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LEVEL OF TUMOR MARKERS IN THE POPULATION OF SOUTHERN YAKUTIA CONSUMING UNTREATED AND FILTERED WATER

The level of tumor markers was assessed in working-age residents of the Aldan district who consume untreated and filtered water. The average level of tumor markers varied within the normal range. Residents of the city of Aldan who consume unpurified water have shown an increase in the average level of cancer embryonic antigen and carbohydrate antigen Ca19-9 compared to other groups. This group also has a high proportion of individuals with elevated levels of carbohydrate antigen Ca15-3, cancer embryonic antigen, and among women, carbohydrate antigen CA-125. Among individuals who consume filtered water, there is a high proportion of individuals with elevated levels of alpha-fetoprotein, which is more commonly found among residents of the city of Tommot, indicating a need for more in-depth study.

Keywords: tumor markers, filtered water, untreated water, South Yakutia

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Introduction. Cancer incidence is of social significance worldwide. Mortality from cancer in Russia ranks second, in Yakutia in 20 districts the mortality rate from neoplasms for 2022 exceeded the average for the republic, while the Aldan district was one of the districts with the highest cancer mortality rate, the rate per 100,000 population was (217,7), exceeding the average republican rate was 72,3% [3]. In the modern world, screening of tumor markers (oncomarkers - biological substances that are produced by the cancer tissue itself or the body in response to cancer growth) is one of the methods for detecting cancer, determining the stage of the disease and the prognosis of the treatment. However, a temporary increase in the level of tumor markers can also be provoked by other factors, such as a relapse of chronic diseases, as well as environmental pollution with toxic, chemical substances [11, 5, 8]. Among residents of Primorsky Krai, a dependence of the prevalence of oncological diseases on the quality of the external environment has been identified; in areas of environmental stress, a high incidence of lung, stomach, intestinal and skin cancer is observed [13].

The Aldan district belongs to the industrial regions of the Republic of Sakha (Yakutia), where open-pit mining is carried out, which contributes to the deterioration of the environmental situation, mainly water sources [7]. As a result of the activities of gold mining organizations, 9-12 million cubic meters are returned to water bodies. In 2021 and 2022, the water quality of the Aldan River was characterized as "very polluted", 3rd class of category "b", where out of 14 hydrochemical indicators examined, 9 were polluting, which can contribute to the development of various diseases, including cancer, therefore, medical and environmental monitoring, screening to determine the level of tumor markers in residents of the Aldan district is relevant [1, 2, 10, 15].

The aim of the study was to assess the level of tumor markers in residents of the Aldan region who consume filtered and unpurified water.

Materials and methods of the study: A survey of 170 people of working age from the Aldan district was conducted: 115 people from the city of Aldan (58 men, average age 44 (33; 52) and women 57 and 39 (32; 45) respectively) and 55 people from the city of Tommot (7 men and 48 women), average age of men 62 (41; 64), women 48 (37; 59) years (Table 1). The study was approved by the decision of the Local Ethics Committee at the Federal State Budgetary Scientific Institution "Yakutia Scientific Center for Clinical and Medical Research". The study participants were informed in advance about the goals and nature of the study, and all of them provided written voluntary consent for it to be conducted.

The main source of centralized drinking water supply in the settlements of the Aldan district is underground water, which enters the water supply system from special water intake wells. To determine the type of water consumed for food, all participants completed a survey: "What kind of water do you most often drink?" and selected an answer (1 - water from harvested ice; 2 - packaged, 3 - filtered (household filters), 4 - unpurified (tap). Persons who answered that they drink packaged (bottled water in a polycarbonate container) and filtered water were combined into 1 group, as those who drink purified filtered water.

Blood sampling was performed in the morning before 11 a.m., on an empty stomach. The enzyme immunoassay method was used to determine the level of tumor markers alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), carbohydrate antigens CA 15-3, CA 19-9 and CA-125 in women only, using test kits from Vector-Best (Novosibirsk, Russia) on the Uniplan enzyme immunoassay analyzer (Russia).

Statistical data processing was performed using the IBM SPSS Statistics

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23 software package. The data are presented as median (Me) and interquartile range [Q25; Q75]. The nonparametric Mann-Whitney U-test was used to compare two independent samples. The normality of distribution was tested using the Kolmogorov-Smirnov method. Differences were considered statistically significant if the level of significance was p < 0.05. Correlation analysis was performed using the Spearman method.

