THE DIOXIN POLLUTION AS AN ENVIRONMENTAL RISK OF BREAST CANCER IN CHAPAEVSK CITY, RUSSIA

B.Revich[1], T.Ushakova[2], V.Levshin[2], O.Sergeev[3], V.Zeilert[3]

[1] Center for Demography and Human Ecology of Institute for Forecasting, Russian Academy of Sciences, Nakhimov's prosp. 47, Moscow, Russia, 117418
* tel. (07-095) 3324313, fax (07-095) 7189771, e-mail: revich@mail.ecfor.rssi.ru
[2] Cancer Scientific Research Center, Russian Academy of Medicine Sciences, Kashirskoe Drive 24, Moscow, Russia, 115478
[3] Chapayevsk Central Hospital, Chapayevsk, Russia

Introduction

In recent years, more studies have in fact demonstrated small but statistically significant increases in the number of breast cancer cases in groups exposed many years ago to high doses of dioxins. Epidemiological evidence supports the link between exposure to organochlorines and breast cancer. The focus has been on chemical industry workers. The results of epidemiological research on environment risk factors and breast cancer vary, but in certain case-control studies the role of these factors has been confirmed [1 – 6].

Organochlorines affect or mimic sex hormones that may be mentioned as causes of some types of cancer. Future more, they are excreted in breast milk, suggesting that ductal and other cells in the breast are exposed directly. Natural estrogens are usually metabolized and excreted rapidly, but synthetic estrogens can have long half-lives and bioaccumulate in fat. However, one point on which all investigators agree at this time is that the greater the lifetime exposure to estradiol, the greater the risk of developing breast cancer. An increase in risk is seen if the estrogen exposure occurs during the fetal, rapid breast formation time, pregnancy or menopause periods [7-8].

Object description

The object of study was taken the Chapaevsk due to more than 30 years production of organochlorine compounds was taken as the object of study the public health and environmental exposure. Prior to 1949, the Plant produced chemical blister agents: mustard gas and lewisite. Industrial plants, mainly related to the military-industrial complex, occupied 51% of the total Region area. From 1967-1987, they produced hexachlorcyclohexan (lindan) and its derivatives. Currently, it is produced crop protection chemicals (liquid chlorine, acids, methyl chloroform, vinyl chloride, and some other chemicals). Previously it was considered that hexachlorane production was responsible for dioxin contamination in the city's environment. Tests seemed to confirm it. But after the production was stopped in 1987, a continued output of dioxin was still observed. The study of the present day chemical production technologies revealed that dioxins and similar compounds can be formed in the production of methyl chloroform, vinyl chloride, dichlor propionic acid, hexachlorethane, sodium pentachlorphenolate and polychloroform [9].

This city is located 43 kilometers to the southwest of Samara, on the Chapaevka River, which flows into the Volga river. The population of the town is 83,000. These plants produced 86 % of the city's income. They employed approximately half of the city's population.

The detection of dioxin exposure begun from 1994. The technique for the isomer-specific analysis of PCDDs and PCDFs in complex lipophilic matrices consists of efficient extraction involving a salting out procedure, followed by the clean-up on the carbon microcolumn that permits to separate lipids. Dioxins were detected in the air (0.116 pg/ m^3), in soil (8,9-298 ng/kg), in cow's milk the content of 2,3,7,8 – TCDD was 17,32 pg TEQ/g fat. The town's drinking water source is groundwater. The water distribution pipes are old and suffer from many breaks (120-225 per year) due to poor technical maintenance. This is an on-going cause of underground water pollution. The results showed high levels of dioxin congeners OCDD and HpCDD, and relatively low concentrations of other congeners. The highest dioxin concentrations were found in samples taken in the City center – 102.4 and 74.1 pg/liter. Significantly lower levels were detected in the drinking water of the residential area 5 – 8 km from the plant (28.4 pg/liter). Private home owners (18,000 in Chapaevsk) grow essentially all their vegetables and fruit for their own use, thus receiving an additional dioxin load. The TEQ values were calculated using the WHO-TEF for human milk and blood. The analysis of dioxins in 7 pooled samples of human milk (40 individual trials) has been carried out. The mean content of dioxins oin human breast milk was 42,26 pg TEQ/g fat. In comparison to data from other sites of Russia and different countries, breast milk in Chapaevsk contained considerably higher levels of the more toxic congeners - 2,3,7,8-TCDD, 1,2,3,7,8-PeCDD, 1,2,3,4,7,8-HcCDD, and also octa-dioxins. The higher concentration of dioxins were found only in the milk of women, living close to cotton fields in Kazakhstan [10]. The analysis of blood serum for dioxin confirmed the excess dioxin concentration in the breast milk samples. A comparison of the dioxin contents in the blood of different groups of the population shows considerably higher levels of dioxin, especially of 2,3,7,8-TCDD and 1,2,3,7,8-PeCDD in female workers' blood. There are distinct differences in the levels of dioxin in women living in two different regions of the town. The comparison of data on dioxin concentrations in blood of the residents of Chapaevsk in 4 female workers' blood samples — 412,4 pg TEQ/g fat, in 6 residents' blood samples (those who lived 1 – 3 km from the Chemical Plant) — 75,2 pg TEQ/g fat, in 4 residents' blood samples (5 – 8 km from the plant) — 24,5 pg TEQ/g fat. It allow us to draw the following conclusions: in comparison with the population of other cities of Russia and a few other countries, there are elevated dioxin and furan concentrations in the blood of the residents of the area close to the chemical factory in Chapaevsk; inside the city, there is a sharp difference in the levels of dioxin in the blood of the general population, living close to the plant and those living far from the plant [11,12].

