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ORIGINAL ARTICLE

Organochlorine pesticide residues in breast milk in Armenia

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Abstract: The study evaluates organochlorine pesticide (OCP) exposure and the possible relationship with adverse birth outcomes through analysis of breast milk samples from a rural Armenian population in 1993-2000. 266 samples were randomly collected during the first 2-3 days after delivery. Residues of OCP (lindane, DDT, DDD/DDE) in breast milk were measured using gas chromatography. DDE consistently ranged from undetectable to 0.14 mg/l. DDT was detected twice (7%) in 2000, providing evidence of the illegal use of this banned pesticide. Total frequency of DDT/DDE detection was 77% and lindane 51%. Almost 8% of breast milk samples contained lindane, exceeding the acceptable daily intake (ADI) estimated by the WHO, and 20% exceeded the ADI for DDT/DDE. No differences in pesticide content were detected between the milk of primiparous and multiparous women. No correlation was found between levels of pesticide body burden and frequency of pregnancy/delivery complications, infant gender ratio, birth defects, or infant weight/height. There was some decrease of body mass and a statistically significant change of chest circumference among infants of mothers with detectable levels of OCP. A doubling in the frequency of pregnancy/delivery complications for those with OCP in their breast milk, though not statistically significant, is worrying. Further research is warranted involving a larger sample, possibly from rural and urban regions.

Keywords: pesticides, agricultural chemicals, breast milk, biomonitoring

INTRODUCTION

Because of its remarkable insecticide activity, DDT [2,2-bis(*p*-chlorophenyl)-1,1,1-trichloroethane], has been the most widely used pesticide in the world since the 1940s. Although discovery of a number of adverse properties, especially extremely high environmental persistence and bioaccumulation in food chains, led to the banning of DDT in the developed countries of Europe and in North America, it continues to be widely used in other parts of the world. DDT is the most common pesticide used to combat the vectors of human transmitted diseases such as mosquitoes and tsetse fly. Mexico uses 3,000 tons of DDT annually in its mosquito control programme. In India, DDT and HCH (gamma-hexachlorocyclohexane) (Lindane) make up 70% of the total pesticides in use [1, 2, 3]. The widespread use of DDT and other organochlorine pesticides (OCP) with extreme environmental stability has resulted in a global problem. There is evidence suggesting that these compounds play a role in causing cancer (particularly of the breast), as well as neurological, reproductive, and other disorders [4].

Monitoring of OCP in the environment has been conducted in many countries using human breast milk. Breast milk as a biomarker has a number of advantages. Humans occupy the top of the food chain, and contaminants contained in breast milk are a good indicator for fat-soluble toxicants and maternal body burden. The mammary gland is an excellent natural dose device, concentrating lipophilic compounds. These enter the mother by different pathways and are passed on to the infant via the breast milk. For instance, lindane's coefficient of transit from blood to the milk is 9.15-23.48 [5]. It has been experimentally estimated that infants have double the concentration of these types of contaminants in blood, compared to their mothers [6]. This observation is also supported by clinical observations [7]. DDT and HCH were found in the abortive tissues and tissues of stillborn infants, and infants who died from inherited disorders [8, 9].

There is a very high correlation between the content of DDT and HCH in adipose tissue and breast milk [10, 11, 12, 13]. Determination of DDT in breast milk has the significant advantage that it is a non-invasive and convenient method. Bearing in mind that approximately 5% of women deliver yearly, data obtained from such monitoring could be considered representative for an entire population. Some authors have found correlations between DDT concentration in breast milk and maternal age, number of deliveries, and diet. On the other hand, many authors have not found these associations [1, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24]. During recent decades, population means of DDT have declined from 5-10 mg/kg milk fat to around 1 in many areas. Although different geographic regions have different means, the decline seen in various countries corresponds to their restriction in the use of DDT [25].

