THE USE OF THERAPEUTIC AGENTS DERIVED FROM THE PLANTS AND FRUITS GROWING IN KYRGYZSTAN FOR THE ELIMINATION OF ORGANOCHLORINE PESTICIDES FROM GASTROINTESTINAL TRACT OF NURSING WOMEN.

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Introduction

- Persistent organic pollutants (POPs), including the most common and dangerous organochlorine pesticides (OCPs) is a problem that remains pressing. In rural areas, uptake of OCPs into the human body occurs by ingestion in 80-90% of cases, in urban areas - in 100%. In women living in the vicinity of the former pesticide storehouses, agro-airstrips and pesticide dumpsites, OCPs are detected in 100% of cases.
- OCP exposure is linked to higher rates of various pathologies of pregnant women, fetuses, newborns and infants [1]. In southern Kyrgyzstan, OCPs are the major cause of a number of pathologies, including cancers, hepatitis, infant encephalopathy, disbacteriosis, immunodeficiency, anemia, intestinal (infection) disorders of unknown etiology, and other pathologies.

Introduction

- For the prevention of the above pathologies, taking into account the fact that 90-100% of OCPs are taken into the body through the gastrointestinal tract (GIT), there is only one way to eliminate OCPs from the GIT and this is a search for therapeutic agents for their elimination from the body.
- It's well known that pectin substances are used to remove ecotoxicants [2-7] as well as antioxidants - dibunol, emoxipin, cytochrome and other agents inhibit lipid peroxidation, i.e. they can be used in complex therapy of different diseases, including in combination with xenobiotics [8].

Introduction

- Numerous data published both in local and foreign literature indicate that there are no effective therapeutic agents for the neutralization and elimination of OCPs from the human body. Not to mention universal, specific antidotes - there are no antidotes; even primitive ones have not been created for OCPs so far.
- The aim of this work was therefore to search for therapeutic agents for the neutralization and elimination of pesticides from the human body (gastrointestinal tract); it is necessary to search for highly effective agents, cheap, accessible to all segments of the population.

Materials and methods

- Breast milk samples were collected from the women who contacted us about the illness of their children from the "maternity hospital" and the women themselves. All samples were collected with the written consent of the participants after explaining to them the purpose of the study. All studies at the Institute of Medical Problems of the Southern Branch of the National Academy of Sciences of the Kyrgyz Republic are carried out only after obtaining the permission (conclusion) of the ethical commission, as well as with the consent of the study participants indicated in medical cards.

Materials and methods

- The developed medical cards contain all necessary information about the woman in labor, her children and spouse (spouse's profession, possible contact with pesticides), place of birth, ethnicity, weight, height, number of pregnancies, childbirth, stillbirths, miscarriages, abortions, information about nutrition (for example, markets where urban women buy food, or gardens/fields where rural women pick fruits or vegetables, consumption of sour milk (national drinks ayran, zhuurat (goat milk airan) suzmo, kymyz) and meat products [9].
- A special attention was given to the cases (and there were most of them) when the examinations were carried out at the request of the examined women (since we covered all the expenses for the examination, further conducting treatment aimed at removing of OCPs from the body of nursing mothers with the use of therapeutic agents we obtained from local endemic plants and their fruits which possess sorbent and detoxic properties [10].

Materials and methods

- Considering the fact that the most common among the OCPs are α-HCH and β-HCH, DDE, and OCPs detection rate and concentration levels in breast milk depend on the time after childbirth [11], we therefore selected the women who came to us on the 28-30th day after childbirth. All women were of the one ethnic group; Uzbek women mainly consume vegetable products, while Kyrgyz women consume meat and dairy products (the above types of OCPs were detected in breast milk of these women).
- All women under observation were allocated into 2 groups. Group I consisted of 27 nursing women and Group II (control group) included 24 women. Women in Group II didn't receive any treatment. In Group I, a concentrate derived from medicinal herbs was used to neutralize and remove pesticides from GT, including crushed seeds which contain unsaturated fatty acids up to 4%, growing in southern region of the Kyrgyz Republic in mid- and high-mountain areas; they are rich in vitamins, pectins, microelements and biologically active substances, with slightly bile, urine and diaphoretic properties.

