THE NEW ARMENIAN
MEDICAL JOURNAL
Vol. 3 (2009), N 2, 41 - 48
www.ysmu.am

PESTICIDES APPLICATION IN AGRICULTURE OF ARMENIA AND THEIR IMPACT ON REPRODUCTIVE FUNCTION IN HUMANS

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Abstract

The healthy environment is one of predictors of population health and well-being. Pesticides have particular place among different environmental pollutants, since their application leads to accumulation of residues and creates grounds for unfavorable effect on human organism. In this respect, organochlorine pesticides are the most dangerous ones due to their ability to persist and circulate in the environment during a long time (for decades). Amongst different manifestations of adverse impacts of pesticides, including organochlorine ones, a significant place belongs to disorders of reproductive function that might be observed at the carriage level. These compounds are also able to penetrate through the placental barrier and considerably affect the course and termination of pregnancy, fetus development, and newborn child's health.

Results of organochlorine pesticides monitoring in breast milk samples are an evidence of their continuing presence in biomedia of country population. The comparison of organochlorine pesticides content revealed that the determination frequency and concentration, as well as their total levels in Artashat region are statistically higher than those in Ashtarak region. Among females of Artashat region the high frequency of pregnancy and delivery complication cases was observed, as well as different disorders of reproductive function (miscarriage, preterm delivery). The organochlorine pesticides content in parturient women with complicated course of pregnancy and/or delivery was higher than in women with the normal course. The calculated values of odds ratio signify that carriage of organochlorine pesticides poses an increased risk of negative impact on human reproductive function.

Keywords: environment, pesticides, persistent organic pollutants, rural population, reproductive function, risk, odds ratio.

Introduction

The healthy environment is one of predictors of population health and well-being. It is well known that the leading role pertains to social and ecological factors among a number of those, which affect human health [*Sobolev V. et al., 2007*]. WHO experts are of the opinion that on the average 20% of all diseases are determined by environmental factors. In this connection the observable negative trends in demographic indices, increase of population morbidity against the background of the environmental state worsening are the nowadays realities. Therefore, investigations aimed at study, appropriate assessment and evaluation of environmental factors impact on health, as well as elaboration of methods for diagnostics, prevention and control of diseases related to the environment are the most important and decisive [*Karelin A., 2006*].

It should be mentioned that among different environmental pollutants pesticides have particular place that is determined, on one hand, by large volumes and scope of their application, and, on the other hand, by their biological activity manifested towards both plant pests and humans. In spite of preventive measures, application of pesticides, particularly organochlorine ones, leads to accumulation of their residues in the environment and thus creates provisions for unfavorable effect on human organism. Pesticides may penetrate and accumulate not only in organism of individuals involved in their production and application, but

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also in persons without any professional contact.

In this respect, the organochlorine pesticides are mostly dangerous due to their ability to persist and circulate in the environment during long time (for decades). Because of these peculiarities, the majority of organochlorine pesticides were considered persistent organic pollutants (POPs), which represent the global threat to human health and environment. Taking into account the scales of hazard represented by POPs, as well as the necessity to manage various issues related to POPs at international level, Governments of many countries came to an agreement and in 2001 signed the International Convention on Persistent Organic Pollutants in Stockholm (Stockholm Convention), which the Republic of Armenia ratified in 2003. Overall, the Stockholm Convention regulates 12 compounds, towards which the appropriate measures should be defined and taken with the aim to reduce related risks.

It is known that the regulation of different chemicals in the environment continues to be based on elaboration of maximum allowable concentrations (MACs). However, there are no doubts on the conditionality of this criterion, as well as its inability to assess the character of interactions between human organism and the environment with its diversity and multi-component impact of factors of various origin [*Pavlov A. et al., 1991*].

It should be mentioned that even in case of acute intoxications the identification of pestcides impact is not always possible. It is especially difficult to reveal pesticides impact on human health under the conditions of actually existing levels of environmental contamination by pesticides and their metabolites. Therefore, many cases of poisoning and diseases caused by pesticides are mostly classified as etiology not connected with them. It is shown that long-term exposure to pesticides low concentrations may be manifested as increase of non-specific diseases frequency and impairment of their clinical course, as well as the increase of population general morbidity, since pesticides, first of all, have general-toxic and polytropic effect on different organs and systems of the human organism [*Pavlov A. et al., 1991; Borisenko N., Khizhnyak N., 1992*].

