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Reduction of Zinc in the Body as a Risk of Developing Early Liver Damage in the Adult Population of the Aral Sea Region

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Abstract

Diseases of the hepatobilar system in the adult population in the zone of ecological trouble in the Aral Sea region have a special damage mechanism. The main factors are environmental pollution among chemicals against the background of use for irrigation of land in the Southern region of Kazakhstan. In recent years, the growth of the disease in the disaster zone of the Aral Sea region has been revealed. The main load in the body takes the liver. One of the functions of the liver is the synthesis and regulation of bio-elements in the body.

Two settlements were selected for the surveys: from the disaster zone of the Aral Sea region of Aralsk and the control zone of the village of Atau of the Karaganda region, which are as close as possible to the population and living conditions. Diseases of the hepatobiliary system are exposed according to the protocols of diagnosis and treatment: clinical examination, biochemical blood analysis, ultrasound examination of the hepatobiliary zone and determination of all the examined individuals in the blood zinc. Emphasis was placed on the time a person lived in the area.

The most sensitive tests for liver damage are triglycerides, cholesterol, aspartate aminotransferase, and a decrease in blood zinc. Ultrasound diagnostics of the hepatobiliary system does not always correspond to laboratory parameters. Consequently, a decrease in zinc is characteristic of the disaster zone of the Priaralye, which is an indicator of damage to the hepatobiliary zone, which requires preventive measures for the population of the Aral Sea region.

Keywords: Ecological distress; Disaster zone Aralsk Priaralie; Diseases of the hepatobiliary system; Reduction of zinc in the blood

Introduction

The urgency of the problem

The Aral problem, as the largest ecological catastrophe of the planet, has become acute. Intensive desertification and steady irreversible processes of environmental degradation, deterioration of living conditions, an increase in the incidence caused new socio-economic and ecological situations that require legislative solutions and legal regulation of measures for social protection of the population living in ecologically unfavorable areas [1,2].

The extremely tense environmental situation in the Aral Sea region has created a direct threat to public health. Among the environmental factors affecting the health of the population in Priaralye, desertification of territories, deficit of benign drinking water, increased salt-dust removal from the dried bottom of the Aral Sea, massive salinization of lands, chemical pollution of natural environments (water, air, soil, plants), increased air dryness should be noted, strong temperature differences [3].

The increased load on the body, due to the widespread production of chemical products harmful to humans that enter the environment, has changed the immunobiological reactivity of residents. This leads to disorders of the main regulatory systems of the body such as the hepatobiliary system, which is responsible for the detoxification of the body, impaired metabolic processes [4,5].

Over the past 20 years, there is a clear upward trend in the number of diseases of the hepatobiliary system throughout the world. Only in the CIS countries annually from 500 thousand to 1 million people are registered suffering from a particular hepatic pathology. There is an increase in the frequency of the pathology of the hepatobiliary system at a young age. In the etiology of biliary tract dysfunction, the share of environmental factors can be from 14% to 36%. It was noted that in areas with unfavorable environmental conditions, hepatobiliary pathology occurs 3-4 times more often than in conditionally "clean" territories [6,7].

There are many poisons, including those that have a so-called affinity for liver cells, and are hepatotropic. These include benzene, phosphorus, fluorine, arsenic, heavy metals, styrene, organophosphorus pesticides, chlorinated naphthalenes and hydrocarbons, azo dyes and other [8]. These toxic substances have a specific negative effect on the liver tissue even in small doses [9].

The accumulation of copper and cadmium in the liver cells reduces the synthesis of ceruloplasmin, leads to an imbalance of zinc in the body, contributes to the development of cirrhosis and liver cancer, having an effect on liver cell microsome transaminases, disrupts liver detoxification function [10,11]. When zinc deficiency decreases the activity of pancreatic carboxypeptidase A and alkaline phosphatase, insulin deposition is disturbed, which leads to the development of diabetes mellitus type I [12,13].

Materials and Methods

The sample was carried out in clinical laboratories. Diagnoses were set, as first revealed by outpatient cards. Two settlements were selected for the survey: from the zone of ecological disaster in Aral sea region-the city of Aralsk, Kyzylorda Oblast, and the control area, and ecological clean-the settlement of Atasu, Karaganda Oblast. On the basis of newly diagnosed diseases by general practitioners, the entire contingent surveyed was divided into 2 groups (having diseases of the hepatobiliary system and not having this pathology).