Sweden has recorded dramatically declining DDT and DDE content in breast milk by 97% and 91%, respectively, over a 20-year period (1972-1992) [15, 26]. In East Germany, total DDT

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and HCH has decreased by 83-84%, but DDE has increased 32% – to 0.755 mg/kg of milk fat. Using a safety factor 100, up to 20% of samples exceeded the 'tolerable concentrations'. In general, significantly higher concentrations of OCPs were found in women's milk from East Germany compared to the West [14, 27, 28, 29]. In North Germany, the median DDT level was 0.202 mg/kg, and decreased by 80-90% over 12 years. Higher HCH and HCB concentration levels were associated with lower birth weights of female infants [30].

The continuing trend of reduction in the concentrations of OCPs and in the percentage of human samples containing residues is also seen in the United Kingdom where concentrations were similar or lower than in Europe [21]. In Greece, Lindane is found in only 57% of breast milk samples, with a mean concentration is 0.58 microgram/l. DDT and DDT are found in 41% and 55% of samples, respectively; however DDE was detected in all samples, ranging from 0.33-278 microgram/l. Three of 112 DDT derivatives exceeded the acceptable daily intake value established by the WHO in 1987 [24].

In a number of industrialized countries, OCP residues in breast milk still remain high and pose a concern for certain subpopulations, even in the USA and Australia [17]. Much higher levels of contamination are reported from developing countries. In Uganda, for example, DDT and DDE were detected in 100% of samples, with a mean of 3.24 mg/kg based on milk fat [31]. Up to 75.7% of milk samples from Swaziland exceeded the ADI estimated by FAO/WHO; moreover, the high content of DDT compared to DDE indicated a relatively recent exposure of the mothers to OCP [22]. In India, a mean value of DDT in maternal milk was reported as 1.27 mg/kg. Hence, a 3 kg infant ingests 0.21 mg/kg/day DDT, a level 42 times greater than the recommended 0.005 mg/kg/day ADI. For HCH, the average daily intake is nearly 5 times higher than the ADI [1, 2]. Higher levels of contamination have been registered in Zimbabwe – up to 25.259 mg/kg milk fat (lowest level 1.61mg/kg). The proportion of contaminated samples was 98-100% [18].

A very similar pattern was found in Mexico, with detection of DDT and DDE in 90% and 100% of samples, respectively. The mean sum content of DDT and its metabolites was 2.05-5.302 mg/kg milk fat (maximal – 78.1 mg/kg) and 4.0 mg/kg in whole milk. The average sum of DDT exceeded the ADI by up to 2.93 times [3, 11, 13]. The levels of DDT residues were studied in 145 breast milk samples collected 25 days postpartum from women living in various rural populations in Venezuela, where DDT has been used in farming activities and to interrupt the transmission of malaria. All participants showed quantifiable milk levels of DDT residues in the range from 5.1-68.3 microgram/l, and their levels significantly increased ($P < 0.05$) with maternal age [16]. In the large metropolitan area of Rio de Janeiro, Brazil, relatively low levels of total DDT and HCH have been reported – 1.7 and 0.005mg/kg milk fat, respectively [32]. The sum content of DDT in Cuban mother's milk was 0.128 mg/l, and in rural areas it was significantly higher [33].

In Egypt, analyses of 60 samples of breast milk from 20 governorates determined DDE, Lindane and DDT residues at 21.37 ppb, 8.42 ppb and 2.93 ppb, respectively, which is significantly lower than in most developing countries [34]. Despite this, in the Kafr El-Zayat governorate the estimated daily intakes of DDT complex by breast-fed infants were 86% of the acceptable daily intakes [35]. Overall levels of DDT and DDE in milk samples from Kuwait were lower than levels reported from other Middle Eastern countries – 0.012 and 0.833mg/kg milk fat, respectively. [36]. In the Al-Kharj area of Saudi Arabia, Lindane was found in 23.5% of screened samples, DDT – 81%, DDE – 94%, in amounts that exceed the WHO ADI for a 5-6 kg infant [37].