Amongst different manifestations of adverse impact of pesticides on human organism, the disorders of reproductive function of both men and women have a significant place. Under conditions of ecological or dietary exposure, when the exposure levels are too much lower than professional ones, the disorders of reproductive function are observed non-constant and they are not so evident. In any case the risk of adverse effect remains, particularly for organochlorine compounds [*Dallinga J. et al., 2002*]. The unfavourable outcomes of pesticides impact on pregnancy may be manifested as noncarrying of pregnancy, late abortions, increase of congenital malformation frequency, intrauterine delay of fetus development, low body weight at birth, etc. Some authors are of opinion that pesticides are able to penetrate into female organism through sperm and thus exert toxic effects on pregnancy course and fetus [*Arbuckle T. et al., 1999a; 1999b; 2001; Bell E. et al., 2006*].

In recent years the issues of persistent organochlorine pesticides content in human organism give considerable concern despite the longstanding prohibition of DDT application (1970) and restriction to use other chemicals from this group. It is shown that organochlorine pesticides may have adverse impact on carriage levels due to effect of several stressful factors that might be the cause of different pathological states manifestation. Against the background of such bearing even the course of ordinary somatic diseases may get another character [*Borisenko N. et al., 1987; Pavlov A., 1987*].

A number of investigations dedicated to issues of organochlorine pesticides accumulation in an organism and study of their impact on human health revealed that children, expectant mothers and several groups of patients are mostly vulnerable to impact of accumulated pesticides. It is shown that persistent compounds may affect health state of carriage organism. POPs are also capable to penetrate via the placental barrier and considerably effect on pregnancy course and its termination, fetus development and newborn child's health. In this connection amongst the entire population, pregnant women and children are considered as a specific risk group [*Komarova L., 1981; Mudry I., 2008*].

There are data on existing risk and possible effect of organochlorine pesticides carriage on course and termination of pregnancy [*Saxena M. et al., 1980; Longnecker M. et al., 2001; Fenster L. et al., 2006*].

The high content of polychlorinated biphenyls and DDT was determined in blood serum of women who suffered from toxicosis of pregnancy (gestosis). Hence, the conclusion was drawn that organochlorine pesticides disturb a normal immunological response of maternal organism to penetrated antigens, which accumulate in exceess that may be the cause of gestational toxicosis. The investigations revealed correlation between blood serum and placental tissue levels of organochlorine pesticides and abortion terms. The high content of organochlorine pesticides in mothers' blood (up to 0.9 *mg/l*) was determined in case of premature delivery [*Borisenko N. et al., 1987*].

The accumulation of pesticides in human organism may have an adverse effect on intrauterine growth and cause physical development lagging in newborns, as well as intrauterine fetal death. In opinion of some researchers, pesticides accumulated in maternal organism by penetrating via placenta have a toxic effect on fetus that resulted in disorders of intrauterine formation and growth [*Hambardzumyan G., 1980*]. It should be mentioned that even in cases when the clear relationship between DDT and its metabolites content in maternal serum and pregnancy/delivery terms, as well as body weight at birth was not revealed, nevertheless the obtained data did not allow to exclude possible effects of organochlorine pesticides on the course and termination of pregnancy [*Farhang L. et al., 2006*].

Due to abovementioned reasons, monitoring of persistent organic compounds content in biomedia is widely used for assessment and evaluation of their load levels in human organism. In many countries the breast milk samples are used for monitoring of organochlorine pesticides residues. As the breast milk contains many lipophilic compounds, which also exist in organism adipose tissues, the levels of organochlorine pesticides determined in breast milk are an evidence of their content in serum, plasma fat, and adipose tissues. Numerous studies revealed the close correlation between DDT and HCH content in adipose tissue and breast milk [*Dorea J. et al., 1997; Wasilszewski S. et al., 1999; Pauwels A. et al., 2000; Terrones M. et al., 2000*]. Thus, monitoring of organochlorine pesticides content in breast milk is widely applied to assess the environment state and to study the possible adverse effect of organochlorine pesticides on human organism [*Borienko N. et al., 1987*].

It is significant that in a number of industrially developed countries the residues of organochlorine pesticides in breast milk still remain high that represent a risk for certain groups of population [*Maien K., 1997*]. Considerably higher levels of these pollutants are recorded in the developing countries. In breast milk of women residing in agricultiral areas of southern regions of Russia the residues of DDT and its metabolites were also determined and their concentration ranged from 0.001 to 0.067 *mg/l* [*Revich B., Shelepchikov A., 2008*]. Mentioned quantities are at the levels close to those determined in Armenia.