The city of Aralsk refers to the “disaster” zone. A total of 910 people living in this region were examined, of which 657 people were ill with the hepatobiliary system. Without this pathology, 253 people were treated.

In the control village Atasu, 799 people were examined, of which 489 had hepatobiliary system diseases, 310 had no liver disease.

Conducted hygienic studies allowed to identify the disaster zone of the Aral Sea region corresponds to the territory of the city of Aralsk according to the order No. 1468-XII of 06/30/1992 "On social protection of citizens affected by the environmental disaster in the Aral Sea region" (modified and supplemented from 03.07.2013) [14].

- The main criteria for determining the boundaries of the ecological disaster zone are:
- The steady increase in mortality of the population
- Forced migration for environmental reasons
- Exceeding the standards of maximum permissible concentrations of pollutants in the environment in size, threatening the life of the population
- Complete destruction of ecosystems and the loss of their ability to heal
- Catastrophic shallowing of water bodies, exceeding the secular fluctuations

The control zone for the surveyed was the village of Atasu, Karaganda oblast, located more than 1000 km from the Aral Sea, characterized as an ecological clean zone. Epidemiological spreads of liver disease in the surveyed areas were obtained according to reported data-forms 12 and individual outpatient cards. For this form, diseases of the hepatobiliary system include chronic non-calculous cholecystitis, chronic calculous cholecystitis, cholangitis, and viral hepatitis. According to reported data, non-infectious liver diseases have not been studied. At the stage of selection of patients, viral hepatitis is excluded by credentials (Form 12).

Considering the presence of cadmium and chromium in drinking water exceeding MPC 1.1-1.2 times, in soil chlorides 2.1 times MPC and sulfates 24 times MPC, in the air fine dust 65% and iron 1.3 times MPC lead to the development damage to the liver of the population in the disaster area. To solve these problems used:

- Clinical examination of the examined (collection of complaints, history of the disease and life, physical examination) with filling in the clinical protocol
- Determination of the biochemical analysis of blood characterized by the state and function of the liver (ALAT, ASAT, GGTP, alkaline phosphatase, bilirubin, cholesterol, TG, total protein, albumin, glucose in the blood), taking into account the time of residence in a given territory
- Ultrasound of the hepatobiliary system with determination of the size of the liver, echo structure, the presence of induration, formations and dilation of the liver vessels
- Determination of heavy metals in the blood: copper, cadmium, iron, chromium, zinc, selenium, iodine

Research Results and Discussion

1. According to the data of the clinical survey, questioning and physical examination of the examined population revealed preliminary pathology of the hepatobiliary system, such as: chronic non-calculous cholecystitis, cholelithiasis, chronic hepatitis, hepatosis, and sludge syndrome. In the catastrophe zone, chronic hepatitis predominates 5.08 times sludge syndrome 55.8 times and hepatosis 3.66 times in relation to the control zone (**Table 1**).

Table 1: The structure of diseases of the hepatobiliary system of the areas examined.

п/п No.	The structure of the diseases of the hepatobiliary system	Disaster area		Control zone	
		Abs.	%	Abs.	%
1	Chronic hepatitis	278	30,55	48	6,00

2	chronic non-calculous cholecystitis	214	23,51	305	38,17
3	Sludge Syndrome	127	13,95	2	0,25
4	Hepatosis	50	5,49	12	1,50
5	Cholelithiasis	24	2,64	22	2,75
Total:		**693**	**76,14**	**389**	**48,67**

2. In the future, clinical and laboratory materials are analyzed depending on the duration of residence in a given area among persons with identified pathologies of the hepatobiliary system. One of the main functions of the liver is a violation of metabolic processes, such as a decrease in total protein, an increase in blood sugar and an increase in TG and serum cholesterol (**Table 2**).

When analyzing the data obtained by Student's criterion in the disaster zone in Aralsk, there is a statistically significant difference with the control zone-Atasu among the examined individuals with hepatobiliary system pathology in terms of hyperglycemia, increased TG and cholesterol ($p<0.005$).

3. Specific liver function: Of the 910 examined persons in the disaster area, the cholestatic syndrome was detected by specific biochemical blood parameters: alkaline phosphatase, bilirubin (total, direct), total cholesterol. The cholestatic syndrome is most common in people living for more than 21 years. In the disaster zone, the increase in alkaline phosphatase is 12.18 times, cholesterol is 4.15 times and 42.72 times compared with the control zone (**Table 3**).

Table 2: The distribution of the examined persons with metabolic disorders, depending on the residence time in the Aral Sea conditions.