Currently, there are increasing concerns about environmental quality in the countries of the former USSR. Recent data have shown levels of OCP residues in human milk higher than in European countries, but lower than in developing countries. In Kazakhstan, almost all samples (98-100%) contained OCP. The mean concentration of DDE was 1.9 mg/kg based on fat; Lindane ranged from 0.4-8.6 mg/kg fat (overall average 2.21 mg/kg) [38, 39]. Samples of breast milk from 197 women from two cities in the Ukraine had median concentrations of HCH – 0.73 mg/kg fat and DDE of 2.46 mg/kg fat, which is higher than most but not all other reports from Europe. [40]. High levels of DDT residues were found in the breast milk of Russian women, even on the Arctic coast. Moreover, the indigenous population had a lower concentration than migrants, but higher than similar groups in Scandinavian countries, and at levels causing medical concerns [41, 42, 43].

Unless breast milk is highly contaminated with organochlorine compounds, it is still best for infants (i.e. better than formula). Breast-feeding should be prompt, but the importance for breast feeding mothers of a healthful dietary regimen in order to prevent body weight lost and mobilization of body fat stores for milk fat synthesis should be stressed [14, 20, 39, 44, 45, 46, 47]. Despite the obvious advantages of breast-feeding, there is a large amount of literature that highlights the adverse effects of OCP on children and infants, substantiating the necessity to monitor breast milk. Determination of actual levels of OCP in breast milk of mothers, to determine if the total OCP levels received by breast-feeding infants approaches or exceeds potentially deleterious levels, could be an important indicator of the burden of persistent lipophilic chlorinated hydrocarbon pesticides in the human body.

The aim of this study was to evaluate OCP exposure, using breast milk as a measure of body burden, and the possible relationship with adverse birth outcomes in a rural population in Armenia.

MATERIAL AND METHODS

Investigations were conducted in 1993-2000 in the Ashtarak pre-mountainous (piedmont) region of Armenia, with a total population of about 14,000 people [48].

Ashtarak is the administrative centre of a rural country with intensive agriculture, located 17 km to the northwest of Yerevan at an altitude of 1,130 m. The types of agricultural commodities are fruits, vegetables and grapes. Armenian peasants largely consume their own products, with wheat as their staple food – the mean bread and pasta consumption in Soviet Armenia was 170 kg/year – more than average in the former USSR. Seafood and fish are not commonly consumed in Armenia.

Approximately 30 samples of breast milk were analyzed annually in autumn, close to the end of agricultural activities, in order to detect possible occupational exposure as well as environmental exposures. A total of 266 samples were collected in the period of 8 years during which the total number of deliveries was 6,823. Breast milk samples were collected from a subgroup of women who gave birth in the maternity ward of the Ashtarak Central Clinic where the donors were asked for their collaboration and provided verbal consent. The age of mothers was ranged from 17-36 years, with median 22 and average 23.1±0.25. One sample of breast milk was collected from individual randomly selected mothers in the maternity the ward during the first three days after delivery. The breast milk samples (50 ml) were collected by the mothers themselves, using standard glass pumps and poured into opaque jars. At the time this study was started an IRB system had not yet been put in place in Armenia. The samples were shipped immediately in a cooler containing blue ice to the laboratory where they were stored in a refrigerator at -12°C.

Residues of the OCP Lindane (gamma HCH), DDT and it's metabolites DDD and DDE were measured in whole milk using gas chromatography at the Institute of Environmental Health and Preventive Toxicology, Ministry of Health, Republic of Armenia. A 50 ml aliquot of milk was treated with concentrated sulphuric acid and extracted with hexanone. If the milk sample volume was sufficient, 3-9 parallel samples were analyzed and the mean value calculated. A 'Tsvet' gas chromatograph (Dzerzhinsk, USSR) with an electron capture detector was used with the following conditions: a carrier gas (nitrogen) rate at the column outlet = 60 ml/min; glass column (2,000×3 mm) filled with SE 30% applied in amount of 5% on the silanized Chromaton N-AW; evaporator t = 220°C, column thermostat t = 190°C, detector t = 220°C; electrometer working scale – 20×10^{-12}. Retention time for Lindane (HCH) was 1.2 min, for DDE = 7 min, DDD = 8.75 min, DDT = 11.9 min. Quantitative evaluation of organochlorine compounds was performed by the method of comparison with commercial standards 99.8% purity. The lowest detection level was 0.0007 mg/l [49]. Blank samples and spikes were also treated periodically in the same way as the trial samples. Spike recovery level was 89%

Data on newborns' anthropometric parameters (body weight, height, head and chest circumference), as well as the frequency of anomalies (such as aspiration of mecum, breach birth), pregnancy (e.g. preclampsia, intrauterine hypertrophy) and childbirth duration, complications and disorders were obtained from the medical records (charts). All data were entered in an Access Database and analyzed using SAS programme (version 6.12).