Methods and Materials

The official statistical data were used to calculate age-specific and ade-ajusted incidence and mortality rates. To remove the errors of official statistical registration of breast cancer cases and to prepare more careful analysis the special database about all diagnosed cases was organized. The personal information was collected from medical forms and records kept in ambulance and Chapaevsk city hospital. This allows to make the analysis of incidence, mortality and survival of

the patients. The criteria of precision of the data is the full annual registration of all breast cancer cases.

The personal information was collected in Oncology department of Chapaevsk city Hospital. It includes the following: date of birth, date of breast cancer diagnosis, stage (TNM), histology, morphological verification, conditions of cancer detection, follow-up data.

All alive breast cancer patients born after 1940 year were included in case-control study to investigate the role of established breast cancer risk factors and to estimate the possible dioxin exposure.

Results

The analysis of incidence and mortality data for 199Chapaevsk women have a higher incidence risk overall due to breast cancer (2.1) or cervix cancer (1.8). The risk of dying from these forms of cancer is significantly higher than for Samara region. It is unexplained that breast cancer incidence rates are much higher in all age groups especially from the age of 35 to 55 years. The observed number of deaths from breast cancer is significant, as it is two times greater than the expected number of deaths for Samara region. The incidence rates are much higher in all age groups from the age of 35 to 55 years.

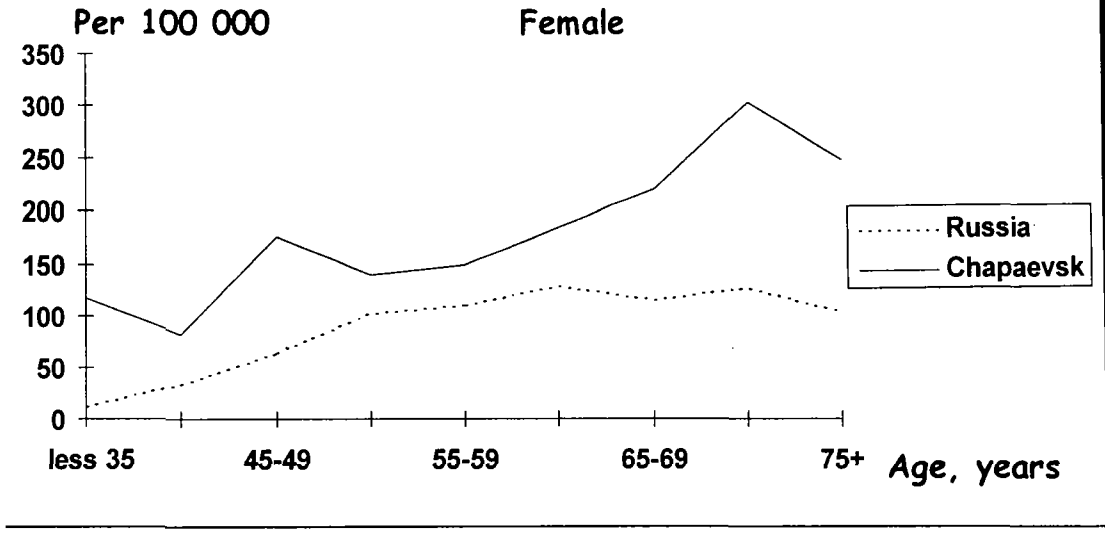

Fig. Age-specific Female Breast Cancer Incidence Rates in Chapaevsk, Samara region and Russia, 1998

For the last 15 years (from 1985 to 2000) 356 breast cancer cases were registered. The young age at the diagnosis before 55 years old had 144 patients (42%). All alive women with breast cancer

diagnosis born after 1940 are involved in the study, 71 persons (tabl. 1). The description of clinical characteristics of case group is performed in table 2.

Table 1.

The statistical rates for breast cancer case group in Chapaevsk city (N=71)

Factor	Mean	SEM	Min	Max	Median	Lower quart	Upper quart
Year of birth	1948	0,65	1940	1963	1948	1944	1953
Age	47,1	0,67	34	58	47,0	43	52

Table 2.

