастральной области до сильных по всему животу. Продолжительность болей в животе в среднем составляла 3-4 дня, они часто сопровождалась тошнотой и рвотой. При пальпации живота, как правило, был мягким, болезненность имела лишь в эпигастральной области, умеренно выраженная ригидность мышц передней брюшной стенки наблюдалась часто, но симптомов раздражения брюшины не было.

Дифференциальная диагностика желудочно-кишечного тракта при COVID-19 и острых заболеваний желудочно - кишечного тракта обычно не вызывает особых затруднений. Ошибки диагностики чаще допускаются в тех случаях, когда не учитывают клиническую картину болезни в целом. А фиксируют внимание лишь на симптомах поражения желудочно-кишечного тракта.

Нами так же было проведено исследование некоторых показателей пепсинообразующей функции желудка у больных с поражением желудочно-кишечного тракта при COVID-19 путем определения пепсиногена плазмы крови и уропепсиногена.

У 13 больных с поражением желудочно-кишечного тракта при COVID-19 определяли натощак уровень пепсиногена в плазме крови, который в среднем ($M \pm m$) был равен $8,1 \pm 1,01$ мг%. У 16 больных в период клинических проявлений болезни содержание уропепсиногена в суточном количестве мочи было в среднем равно $82,1 \pm 8,2$ мг/сутки. В период реконвалесценции содержание уропепсиногена у тех же больных было повышено до $178,5 \pm 28,1$ мг/сутки.

Сопоставление данных нашего наблюдения показывает, что параллелизм между изменениями кислотообразующей функции желудка с одной стороны, и уровнем пепсиногена в плазме, а также выделением уропепсиногена – с другой, при этом заболевании отсутствует.

Различные изменения желудочно-кишечного тракта у больных с COVID-19 наблюдаются довольно часто. При выраженных желудочно-кишечных симптомов COVID-19 для дифференцировки с заболеваниями желудочно-кишечного тракта необходимо учитывать весь комплекс эпидемиологических, клинических и лабораторных данных.

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Perioperative period in the radical treatment of uterine cancer: features of management

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doi: 10.18411/sr-10-08-2021-06

Abstract

Purpose of the study is to characterize the state of coagulation and state of lipid peroxidation and antioxidant potential in cases of women with uterine cancer during surgery, to evaluate the effectiveness of the of antioxidants used in order to correct changes in the hemostatic system. 104 women were examined. Women were separated into 3 groups:

healthy, receiving standard therapy and standard therapy + selmevitum. the patients showed a change in hemostasis which was mostly prevented by using additional vitamin and mineral complex – selmevitum before and after operation.

Keywords: uterine cancer, hemostatic system, antioxidants.

In recent decades, there has been a significant increase in an increase in the incidence of benign and malignant neoplasms of the uterine body. Since 1997, in Russia, maternal body cancer has taken the first place in the structure of malignant qualitative neoplasms of the female genital organs [1, 2, 6, 14]. In the structure of mortality, oncological problems occupy one of the first places, however less known is that thrombosis appears as the second most frequent cause of death of cancer patients [9, 10, 11, 12, 13, 14]. Modern literature suggests that the activation of the hemostatic system connected with the development of chronic DIC syndrome in cancer patients.

Information about the positive effect of antioxidants in the prevention of thrombohemorrhagia caused by effects that initiate hyper-thrombinemia, the relationship of thrombohemorrhagia in neoplasia with hemocoagulation shifts caused by thrombinemia, the absence of contraindications to the use of antioxidant vitamins, their availability and the possibility of outpatient use were the basis for studying the corrective effect of antioxidant vitamins on hemostasis in the surgical treatment of myoma and uterine cancer. In addition, the nature of hemostatic disorders, especially platelet disorders, cannot be considered sufficiently studied in such operations. Data on the close relationship between hemostasis and lipid peroxidation [2, 3, 5, 8, 11] confirm the need to study the state of lipid peroxidation (LPO) in malignant and benign diseases of the uterus.

Purpose of the study

To characterize the state of coagulation (biochemical) and platelet components of hemostasis, the state of lipid peroxidation and antioxidant potential in cases of women with uterine cancer during surgery, to evaluate the effectiveness of the of antioxidants used in order to correct changes in the hemostatic system.