RESULTS AND DISCUSSION

88 of 266 (33.1%) women were primiparaous (Table 1). There was no significant difference in age between women with detectable and non-detectable pesticide biomarkers (23.06 ± 0.28 vs. 23.21±0.61) and primiparaous and multyparaous women (22.67±0.45 vs. 23.27±0.35). There were 10 cases involving complications of the pregnancy duration (3.76%), 38 (14.29%) complications of delivery, and 22 cases (8.27%) of premature labour. Newborn pathology was exclusively intrauterine hypoxia and intrauterine growth retardation (IUGR), no other serious birth defects were observed.

Table 1 Parity of deliveries

Year	Total deliveries	Number of delivery First	Second +	Missing
1993	54	28	23	3
1994	44	12	32	0
1995	22	10	12	0
1996	28	11	14	3
1997	30	11	15	4
1998	30	5	1	24
1999	28	1	3	24
2000	30	10	10	10
Total	266	88	110	68

Table 2 Residues of organochlorine pesticide (OCP) in breast milk

Years	Pesticide	N	Geometric Mean Concentration* Mg/l (± sd)	Frequency of Detection %
1993	Lindane	42	0.00249 (±2.59405)	81
	DDE	52	0.01178 (±3.37722)	93
1994	Lindane	25	0.00327 (±3.13665)	83
	DDE	26	0.02751 (±2.44826)	87
1995	Lindane	13	0.0002 (±2.58372)	59
	DDE	19	0.00043 (±3.97072	86
1996	Lindane	18	0.00162 (±1.6943)	64
	DDE	27	0.02913 (±2.99018)	96
1997	Lindane	0	No/detect.	0
	DDE	29	0.01635 (±2.62457)	97
1998	Lindane	8	0.00226 (±2.34512)	27
	DDE	10	0.01105 (±2.21322)	33
1999	Lindane	3	0.00070 (±1.58307)	10
	DDE	17	0.00497 (±2.83215)	62
2000	Lindane	29	0.00193 (±2.44680)	97
	DDE	29	0.00609 (±2.61752	97

* Non-detected values not included in calculations of geometric mean values.

Pesticide analytical results are presented in Table 2. Analysis of breast milk samples consistently detected the major metabolite of DDT -DDE, ranging from undetectable to 0.14 mg/l, but not the parent pesticide. DDT was detected twice (7%) in 2000, providing evidence of (most likely) recent illegal use of this pesticide which had been banned since 1972. The total frequency of detection of DDT/DDE during the 8-year time period was 77%. Lindane was also frequently detected (51% of all samples during 8 years) with a peak determination in 1993-94 – reaching 81-83%. The concentration of Lindane ranged from undetectable to 0.033 mg/l. The fact that Lindane was not detected in 1997 cannot be satisfactorily explained. An abrupt increase in the frequency of detection of Lindane – up to 97%, as well as DDT residues, most likely indicates recent environmental pollution (Table 2).

There were no significant differences between the concentration of DDE and Lindane in the primiparous (n = 88) and multiparous (n = 178) breast milk (0.0214 mg/l vs. 0.0221 mg/l and 0.0028 mg/l vs. 0.0037 mg/l, respectively). The group of women in whom no detectable amounts of pesticides were found in their brest milk – the 'non-detectable' group (n=48), was compared to those whose milk did contain detectable levels (n=218) of OCP (Table 3). There were no statistically significant differences in mean age (23.2±0.61 vs. 23.1±0.28), the frequency of complications of duration of pregnancy, complications of delivery, intrauterine hypoxia, or IUGR of newborns among detectable and non-detectable women (Table 3).