Clinical characteristics for breast cancer cases (N=71)

Factor	N	%
Stage of disease:		
T1	12	16,9
T2	38	53,5
T3	12	16,9
T4	7	9,9
Unknown	2	2,8
Localized stage	38	53,5
Regional metastasis	28	39,5
Advanced stage	3	4,2
Unknown	2	2,8
Morphological verification:		
Low	4	5,6
Moderate	32	45,1
High	11	15,5
Unknown	24	33,8
Conditions of cancer detection:		
Unknown	9	12,7
Consultation	46	64,8
Screening	16	22,5

A special questionnaire was developed and it includes questions on birth place, occupation and residence of woman and her parents, diet, lifestyle, reproductive function and behavior, medical history. As it was planed the list of patients who had the diagnosis of breast cancer during 15 last years was prepared. The interviewing of this group is already done. We planed to interview 71 women. The response in case group was 67 persons. Tree women left the city and one died. It is important that there were no refuse. The most difficult questions concerned with diet, fat intake and lifestyle.

The selection the controls was taken from the general medical insurance database. This group will be matched by age. For the higher reliability the ratio of number cases/controls was 2:1. The pilot estimation about the association of dioxin exposure and breast cancer is not available because we have no information about controls yet. The brief results of case group statistics are shown in table

3. But our research demonstrate that it is unexplained that breast cancer incidence rates are much higher in all age groups especially from the age of 35 to 55 years.

It can be assumed that high levels and long-term dioxin pollution influence to a certain degree the high level of incidence and mortality from female breast cancer.

The study is ongoing.

Table 3.

Results of questionnaire administration to breast cancer case group (N=67)

Factor	Abs.number	%
Average resident time in Chapaevsk city 40,4±1,9 years	65	100
Were born in Chapaevsk city	34	52,3
Father was working before patients birth chemical plant	12	18,5
The mother worked before the birth chemical plant	5	7,7
Chemical plant workers with mean years of work 14,6±2,1 years	12	18,5
Family history of breast cancer	13	20,0
Oral contraception usage	12	18,6
The age of menarche before 13 years old	9	12,9
Regular menstrual cycle	63	96,7
The duration of menstrual cycle more than 30 days	16	22,9
Kept normal sex life prior to the cancer diagnosis	52	80,0
Mean age at first birth 21,9±0,41 (from 17 to 36 years)	61	93,8
Breast feeding up to 3 months	17	24,3
Mean age of menopause 47,2±0,76	53	81,5
Smoking	7	10,0
Alcohol assumption more than one time a month	16	24,6

Acknowledgments

The authors are grateful MacArtur Foundation for financial support of the project (grant 00-62747).

References

1. Falck F Jr, Ricci A Jr, Wolff MS, Goldbold J, Deckers P. Pesticides and polychlorinated biphenyl residues in human breast lipids and their relation to breast cancer. Arch Environ Health 47:143-146 (1992).
2. Flesch-Janys D, Berger J, Manz A, Nagel S, Ollroge I. Exposure to polychlorinated dibenzo-*p*-dioxins and -furans and breast cancer mortality in a cohort of female workers of a herbicide producing plant in Hamburg, FRG. In: Proceedings of the 1993 Dioxin Conference. 381-384.
3. Krieger N, Wolff MS, Hiatt RA, Rivera M, Vogelman J, Orentreich N. Breast cancer and serum organochlorines: a prospective study among white, black, and Asian women. J Natl Cancer Inst 86:589-599 (1994).

4. Lopez-Carillo L, Blair A, Lopez-Cervantes M, Cebrian M, Rueda C, Reyes R, Mohar A, Bravo J. Dichlorodiphenyl trichloroethane serum levels and breast cancer risk: a case-control study from Mexico. Cancer Res 57:3728-3732 (1997).
5. van't Veer P, Lobbezoo IE, Martin-Moreno JM, Guallar E, Gomez-Aracena J, Kardinaal AFM, Kohlmeier L, Martin BC, Strain JJ, Thamm M, et al. DDT (dicophane) and postmenopausal breast cancer in Europe: case-control study. Br Med J 315:81-85 (1997).
6. Manz A, Berger J, Dwyer JH, Flesch-Janys D, Nagel S, Waltsgott H. Cancer mortality among workers in a chemical plant contaminated with dioxin. Lancet 338:959-964 (1991).
7. Colditz G., Fraizer A. Models of breast cancer show that risk is set by events of early life: prevention efforts must shift focus. 1995, Cancer Epidemiol. Biomarkers Prev. 4: 567-71
8. Davis, D., 1998. Rethinking breast cancer risk and the environment: The case for the precautionary principe. Envirnm. Health Perspect 106, 523 – 529.
9. Sotskov U., Liptchenko U., Revich B. et.al. , 2000, Environmental and public health in Chapaevsk city, Moscow, 105 p. (in Russian).
10. Hooper K. et al. (1999). Analysis of Breast Milk to Assess Exposure to Chlorinated Contaminants in Kazakhstan: Sources of 2,3,7,8–Tetrachlorodibenzo–p–dioxin (TCDD) Exposures in An Agricultural Region of Southern Kazakhstan. Env. Health Persp. 107(6), 447 – 457.
11. Revich B., Brodsky E., Sotskov Yu. // Dioxin'99. Organohalogen Compounds. – 1999. – Vol.44. – P.229 – 232.
12. Revich B., Aksel E., Ushakova T., Ivanova I., Zhuchenko N., Klyuev N., Brodsky Ye., Sotskov Y. Dioxin Exposure and Public Health in Chapaevsk, Russia // Chemosphere, 2001 (in press).