Results and discussion. Analysis of the content of tumor markers in the blood serum showed that the average levels of CEA, AFP, CA-19-9, CA-15-3, CA-125 in residents of Aldan and Tommot were within normal values in all groups (Tables 1, 2, 3).

Analysis of the level of tumor markers by place of residence and gender revealed that men and women in Aldan had an increase in the level of CEA by 36 and 21%, compared with men and women in Tommot, respectively, while the level of CEA in men in Aldan was 25% higher than in women in Aldan. Men in Aldan also showed an increase in Ca15-3 by 35%, compared with women in Aldan (Table 1). The level of other tumor markers did not statistically change depending on place of residence and gender.

Analysis of the level of tumor markers depending on the type of water consumed showed that the average concentration of CEA in Aldan residents consuming untreated water was increased by 22,3% (p=0.033) compared to those consuming filtered water from Aldan, and by 46,6% (p=0.002) compared to Tommot residents consuming untreated water and by 44,7% (p=0.000) filtered water. In Aldan residents consuming filtered water, the level of CEA was also higher by 28,8% (p=0.041) compared to Tommot residents consuming untreated water and by 26,9% (p=0.000) consuming filtered water (Table 1).

Carcinoembryonic antigen is a glycoprotein protein that is produced in small quantities in the cells of healthy people (0-5 ng/ml), an increase of 7-10 ng/ml is noted in people suffering from alcoholism and from 5 to 10 ng/ml in smokers, a slight increase in the level of CEA can be associated with various inflammatory processes (with liver cirrhosis, chronic hepatitis, pancreatitis, ulcerative colitis, Crohn's disease, pneumonia, bronchitis, tuberculosis, emphysema, cystic fibrosis), autoimmune, benign diseases of internal organs, with oncological diseases it can reach very high values. The CEA test is most sensitive for colon and rectal cancer, so it is used in primary diagnostics, but an increase is also noted in cancer of the stomach, pancreas, breast, lung, prostate, ovaries, metastases of cancer of various origins to the liver and bones, but in these diseases the sensitivity of the method is significantly lower [14].

The average concentration of AFP in the groups did not statistically change significantly depending on the quality of the water consumed, but among residents of Tommot who consumed filtered water, it tended to increase (Table 2).

Alpha-fetoprotein (AFP) is a glycoprotein produced by the yolk sac of the embryo. It has high diagnostic sensitivity in hepatocellular carcinoma. It increases in teratocarcinoma containing elements of the yolk sac. Indications for AFP testing: diagnostics of primary hepatocellular carcinoma; liver cancer screening in patients with liver cirrhosis and chronic hepatitis once every 6 months; monitoring treatment of primary liver cancer (with successful treatment, normalization within 1 month); early detection of liver cancer recurrence; prenatal diagnostics of fetal neural tube lesions and Down syndrome. AFP level in some pathologies (in IU/ml): - hepatocellular carcinoma > 800, - hepatoblastoma (children) > 400, - testicular teratoblastoma > 500, - ovarian dysgerminoma > 1000, - liver metastases > 10, - hepatitis B and C > 10–50, - acute poisoning up to 100 [14].

The average level of CA-15-3 in all residents (men and women) and CA-125 in women of Aldan and Tommot did not differ from the type of water consumed (Tables 2, 3). The tumor marker CA-15-3 is often used in diagnosing tumors in the mammary gland, but at the initial stages of cancer its level may not exceed the norm, and therefore it is recommended to carry out it in combination with CEA. This analysis is prescribed to people with benign or malignant neoplasms in the mammary glands, lungs, ovaries, pancreas, cervix, liver cirrhosis and endometrial carcinoma.

CA-125 is a glycoprotein, a highly sensitive test for detecting ovarian cancer in women, its values vary from 35 IU/L to several thousand and depend on the stage of the disease and the histological structure of the cell type, but an increase in CA-125 from 35 to 150 IU/L in women of reproductive age may be associated with other conditions (pregnancy, tuberculosis, pneumonia, pancreatitis, endometriosis, uterine fibroids, during menstruation, etc.), which in some cases requires additional research, therefore, the determination of tumor-associated antigen CA-125 is not a strictly specific screening marker for the early diagnosis of ovarian cancer [6].