Table 3 Duration and outcomes of pregnancies, N=266

Group	Complications – % Pregnancy	Delivery	Pathology of newborns	Rate of gender m/f	Timely delivery %
Detectable	4.13	15.60	7.80	1:1.09	72.48
Non- detectable	2.08	8.33	12.5	1:1.12	70.83
P	0.500	0.193	0.294	0.933	0.818

There were 11 cases of delivery complications in a top quartile group of women (sum of content of OCP in breast milk above 0.0262 mg/l) vs. 5 cases in a bottom quartile (OCP concentration below 0.0055 mg/l). Odds ratio 2.5, 95% confidence interval 0.81 – 7.75. All cases of delivery complications were mild and included powerless labour, early rupture of amniotic fluid sac, perineal rupture. However, there was a trend for higher frequency of complications during pregnancy and delivery in the detectable group (4.13% and 15.60% vs. 2.08% and 8.33% for non-detectable) that may not have reached statistical significance due to insufficient sample size. This suggests the need for further investigation.

No statistically significant differences were found in height and head circumference between newborns of the detectable and non-detectable groups. Although some changes in weight were observed they were not significant, and only chest circumference was statistically significantly different (smaller) ($F = 6.44$, $P = 0.0003$). Correlation analysis was performed to determine possible relationships between anthropometric parameters of newborns and the concentration of OCP in breast milk. Spearman's coefficient of rank correlation did not reveal any significant correlation between pesticide (DDT or Lindane) content of breast milk, and weight, height or head and chest circumstance.

DISCUSSION AND CONCLUSION

The aim of the presented investigation was to determine the prevalence of OCP residues in breast milk among a rural Armenian population, assess the maternal burden, and to investigate possible adverse impacts on the duration of pregnancy and delivery, and helth status of the newborns. Analysis of data have shown that in spite of 30 years of total prohibition of the use of DDT and HCH, their residues still circulate in the environment in significant concentrations and enter humans in sufficient amounts which are cause for concern.

The main implications of this investigation are that there may be continued use of DDT, or more likely, environmental reservoirs with a persistence of DDT metabolites in animal fat, fish, dairy and other food sources. In previous years, only DDE was detected, reflecting the presence of this metabolite in the food chain. The detection of the parent compound DDT in the most recent analysis suggests recent reintroduction (or use) of DDT in this region.

The frequency of detection, as well as the mean levels of organochlorine pesticides in breast milk, generally corresponds to findings in other countries where OCP were banned long ago. The current levels of OCPs in these countries are perhaps connected with the global circulation of remarkably stable compounds, and successful future reductions in their environmental and human concentrations require universal abstinence. In general, DDE concentrations were a little higher than in most developed countries (Northern Europe, former West Germany, Japan), and similar to levels reported from Greece, former East Germany, and Egypt. The concentrations in Armenia were a little lower than in other parts of the former Soviet Union. In spite of this, 2 facts are very important:

1) The appearance of DDT in recent samples and the general increase in the frequency of detection of OCPs in breast milk. This may indicate recent contamination and/or usage and exposure. This is a consequence of the difficult economic situation in Armenia and in other former Soviet Union countries, with a total dissolution of regulatory and control structures responsible for environmental protection and human health in this slow, burdensome transition period to a free-market economy.

2) Almost 8% of breast milk contained HCH in amounts exceeding the ADI estimated by the WHO (1990) [50] and 20% of samples exceeded the ADI for DDT (as its metabolite DDE) (WHO, 1985) [51]. There were no differences in the pesticides content in breast milk of primiparous and multiparous women. There was also no correlation between levels of pesticide body burden and frequency of complications of pregnancy and delivery, gender rate, birth defects of newborns, weight and height of infants. There did appear to be some decrease of body mass, and a statistically significant change in chest circumference in those with detectable levels of OCP in their breast milk. The doubling of the frequency of complications of pregnancy and delivery for those with OCP in their breast milk, even though not statistically significant, is troubling. Further research involving a larger sample size, and possibly comparing exposures among women from different rural and urban regions of Armenia is warranted.

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