Research objectives:

1. To assess the state of the coagulation and platelet components of hemostasis, the intensity of LPO and Antioxidant potential (AOP) of blood in patients with uterine cancer, depending on the type of preoperative preparation (traditional or supplemented with selmevitum).
2. Along with the clinical characteristics, to assess the state of hemostasis, LPO, and AOP of blood in patients with uterine cancer after hysterectomy by laparotomy access.
3. To determine the effectiveness of the use of a complex antioxidant (selmevitum) in order to correct hemostasiological disorders in the postoperative period in patients with uterine cancer before and after surgery.

Content of the work

Scientific research is of a clinical nature. 104 women were examined, including 20 healthy donors in the second phase of the menstrual cycle and 84 women with uterine cancer or uterine fibroids who received surgical treatment (extirpation of the uterus with appendages).

To study the changes in hemostasis, LPO, and AOP, and to study the effect of the vitamin-mineral complex – selmevitum on these cases, homogeneous groups of patients were formed: control group (healthy woman)(n=20), the comparison group (normal pre-operative preparation and postoperative treatment)(n=39) and the main group (women received additional selmevitum)(n=45). Vitamin and mineral complex-selmevitum (registered by the State Pharmaceutical Committee of the Russian Federation, Protocol No. 10 of September 25, 1997) was prescribed one tablet a day 14 days before the operation and 14 days after it.

The criteria for inclusion in the groups are following: the presence of indications for planned surgical intervention, informed consent of patients for follow-up and surgical intervention, and the implementation of recommendations for treatment and prevention by women in the perioperative period. Exclusion criteria – refusal of examination and implementation of recommendations for treatment in the perioperative period, the presence of severe somatic diseases that are a contraindication to surgical treatment. Observations were carried out in the gynecological departments of the Tyumen Regional Oncological Dispensary, maternity hospital No. 3 in Tyumen, and the regional perinatal center in Tyumen.

Clinical and laboratory examinations were performed one day before, 1, 3-4 and 5-7 days after the operation. The duration of the operation, the type of anesthesia, and intraoperative blood loss were taken into account. In the postoperative period, the frequency of thrombohemorrhagic complications, the length of hospital stays, and the number of days after surgery were evaluated.

Platelet hemostasis was assessed by determining: the number of P; the distribution of their forms; the number of active forms of P (the sum of DE, SE, and S); the number and size of aggregates per 100 free cells, the number of small aggregates (2-3 P) per 100 free cells and large aggregates (4 or more cells) per 100 free cells.

Coagulation hemostasis was assessed by determining: 1) activated recalcification time (ART), 2) activated partial thromboplastin time (APTT), 3) prothrombin ratio - PR; international normalized ratio (INR), 4) fibrinogen concentration, 5) soluble fibrin – monomer complexes (RFMC), 6) products of fibrin degradation (PDF) - in the modification of A. Sh. Byshevsky et al. (1989)], 7) activity of antithrombin III (AT-III), 8) the index of plasminogen reserve (IRP). LPO was evaluated by the content of lipid peroxides-diene conjugates (DC) and malondialdehyde (MDA). AOP was judged by the content of vitamin E in red blood cells, superoxide dismutase, and glutathione-S-transferase (G-S-T).

Statistical processing of the obtained data was carried out using the Excel program by the Student method. The analysis of the relationships of the variables was carried out by the Spearman rank correlation (r_s) method. The graphical analysis was carried out in the Microsoft Graf system (MS Word 2000 application) with the construction of approximation graphs, the correctness of which was characterized by the value of the approximation coefficients (R^2).

Results

Clinical characteristics, state of hemostasis, lipid peroxidation and blood antioxidant activity in patients with malignant diseases of the uterus before and after surgical treatment. 84 women with cancer of the uterus were examined. The average age in the comparison group was 53.6 ± 13.4 years, in the main group 52.7 ± 11.5 years. According to the diagnosis and stage of the disease, both groups were comparable (Table 1).