It should be mentioned that Armenia was always characterised as an agriculturally developed country. Untill the end of 1980s the republic was considered among a number of regions distinguished by intensive pesticides application, including the most persistent ones such as organochlorine compounds. Country total area burden of pesticides exceeded the all-union application levels many times. In separate areas the pesticides consumption ranged from 9 to 37.5 *kg/ha.*

Recently, the role of agriculture in National Economy is increasing again that is reflected in considerable rise of gross production indices in agriculture by all types of farms (commercial organizations, individual farms). The increase of agricultural production volumes is certainly connected with the increase of application volumes of plant protection means and, as a result, is fraught with risk of environmental contamination. Therefore, the solution of pesticides application problem as well as agricultural production safety is inseparably linked with principles of sustainable development aimed at ensuring the ecological well-being and human health protection. In this respect, nowadays ensuring the safe conditions for pesticides application is one of the priority problems from both public health and environmental protection viewpoints.

Based on aforementioned, the research aimed at study of organochlorine pesticides' levels in human organism and their possible adverse effect on reproductive function (pregnancy and delivery abnormalities, different malformations, etc.) and physical development of newborns was carried out.

Material and Methods

Epidemiological and monitoring studies were performed in a region with the most active agricultural production, Ararat Valley, in 2008. Epidemiological studies were carried out with face-to-face interviews among rural female population of Artashat region (Ararat marz) by a specially developed questionnaire. Thirty recently confined women from different villages (Shahumyan, Aygestan, Baghramyan, etc.) were randomly selected for interviewing. The questionnaire embraced issues related to description of pregnancy and delivery course with indication of occurred complications, premature delivery, stillbirth, miscarriage and birth defects, as well as newborns physical development data (sex, weight, height, head and chest circumference), respondents' possible contacts with pesticides or participation in farm job, etc.

In the same group of respondents monitoring of organochlorine pesticides content in biomedia (breast milk) was conducted in parallel with epidemiological studies to assess the anthropogenic contamination of environment with their residues: γ-isomer of HCH, DDT and its metabolites: DDE and DDD.

To determine the levels of organochlorine pesticides residues during the first 2-3 days after the delivery the samples of breast milk were taken and kept under the appropriate cold conditions until analytical studies. The determination of organochlorine pesticides in breast milk of nursing mothers was done by gas-liquid chromatography methods with electron capture detector on "Tsvet" gas-liquid chromatograph [*Klisenko M. et al., 1992*]. Determination sensitivity is 0.0007 *mg/l*. The findings were processed with the use of standard statistical programs such as Biostat, Excel, and Epi Info 2000. The obtained data validity was estimated at significance level equal to $P<0.05$.

Results and Discussion

The results of organochlorine pesticides monitoring in breast milk samples of women recently confined (Artashat region) testify to continued presence of their residues in biomedia of studied cohort. Determination frequency of main contaminants (γ-isomer of HCH and DDE) was high and ranged from 97 to 100%; the average concentrations were 0.0033 and 0.0130 *mg/l*, appropriately.

To assess the levels of environment contamination in different regions of Armenia (premountain zone and Ararat Valley) the comparative analysis of organochlorine pesticides content in breast milk samples of female population of Ashtarak region (Aragatsotn marz) and Artashat region (Ararat marz) was carried out (Table 1).

The obtained data testify that both determination frequency and concentration of separate organochlorine pesticide, as well as their total amount in Artashat region were higher than in Ashtarak region. At the same time the difference of both DDE and total amount of organochlorine pesticides content reached high level of statistical significance: p=0.00002 and 0.00011, appropriately. The obtained results were predictable, since it is well known that among different regions of country the rural areas of Ararat Valley differ by active agricultural production that, in its turn, is inseparably linked with intensive application of plant protection chemicals. At the same time, determined high levels of DDE (main metabolite of DDT) indirectly confirm unofficial information on DDT application in either plant cultivation, or in poultry farming and cattle breeding. It should be

Table 1.

The average content of organochlorine pesticides in the breast milk of rural female population, Armenia, 2008 (X±Sx)

Pesticide	Ashtarak region, Aragatsotn marz		Artashat region, Ararat marz	
	average concentration, *(mg/l)*	determination frequency, (%)	average concentration, *(mg/l)*	determination frequency, (%)
DDE	0.00275±0.0005	80	0.0130±0.0026 p=0.00002	100
γ-isomer of HCH	0.00296±0.0013	83	0.00329±0.00089 p>0.05	97
Total amount of organochlorine pesticides	0.005425±0.0013	83	0.022412±0.0083 p=0.00011	100

mentioned that pesticides considered POPs are not included in the "List of Plant Protection Means Allowed for Application in the Republic of Armenia" approved by the Ministry of Agriculture of the Republic of Armenia (Order No.301-N dated December 28, 2007).

Summarizing the results of epidemiological study on pregnancy and delivery courses among female population of Artashat region, we revealed a very troubled situation. Thus, 66.7% of respondents indicated the cases of current pregnancy and delivery courses complications, as well as different disorders of reproductive function (miscarriage, premature delivery). At this stage of research, it was difficult to analyze the indices of newborns' physical development in connection with organochlorine pesticides exposure (levels in the breast milk of their mothers) because of limited number of cases. In future, enlarging the research scope will facilitate to study this issue.