Zones	Indicators	Normal swing	X	σ	t	P	Years of residence (ages)				
							Up to 5	06-Oct	Nov-15	16-20	21<
							Abs.	Abs.	Abs.	Abs.	Abs.
catastrophe	Protein (total)	65-85 (g/l)	55,15	0,82	0,06	0,96	11	1	1	-	118
control							1	-	1	9	31
catastrophe	Glucose	4,2-6,1 mmol / l	9,59	1,43	6,72	0,00	-	-	1	1	37*
control							-	1	-	-	9
catastrophe	TG	0,14-1,82 μmol / l	2,48	0,07	35,71	0,00	-	1	2	3	190*
control							-	1	-	-	8
catastrophe	cholesterol	>5,17 mmol / l	6,40	0,14	46,85	0,00	-	1	2	5	249*
Control							5	-	-	3	60
Note: X: average value; σ: standard deviation; Student's t-test; -p<0,005 reliable significance in the catastrophe zone											

Table 3: The distribution of the surveyed persons by cholestasis depending on the time of residence in the Aral Sea conditions.

Residence time	Syndrome	Biochemical indicators	Norm	The spread of enzyme activity (increased)				OR
				catastrophe		control		1,2<
				Abs.	%	Abs.	%	
Up to 5 years	Cholestasis	Alkaline phosphatase	31-40 μ/l	-	-	1	0,11	
6-10 years				1	0,11	-	-	
11-15 years				-	-	-	-	
16-20 years				3	0,33	1	0,11	
Over 21 years old				61*	6,70	5	0,55	11,19
Up to 5 years		cholesterol	5,17 mmol/l	-	-	1	0,11	
6-10 years				1	0,1	-	-	

11-15 years				2	0,22	-	-	
16-20 years				5	0,55	3	0,33	
Over 21 years old				249*	27,36	60	6,59	3,78
Up to 5 years		Bilirubin	1,7-21 µmol/l	1	0,11	1	0,11	
6-10 years				1	0,11	-	-	
11-15 years				-	-	-	-	
16-20 years				4	0,44	-	-	
Over 21 years old				38*	4,17	1	0,11	3,48
Note: *-p<0,005 reliable significance in the catastrophe zone								

The cytolytic syndrome is exposed according to the level of transaminase activity (ALAT and ASAT) and Gammaglutamine Transpeptidase (GGTP). The cytolytic syndrome in the disaster zone of the Aral Sea region was found in 657 of 1813 people examined. The analysis of ALAT, ASAT and GGTP values are divided depending on the residence time in a given territory (on the duration of exposure to harmful factors). The time of residence of the examined were divided into 5 categories: 1-5 years, 6-10 years, 11-15 years, 16-20 years, and more than 21 years (**Table 4**).

Table 4: The distribution of the examined individuals to cytolysis depending on the residence time.

				Increased (zones)					**OR**
				Catastrophe			**1<**		**1<**
				Abs.		**%**	**Abs.**	**%**	-
Residence time	**syndrome**	**Biochemical indicators**	**Norm**	**up to 3**	**up to 10**			-	
Up to 5 years				-	-	-	1	0,12	-
6-10 years				-	-	-	-	-	-
11-15 years				-	-	-	-	-	-
16-20 years				2	1	0,33	2	0,25	-
Over 21 years old		ALAT	31-40 µ/l	73*	3	8,35	5	0,62	13,39
Up to 5 years				-	-	-	1	0,12	-
6-10 years				-	-	-	1	0,12	-
11-15 years				-	-	-	1	0,12	-
16-20 years				4	-	0,44	1	0,12	-
Over 21 years old		AST	31-37 µ/l	116*	-	12,75	15	1,88	7,09
Up to 5 years				-	-	-	4	0,50	-
6-10 years				-	-	-	1	0,12	-
11-15 years				-	-	-	-	-	-
16-20 years				1		0,11	4	0,50	-
over 21 years old	Cytolysis	GGT	32 µ/l	78		8,57	71	8,89	-
Note: *-p<0,005 reliable significance in the catastrophe zone									

4. According to the ultrasound of the hepatobiliary zone. Of the total 910 people surveyed in the disaster area. Data for hepatosis was found in 50 examined individuals, the gold standard for setting a diagnosis of hepatosis was liver ultrasound:

- Increased liver echogenicity in comparison with the cortical layer of the kidney and spleen
- Increase the size of the liver
- The phenomenon of echo attenuation
- Difficult visualization of the diaphragm, architectonics of the liver

- Sites reduce the echogenicity of individual areas (unchanged parenchyma)
- Changes are visualized with fat infiltration in excess of 30%

Among patients with ultrasound hepatosis, symptoms were found in 100% of the case, that is, as in 50 patients in the catastrophe zone and 12 patients in the control zone (**Table 5**).