Table 1

Localization and stage of malignant neoplasm, n ($M \pm m$ %)

Diagnosis	Comparison group, n = 39			Main group, n = 45		
	I stage	II stage	III stage	I stage	II stage	III stage
Cancer of the body of the uterus	22 (56,4±8,0)	4 (10,9±5,1)	2 (5,1±3,6)	27 (60,0±7,4)	4 (8,9±4,3)	2 (4,4±3,1)
Cervical cancer	9 (23,1±6,8)	2 (5,1±3,6)	0 (0,0)	10 (22,2±6,3)	2 (4,3±3,1)	0 (0,0)

The patients of both groups are comparable in the frequency and severity of the pathology. The size of the uterus in patients with malignant diseases of the uterus was 6.8 ± 0.4 weeks in the comparison group, and 8.0 ± 0.9 weeks in the main group. Extirpation of the uterus with appendages was performed in 76.9% of women in the comparison group and in 80% of the main group. Wertheim surgery was performed in 17.9% of women in the

comparison group and 13.3% of patients in the main group. Removal or resection of the large omentum was performed in 5.1% of patients in the comparison group and 6.7% of patients in the main group. The volume of intraoperative blood loss was 217.0 ± 94.0 in the main group, and 205.1 ± 65.7 ml in the comparison group.

The patients of the main group also showed an elongation of APTT (by 42%), ART (by 21.7%), an increase in PA (by 150%), INR (by 144%), an increase in fibrinogenemia (by 256%), a high level of RFMC (by 34%) and PDF (by 52.3%), a decrease in AT III (by 32%), and IRP (by 39%) when compared with healthy women. An increase in the concentration of RFMC and PDF in the blood plasma of patients with uterine cancer before surgery indicates an increase in thrombinemia.

A significant increase in the content of FG, RFMC, and PDF in women of the comparison group was revealed on the 3rd and 4th days in comparison with the indicators before the operation (by 38, 27, and 20%, respectively) and with the first days after it (by 45, 28, and 22%).

Table 2

Coagulation hemostasis after surgery in patients with cancer of the uterus on the background of taking selmevitum ($M \pm m$)

Indicators	Before the operation n=10	1st day, n=10	3-4 days, n=10	5-7 days, n=14
ART, s	$71,8 \pm 5,7$	$84,5 \pm 6,9$ *	$66,2 \pm 5,2$ #	$54,5 \pm 4,2$ **
APTT, s	$57,7 \pm 3,3$	$72,0 \pm 4,3$ *	$61,0 \pm 5,9$ #	$48,2 \pm 1,6$ **
TT, s	$19,6 \pm 1,7$	$19,4 \pm 2,6$	$18,2 \pm 1,7$	$21,8 \pm 1,1$
PO	$3,5 \pm 0,5$	$1,9 \pm 0,2$ *	$2,2 \pm 0,5$ *	$2,7 \pm 0,4$ #
MNO	$3,9 \pm 0,6$	$2,1 \pm 0,3$ *	$2,4 \pm 0,6$ *	$3,2 \pm 0,5$ #
FG, g/l	$8,9 \pm 1,0$	$5,8 \pm 0,8$ *	$6,0 \pm 1,0$ *	$6,9 \pm 0,6$ *
RFMC, mg %	$4,7 \pm 0,7$	$4,9 \pm 0,5$	$4,9 \pm 0,6$	$6,1 \pm 0,3$ **
PDF, mg %	$0,84 \pm 0,06$	$0,78 \pm 0,04$	$0,85 \pm 0,07$	$0,84 \pm 0,08$
AT III, %	$64,5 \pm 3,5$	$69,1 \pm 3,8$	$79,6 \pm 1,9$ **	$58,5 \pm 2,9$ #
IRP, %	$67,1 \pm 3,4$	$64,6 \pm 5,9$	$77,5 \pm 2,4$ **	$59,2 \pm 3,9$ *

Note: the * sign indicates that the differences are statistically significant ($p < 0.05$) compared to the indicators before the operation, the # sign indicates the differences within the first day after the operation

In the study of the platelet component of hemostasis (Table. 4) before the operation, the patients of the comparison group showed a decrease in the number of D (by 36%, $p < 0.05$), an increase in DE (by 28%), C (by 21%), SE (by 50%), APF (by 28%), and BBA (by 180%) relative to healthy women and patients of the main group. In the main group of patients before surgery, the number of TRS (by 46%) and the concentration of PMA (by 39%) and P3 (by 38%) were reduced in comparison with healthy women.