Materials and methods

- The concentrate was used in the form of tea daily, 2 teaspoons (15 grams) per 300 ml of boiling water, brewed in a thermos and administered during a day [12]. A golden root tincture (analogous to ginseng) (produced by the Institute of Medical Problems, Southern Branch of the National Academy of Sciences of the Kyrgyz Republic) derived from Rhodiola Rosea (1:10 in a 30% alcohol solution) which grows in a high mountainous region (2500-3500 meters above sea level) in Chon-Alay district of the Osh Region of the Kyrgyz Republic. The tincture was administered by 25-30 drops twice a day. The course of treatment was 10-12 days.
- Breast milk samples were collected for microbiological and toxicological analysis in accordance with the methodological recommendations of the Central Research Institute of Ecology of the Ministry of Health, MNIIEiM, TSOLIUV, Research Institute of Pediatrics and Pediatric Surgery [9].

Materials and methods

- Morning anterior (initial) and posterior (residual) portions of breast milk were collected from 82 nursing mothers. Breast milk samples (10 ml) were collected in a sterile disposable tube with a lid and then transported to the laboratory in the same container. Sampling of breast milk, blood (5 ml) and urine (10 ml) for OCPs was carried out in accordance with the methodological recommendation [13] on the gas chromatograph "Tsvet -500 M", (Dzerzhinsk, Russia, 1990, upgraded, with software). The presence of the following pesticides was determined: hexachlorocyclohexane (HCH) (α-, β-, γ-, δ- isomers), dichlorodiphenyltrichloroethane (DDT), dichlorodiphenyldichloroethane (DDD) and dichlorodiphenylethylene (DDE) isomers, aldrin, dieldrin, and heptachlor.

Materials and methods

- Statistical analysis of the obtained results was carried out using the methods of variation statistics recommended for biomedical research (https://www.medcalc.org/calc/odds_ratio.php).
- Odds Ratio and Relative Risk Calculator (MedCalc software, free online) on a Pentium Core Duo PC. The results were processed using MS Access 2003 and MS Excel 2007 for Windows XP, BIOSTAT.

Results and Discussion

- The following types of OCPs were found in breast milk of the women under observation: hexachlorocyclohexane isomers: α-HCH, β-HCH, γ-HCH, dichlorodiphenylethylene (DDE). Other types of OCPs - δ-HCH, DDT, DDD, heptachlor, aldrin and dieldrin were not detected in the examined samples of breast milk samples, i.e. α-, β- and γ-HCH and DDE are the most common OCPs. The number of examined and the proportion of women with OCPs in BM samples by groups are shown in Table 1.

Table 1. Detection rates and concentration levels of OCPs in breast milk samples before and after the treatment

Group	Type of OCP	Before the treatment				After the treatment				
		Number of samples	Number of detected	%	Concentration level, mg/l	Number of samples	Number of detected	%	Concentration level, mg/l	P
I	HCH	27	15	55.5	0,0278 ±0,0,004	27	15	55,5	0,0135± 0,006	
									2,05 times decrease	
	DDE	27	24	88.9	0,006238± 0,0042	27	18	66,7	0,0031± 0,0006	**0.5511**
									2. 2,01 times 3. decrease	
II	HCH	24	16	66.7	0,0084± 0,0026	24	16	66,7	0,0072± 0,003	
									1,16 times decrease	
	DDE	24	16	66.7	0,0086± 0,003	24	16	66,7	0,01 ±0,006	

Results and Discussion

- In Group I, of the 27 examined women HCH in BM before and after the treatment was detected in 15, concentration levels were 0.0278±0.0.004 and 0.0135± 0.006 mg / l, respectively, DDE - in 24 (88.9%), concentration level was 0.006238 ± 0.0042, after the treatment - in 18 (6.7%), concentration level 0.0031 ± 0.0006 mg/l, $P < 0.05$.
- As shown in Table 1, concentration levels of HCH in BM in Group I after the treatment decreased by half, but the detection rates remained unchanged. The number of detected with DDE decreased from 24 (88.9%) to 15 (55.5%), concentration levels were also decreased by half.
- In Group II no changes were registered. In control group, the detection rate of HCH and DDE remained unchanged amounting to 66.7%, and concentration levels decreased by 1.16 times, but by 2.01 times against Group I. This is probably due to the intake of OCPs or with an increase in lactation. Concentration levels of DDE slightly increased from 0.0086±0.003 mg/l, after 10 days to 0.01±0.006 mg/l, $P = 0.3947$.