Analysis of the obtained data showed that hepatosis develops in the disaster area when living for more than 21 years, due to obesity in 64.00% of patients, cytolysis 2.28 times, cholestasis 3.84 times and an increase in TG 3.36 times, more often than in the zone control (**Table 5**).

Table 5: Distribution of patients with hepatosis with the detection of ultrasound signs.

Zones	Living for more than 21 years		Obesity (1-3s.)		Ultrasound signs		Cytolysis		Cholestasis		TG<1,82 µmol/l	
	Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%
Catastrophe	50	100	32	64,00	50	100	29	57,00	32	64,00	14	28,00
Control	10	83,33	4	31,25	12	100	3	25,00	2	16,66	1	8,33

Ultrasound signs of chronic hepatitis:

- enlarged liver
- diffuse changes in the structure of the liver
- increase in liver echo-density

The analysis of patients with chronic hepatitis exhibited by biochemical indicators of 278 patients with ultrasound examinations showed that liver changes were detected in the catastrophe zone in 16 patients, cholestasis in 63.67% of patients and 96.04% of patients live for more than 21 years (**Table 6**).

Table 6: The distribution of patients with chronic hepatitis with the identification of ultrasound signs.

Zones	Total	Living for more than 21 years		Ultrasound signs		Cytolysis		Cholestasis	
		Abs.	%	Abs.	%	Abs.	%	Abs.	%
Catastrophe	278	267	96,04	16	5,75	278	100	170	63,67
Control	48	37	77,08	2	4,17	48	100	9	18,75

Thus, when making a diagnosis of chronic hepatitis in the area of ecological catastrophe is biochemical liver tests, ultrasound signs of chronic hepatitis detected only 5.75% of cases. The diagnosis of hepatosis is made on the basis of the characteristic ultrasound signs of hepatosis.

Considering the harmful environmental factors of the city of Aralsk, studying zinc levels in patients with liver pathology such as chronic hepatitis and hepatosis is more relevant. Zinc was determined in all studied individuals. Reducing zinc is characteristic only for the disaster area. A decrease in zinc in the blood was found even in relatively healthy individuals (297 individuals examined). Among patients with chronic hepatitis in 172 individuals and with hepatosis, a decrease in zinc in the blood was detected in 39 patients, mainly when living for more than 21 years in a given territory (164 and 39 cases) (**Table 7**).

Table 7: The spread of patients to reduce zinc in the disaster area.

	Reduction of zinc in the blood (normal 4000-8600 mg/l)									
	With early signs of damage (relatively healthy faces)					Liver damage (among patients)				
	Residence time									
Zone	0-4	05-09	10-14	15-20	21 or more	0-4	05-09	10-14	15-20	21 or more
Catastrophe	3	3	2	13	276	-	-	-	8	203
Total:	297					211				
Liver nosology										
Zone	Chronic hepatitis Residence time					Hepatosis				

	0-4	05-09	10-14	15-20	21 or more	0-4	05-09	10-14	15-20	21 or more
Catastrophe	-	-	-	8	164	-	-	-	-	39
Total:	**172**					**39**				

Conclusion

In the disaster zone, damage to the hepatobiliary system was detected in 657 (72.19%) of the examined persons in the city of Aralsk. Of these, more than 21 years living in this territory, 617 (73.19%) patients. Laboratory and functional signs of liver damage in the background of a decrease in zinc in the body was detected in 391 (59.51%) patients. In 141 persons (36.06%) cytolysis is accompanied with cholestasis. Signs of hepatosis were detected in 50 people; the diagnosis was made by ultrasound with a sign of hepatosis. The diagnosis of chronic hepatitis is set on the basis of the cytolytic syndrome (increase in ALAT, ASAT, and GGTP) to 278 subjects (42.31%). An ultrasound scan showed signs of hepatitis in only 16 patients (5.75%).

In the control group, zinc in the blood was normal (4000-8600 μg/l).

Thus, the reduction of zinc in the blood among the adult population of the zone of ecological disaster in Aral Sea region, in particular, the city of Aralsk, is a clear risk factor for liver damage against the background of environmental stress, which requires preventive measures.

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