A statistically significant decrease in the number of P (by 18% relative to the level of day 1), an increase in the APF content (by 15%) was detected on 3-4 days after surgery, and did not decrease until 5-7 days (comparison with preoperative indicators). At the same time, NMA decreased by 3 times, NA by 41%, and D by 22% (in comparison with preoperative values). Until 5-7 days after surgery the amount of Spherocytes continued to grow (68,6%), decreased NMA (45%), NA (106%) and the number of TTS in the peripheral blood (38%) (compared with the level before surgery and 1-st day after it) (Table 3).

Table 3

The state of platelet hemostasis after surgery in patients with cancer of the uterus against the background of traditional treatment ($M \pm m$)

Indicators	Before the operation n=13	1st day, n=10	3-4 days, n=10	5-7 days, n=10
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TC ($\times 10^9/l$)	225,7 $\pm$ 8,7	223,3 $\pm$ 11,7	164,6 $\pm$ 18,0 *#	185,8 $\pm$ 16,2 *#
D, %	29,8 $\pm$ 0,8	29,3 $\pm$ 1,5	30,3 $\pm$ 1,6	32,3 $\pm$ 1,2
DE, %	31,9 $\pm$ 1,9	31,9 $\pm$ 2,8	31,9 $\pm$ 2,0	31,0 $\pm$ 1,4
S, %	21,8 $\pm$ 1,1	23,2 $\pm$ 1,1	23,3 $\pm$ 0,9	20,5 $\pm$ 2,1
SE, %	15,8 $\pm$ 0,6	15,6 $\pm$ 0,4	14,6 $\pm$ 1,0	16,3 $\pm$ 1,3
AF, %	68,7 $\pm$ 1,5	70,7 $\pm$ 1,5	69,7 $\pm$ 1,6	67,8 $\pm$ 1,2
NSA (per 100 cells)	8,4 $\pm$ 1,1	13,4 $\pm$ 0,8 *	6,1 $\pm$ 1,3 #	8,7 $\pm$ 1,3 #
NLA (per 100 cells)	2,8 $\pm$ 0,4	2,8 $\pm$ 0,7	2,7 $\pm$ 0,9	2,6 $\pm$ 0,7
NA (per 100 cells)	11,2 $\pm$ 1,4	16,2 $\pm$ 1,2 *	8,9 $\pm$ 2,2 #	11,3 $\pm$ 1,9 #
P ₃ , %	43,9 $\pm$ 5,0	39,1 $\pm$ 5,0	36,4 $\pm$ 8,4	38,9 $\pm$ 3,2

Table 4

The state of platelet hemostasis after surgery in patients with cancer of the uterus on the background of taking selmevitum ($M\pm m$)

Indicators	Before the operation n=10	1 st day, n=10	3-4 days, n=10	5-7 days, n=14
P ($\times 10^9/l$)	133,4 $\pm$ 10,8	138,1 $\pm$ 11,0	113,5 $\pm$ 6,2 #	99,8 $\pm$ 4,6 *#
D, %	42,3 $\pm$ 2,4	35,2 $\pm$ 1,7 *	32,9 $\pm$ 2,4*	33,53 $\pm$ 1,9 *
DE, %	28,0 $\pm$ 1,6	28,0 $\pm$ 1,7	28,3 $\pm$ 1,8	20,6 $\pm$ 1,2 *#
S, %	20,4 $\pm$ 1,1	23,9 $\pm$ 1,1	30,1 $\pm$ 3,7 *	34,4 $\pm$ 1,7 *#
SA, %	9,3 $\pm$ 0,9	12,3 $\pm$ 0,9 *	10,7 $\pm$ 0,7	11,1 $\pm$ 1,0 *
AF, %	58,3 $\pm$ 2,7	64,8 $\pm$ 1,7 *	67,1 $\pm$ 2,4 *	66,5 $\pm$ 1,9 *
NSA (per 100 cells)	5,1 $\pm$ 0,6	6,4 $\pm$ 1,6	3,5 $\pm$ 0,5	2,8 $\pm$ 0,8 *
NLA (per 100 cells)	1,3 $\pm$ 0,3	0,8 $\pm$ 0,1 *	0,4 $\pm$ 0,2 *#	0,4 $\pm$ 0,1 *#
NA (per 100 cells)	6,4 $\pm$ 0,8	7,2 $\pm$ 1,6	3,9 $\pm$ 0,5 *#	3,1 $\pm$ 0,9 *#
P ₃ , %	27,1 $\pm$ 5,0	36,5 $\pm$ 4,0	26,6 $\pm$ 2,9 #	27,1 $\pm$ 1,6 #