Concentration levels of OCPs in blood samples before and after the treatment in control group are shown in Table 2. OCPs detected in blood samples before and after the treatment

Group	Type of OCP	Before the treatment				After the treatment				
		Number of samples	Number of detected	%	Concentration level, mg/l	Number of samples	Number of detected	%	Concentration level, mg/l	P
I	HCH	27	9	33,3	0,026744 ± 0,009934	27	6	22,2	0,0005± 0,000189	**0.29**
									53,5 times decrease	
	DDE	27	15	55,5	0,00257 ± 0,0006	27	15	55,5	0,0009 ± 0,000063	
									28,5 times decrease	
II	HCH	24	16	66,7	0,0093± 0,0031	24	16	66,7	0,0068± 0,0021	
									1,36 times decrease	
	DDE	24	12	50,0	0,0033± 0,0014	24	16	66,7	0,0038± 0,0013	
									1,15 times increase	

Results and Discussion

- HCH in blood samples was detected in 9-33.3%, concentration level was 0.026744±0.009934 mg/l; after the treatment HCH was found in 6 – 22.2%, P=0.29, concentration level was 0.0005 ±000189 mg/l or decreased by 53.5 times. DDE detection rate remained at the same level, amounting to 55.5%, but concentration level decreased from 0.00257 ± 0.0006 to 0.0009 ± 0.000063 mg/l or by 28.5 times.
- Detection rate of HCH in blood in control group remained unchanged, amounting to 66.7%, but concentration level decreased by 1.36 times, the rate of DDE detection in blood, on the contrary, increased from 50.0% to 66.7% , and concentration– by 1.15 times.
- Concentration levels of OCPs in urine samples before and after the treatment (in control group) are given in Table 3.

Table 3. OCPs detected in urine samples of women before and after the treatment

Group	Type of OCP	Before the treatment				After the treatment				
		Number of samples	Number of detected	%	Concentration level, mg/l	Number of samples	Number of detected	%	Concentration level, mg/l	P
I	HCH	27	3	11,1	0,0002	27	6	22,2	0,0005± 0,00013	**0.3544**
									58 times decrease	
	DDE	27	9	33,3	0,0029±0,001	27	1	3,7	Traces	
II	HCH	24	12	50,0	0,005±0,0013	24	12	50,0	0,00047 ±0,0002	
									1,06 times decrease	
	DDE	24	3	12,5	0,0002±0,00	24	4	16,7	0,00018±0,00	

Results and Discussion

- Detection rate of HCH in urine samples of women in Group I after the treatment increased from 11.1% to 22.2%, P = 0.3544. Traces of DDE were found in one case after the treatment, P = 0.2051, P = 0.0004, concentration level of HCH decreased by 58 times. In Group II, the detection rate and concentration levels of HCH remained unchanged. Detection rate of DDE in urine samples increased by 4.2%, concentration levels remained unchanged.

Results and Discussion

- Thus, a 10-12 day administration of therapeutic agents produced from local medicinal plants, including endemic herbs and fruits made it was possible to reduce the concentration rates of hexachlorocyclohexane (HCH) - α-, β-, γ isomers and dichlorodiphenylethylene (DDE) in breast milk. Concentration level of HCH decreased by 2.05 times, but the detection rates remained unchanged, DDE - from 88.9% before the start of the treatment up to 66.7%, P = 0.551after the course of treatment. The concentration level decreased by 2.01 times. The level of HCH in blood samples decreased from 33.3% to 22.2%, P= 0.29, concentration decreased by 53.5 times. DDE levels remained at 55.5% even after the course of treatment, but its concentration decreased by 28.5 times.

Results and Discussion

- The level of HCH in urine samples increased from 11.1% before the treatment to 22.2% after the course of treatment, but concentration level decreased by 58 times, DDE - from 33.3% before treatment to 3.7% after the treatment, and only DDE traces were detected, P=0.0004. In control group, the levels HCH and DDE in breast milk samples and HCH level in blood samples remained at 66.7%, in urine samples - remained unchanged. DDE level in breast milk, on the contrary, increased from 50.0% to 66.7%, in urine - the level of HCH remained at 50%, and DDE - increased from 12.5% to 16.7%.

Results and Discussion

- Despite the results obtained, there are still many questions to be answered. First, a question concerning the therapeutic agents derived. These agents are multicomponent, they contain pectin substances with sorbent properties, contain lipids that can absorb OCPs (because OCPs are mostly found in fats - lipotropic), antioxidant vitamins, trace elements and other biologically active substances, which can probably form compounds with OCPs, preventing absorption from the GT and subsequently eliminated from the body via feces. But this issue requires studies of stool samples for OCPs before and after the treatment. On the other hand, we cannot exclude a possible "decay" or 'decomposition" of OCPs in GT. This issue requires more detailed experimental studies.

Results and Discussion

- Thus, therapeutic agents obtained from medicinal plants, including endemic plants and fruits, as well as a tincture of the golden root (*Rhodiola Rosea*) are effective for the neutralization and elimination of OCPs from GT, but further targeted experimental studies are needed on a larger number of patients.

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