The average content of CA-19-9 in all residents did not exceed the norm, but in Aldan residents drinking untreated water it was slightly higher (p=0,039) than in those drinking filtered water in Aldan. Correlation analysis showed the presence of a direct connection with REA (r=0.427, p<0,000).

The cancer antigen CA 19-9 is a glycoprotein normally produced by epithelial cells of the gastrointestinal tract. Its level increases in almost all patients with tumors of the gastrointestinal tract, especially the pancreas. An increase in the concentration of CA 19-9 is also noted

Table 1

Level of tumor markers in men and women of the Aldan region depending on the place of residence, Me (25-75% percentiles)

Indicators	Aldan		Tommot	
	Men n=58	Women n=57	Men n=7	Women n=48
	1	2	3	4
Age, years	44 (33; 52)	39 (32; 45)	62 (41; 64)	48 (37; 59)
СЭА up to 5 ng/ml	3.41 (2.47; 4.36) p=0.000 1-2 p=0.002 1-3	2.55 (2.99; 3.04) p=0.000 2-4	2.17 (1.84; 2.38)	2.01 (1.15; 2.89)
AFP up to 12 IU/L	2.98 (1.87; 4.70)	2.68 (1.74; 4.34)	3.69 (3.47; 8.52) p=0.087 1-3	3.32 (1.73; 7.25)
CA 15-3 3-30 U/ml	15.80 (6.68; 26.45) p=0.014 1-2	10.22 (3.49; 17.79)	15.22 (10.77; 23.57)	10.49 (5.37; 15.02)
CA 19-9 up to 30 U/ml	0.00 (0.00; 1.29)	0.09 (0.00; 3.00)	0.37 (0.00; 2.96)	0.00 (0.00; 1.92)
Ca 125 0-35 U/ml		7.35 (4.83; 10.81)		8.38 (4.53; 11.29)

with the localization of other oncological processes (colorectal cancer, liver cancer, stomach, gallbladder or bile ducts, ovaries), liver diseases (hepatitis, cirrhosis), cholelithiasis, pancreatitis, cystic fibrosis. The CA 19-9 test is of great importance for the early detection of pancreatic tumor metastases, but some people (7-10%) do not have the gene encoding the CA 19-9 antigen and CA 19-9 is not synthesized and is not detected even in malignant tumors, so it is necessary to simultaneously conduct the test with CEA [9].

The proportion of people with elevated tumor marker levels (above the norm) was higher in Aldan than in Tommot. A slight increase in the CEA level was noted in 8 people (4,7%) from Aldan, in 3 (12,5%) consuming untreated water and 5 (5,5%) filtered water. CA -125 was above the norm in 4 people (3,8%), in 3 women (5,5%) from Aldan, one consuming untreated water and two consuming filtered waters, in Tommot in one woman (2,5%) consuming filtered water. CA 15-3 above the norm was noted only in Aldan residents, in 6 people (3,5%) - two (1,2%) consuming untreated and four (2,4%) filtered water. The concentration of AFP above the norm was noted in people consuming filtered water in the city of Aldan in 4 people (2,4%), in the city of Tommot in 7 (4,1%).

Moderate increase in AFP is not always a characteristic sign of cancer; according to literature data, residents of the village of Tommot showed a tendency for AFP levels to increase with age, compared to the control group in the village of Modut, Namsky district, with a satisfactory environmental situation [12]. Increased levels of tumor markers can be caused by drinking water with increased hardness; direct strong correlations between water hardness and tumor marker levels were found in residents of Yakutia: AFP (r=0,134; p=0,000), CEA (r=0,211; p=0,000), PSA (r=0,360; p=0,000) in men and CA-125 (r=0,290; p=0,000) in women [4].

Thus, the average level of tumor markers CEA, AFP, CA-19-9, CA-15-3, CA-125 among residents of the Aldan district did not exceed normal values for both residents of Aldan and residents of Tommot. However, among residents of Aldan who drink untreated water, the average values of CEA and CA-19-9 were significantly higher compared to other groups. An analysis of the proportion of people with elevated tumor marker levels showed that higher levels (above normal) of CA-125, Ca15-3 and CEA are more common among residents of Aldan who drink untreated water.