From the data in Table 5, it can be seen that in the women of the main group, high activity of SOD persisted throughout the postoperative period, and this led to a compensatory decrease in the concentration of G-S-T by 3-7 days, and by 5-7 days to a decrease in the level of lipid peroxides.

Table 5

The state of LPO and AOP after radical operations in patients with uterine oncopathology on the background of selmevitis ($M\pm m$)

Indicators	Before the operation, n=16	1 st day, n=15	3-4 days, n=13	5-7 days, n=18
DC, nmol / ml	114,4 $\pm$ 6,1	114,3 $\pm$ 7,3	102,9 $\pm$ 6,8 *#	100,8 $\pm$ 3,8 *#
MDA, nmol / ml	15,3 $\pm$ 1,3	13,7 $\pm$ 0,9	17,1 $\pm$ 1,5 *#	16,6 $\pm$ 1,0 *#
Vit. E, nmol / ml	4,9 $\pm$ 0,3	5,3 $\pm$ 0,7	4,4 $\pm$ 0,3	3,4 $\pm$ 0,3 *#
SOD, c.u.	27,5 $\pm$ 5,6	43,9 $\pm$ 6,6 *#	31,0 $\pm$ 6,9 #	34,1 $\pm$ 6,7 *#
G-S-T, nmol / (min.l)	940,6 $\pm$ 175,1	793,3 $\pm$ 125,1	523,2 $\pm$ 105,5 *#	675,7 $\pm$ 127,9 *

The women in the comparison group showed a high degree of correlation between the level of LPO products and the concentration of FH, IRP, and the number of P. There was a strong positive relationship between G–S–T and ART and INR, and a strong negative relationship between G–S–T and IRP, G–S–T and the number of P.

Thus, oncopathology of the uterus, extensive gynecological surgery (removal of the uterus with appendages) contributes to the intensification of LPO and the associated activation of platelet and coagulation units of hemostasis.

In addition to traditional therapy with selmevitum, which was accompanied by an increase in AOP and inhibition of LPO, hemostatic disorders caused by malignant uterine disease and their surgical treatment are significantly weakened and hemostatic indicators quickly returned to original values. This confirms the connection of hemostasiological

changes with the intensification of LPO and provides grounds for including the antioxidant selmevitum in the complex of conventional therapy.

Conclusions

1. In patients suffering from uterine cancer, lipid peroxidation was accelerated and antioxidant protection was activated (a twofold increase in the level of glutathione-S-transferase) and signs of the development of the "transitional" stage of disseminated intravascular coagulation (elongation of APTT, TT, an increase in PR, INR, RFMC, PDF and fibrinogen levels, a decrease in AT III, IRP, an increase in the number of APF and the number of large aggregates) were found, which persisted after radical surgery for oncopathology of the uterus up to 7 days.
2. Activation of hemostasis in all surgical interventions in patients with uterine cancer is synchronized with the acceleration of LPO and a decrease in the content of vitamin E in red blood cells. The addition of traditional therapy with selmevitum limits the activation of LPO and leads to an increase in the antioxidant potential.

Practical recommendations

1. To limit hemostasiological changes in the surgical treatment of patients with uterine cancer, it is recommended to prescribe selmevitum 1 tablet per day (14 days before and 14 days after surgery against the background of traditional therapy).
2. Before performing laparotomic radical operations for the treatment of malignant diseases of the uterus, and in the postoperative period, it is recommended to establish the number of P, the number of small platelet aggregates, determine ART, APTT, TT, PR, INR, FG, RFMC, PDF, AT III, IRP, the level of primary and secondary products of LP and G-S-T.

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