Table 2

Level of tumor markers in residents of the Aldan region depending on the type of water consumed, Me (25-75% percentiles)

Indicators	Aldan		Tommot	
	Unpurified water n=24	Filtered water n=91	Unpurified water n=10	Filtered water n=45
	1	2	3	4
СЭА up to 5 ng/ml	3.67 (2.38; 4.74) p=0.033 1-2 p=0.002 1-3 p=0.000 1-4	2.78 (2.17; 3.43) p=0.041 2-3 p=0.000 2-4	1.96 (1.47; 3.13)	2.03 (1.22; 2.38)
AFP up to 12 IU/L	2.51 (1.79; 4.51)	2.85 (1.84; 4.78)	2.89 (1.15; 4.05)	3.47 (1.73; 7.34) p=0.081 3-4
CA 15-3 3-30 U/ml	13.20 (8.11; 21.16)	11.57 (4.55; 22.28)	13.14 (5.69; 21.71)	11.49 (5.53; 16.07)
CA 19-9 up to 30 U/ml	1.77 (0.00; 2.99) p=0.039 1-2	0.00 (0.00; 1.48)	0.00 (0.00; 0.37)	0.00 (0.00; 1.15)

Table 3

The level of the tumor marker CA-125 in women of the Aldan region depending on the type of water consumed, Me (25-75% percentiles)

Indicators	Aldan		Tommot	
	Women			
	Unpurified water n=12	Filtered water n=45	Unpurified water n=8	Filtered water n=40
Ca 125 0-35 Ед/мл	8.17 (4.95; 14.06)	6.96 (4.88; 10.98)	5.76 (3.86; 9.83)	8.38 (4.51; 11.82)

Among residents of Aldan and Tommot who drink filtered water, the proportion of people with elevated AFP levels (above normal) is more common than among those who drink untreated water. This fact requires further study, since other negative factors may be superimposed in this city.

The authors declare no conflict of interest.

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PROSPECTS FOR THE DETECTION OF OVARIAN CANCER BY GENETIC TESTING OF ASPIRATE FROM THE UTERINE CAVITY

In the article, a genetic study of biological samples from uterine cavity aspirate was performed in patients with serous ovarian carcinoma in order to identify gene mutations characteristic of ovarian tumor lesions. It has been proven that the aspiration from the uterine cavity contains diagnostically significant numbers of cells or fragments of ovarian cancer cells necessary for molecular genetic analysis and detection of mutations in the *TP53, FAT3, CSMD3, BRAF*, and *KRAS* genes. Mutations of the *BRCA1/2* genes are rare. The detection of *TP53, FAT3, CSMD3, BRAF,* and *KRAS* gene mutations in uterine aspirate cells requires an active diagnostic search for the detection of ovarian serous carcinoma.

Keywords: ovarian cancer, serous carcinoma, morbid obesity, oncogenic mutations, aspiration biopsy.

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Introduction. Ovarian cancer is the ninth most common type of cancer in women in Russia, accounting for approximately 3,7% of all cancers and 4,7% of deaths among patients with oncological pathology [2]. Malignant ovarian tumors occupy the first place among the causes of death of women with oncogynecological pathology [16]. Most cases of ovarian cancer are first diagnosed at late stages, which is due to the lack of effective methods of early diagnosis and the almost asymptomatic course of the disease [11]. It is extremely difficult to identify clear clinical signs of ovarian tumors, which explains the interest of oncologists in the risk factors for the development of this pathology and the development of effective methodological approaches for its early detection [14].

The use of ultrasound, tomographic (X-ray and magnetic resonance) diagnostic methods helps to identify malignant ovarian pathology in many ways, but these approaches cannot be considered as generally available to a wide range of women, especially at the screening stage [8]. Unfortunately, the determination of the concentration of adenogenic cancer antigen CA-125, the secretory protein of human epididymis 4 (HE4) in the blood, is of little informative value for detecting ovarian cancer at the initial stages [13]. In clinical practice, multiple determination of markers in the blood is used primarily to monitor treatment results and timely detect relapses [15].

Recently, there has been a growing number of proponents that screening should be performed only for primary