It should be mentioned that organochlorine pesticides content in the group of recently confined women with complicated course of pregnancy and delivery was higher (from 29 to 75%) than in a group with normal course of pregnancy and delivery. At the same time, determined levels of organochlorine pesticides in breast milk of secundipara were by one third or almost twice higher (from 34 to 90%) in comparison with primipara. However, because of limited number of cases mentioned differences did not reach the statistical significance.

It should be added that according to conducted interviews none of the respondents had professional contact with pesticides. However, a certain part of rural female population (17%) indicated the application of different pesticide formulations on homestead land and truck farms. Unfortunately, none of the respondents could remember names of applied pesticides and no one used personal protection clothing and equipment during their use.

In order to study the possible adverse impact of pesticides on human organism and to assess the risk of reproductive health disorders the comparative analysis of results obtained in Artashat region was done versus results of the same research conducted in Ashtarak region. The obtained value of relative risk calculated for female population of Artashat region confirmed the available misgivings. The high values of odds ratio (OR=6.00; exact limits = 1.32÷3.66; χ^2 with Yates' correction is 5.69 and p=0.0017) testify that organochlorine pesticides carriage is associated with the increased risk of negative effect on human reproductive function.

It should be mentioned that obtained findings are complementary and confirm results of cross-sectional research previously conducted in a number of villages in Ararat Valley in 2005-2006. The study implemented using face-to-face interviews method was aimed at revealing certain regularities of impact on rural population health resulting from pesticides intensive application. Thus, according to obtained data the pesticides application in agriculture of Ararat Valley had widespread character. During the recent 5 years prior to reseach, plant protection chemicals were actively applied in a broad assortment at 1917 individual farms that made 82.1% of totally interviewed 2336 farms. In the list of applied pesticide formulations the considerable part fell to the banned chemicals or those not included in the mentioned official "List". According to research data, DDT application in Armenia is continued, particularly in cattle breeding, and peasants of 290 farms (or 12.4% of total sampling) indicated its usage in agriculture.

As a whole**,** the awareness of farmers about main rules on pesticides safe application was very low. A very limited part of respondents knew about the "List of Pesticides Banned for Application in the Republic of Armenia" and only few of them were able to name at least one example from this List. At the same time, if respondents were informed about prohibition of DDT application, its usage frequency singificantly decreased. In this case only 9.3% of respondents were aware on DDT ban and kept on its application in comparison with 13.3% of farmers who did not know about the existing List of banned pesticides.

In addition, more than half of interviewed farmers did not keep the expiration dates of pesticides. The obtained data analysis also revealed troubled situation with keeping the re-entry period on farmlands treated by pesticides and, as result, 65% of farmers did not keep these regulations. Only a small part of respondents (on average about 17%) kept some re-entry period minimum 1 day. However, it should be admitted that such short period fails to ensure the safe working conditions in all cases. "Re-entry period" concept was so unfamiliar for farmers that many respondents

even did not understand the meaning of a question. In addition, the "pre-harvesting period" was also badly kept. This period is established for the last allowed treatment of agricultural plants prior to harvest. In overwhelming majority, the farmers (82%) did not keep established hygienic regulations and followed "own" voluntary periods considering that 3-5 days or even 1-2 days are sufficient for harvest safety. However, as research output it was revealed that practically all interviewed farmers complained of different symptoms that were typical for pesticides acute poisoning.

Under conditions of existing agricultural practice, while assessing health status of population among other issues we considered the issues on pesticides possible impact on reproductive function of rural population of Ararat Valley in dependence of extent of agrochemicals' wider application and pesticide exposure levels. The possible pesticide effect was assessed by a set of indicators such as pesticides application evidence ("apply/not apply"), application duration (duration of contact with pesticides in the course of a year), amount of pesticide formulations applied in the course of a year, etc. The state of reproductive function of rural population was assessed by frequency of infertility cases, miscarriages, premature delivery, stillbirth, as well as birth defect cases, etc.

The obtained data were analyzed by separate pesticide formulations (insecticide, fungicide, seeds dressing chemicals, etc.) as well as by sex, contact duration, and amount of applied chemicals. Among several groups of plant protection chemicals, the most manifested adverse effect on reproductive function was revealed for seeds dressing formulations and livestock treatment chemicals. In addition to comparative analysis done by separate groups of plant protection chemicals, the study of possible harmful effect of DDT application on the reproductive function of rural population of Ararat Valley was conducted. The research results revealed that DDT has an unfavorable effect on reproductive function (Table 2).

Table 2.

Effect of DDT on reproductive function of rural population of Ararat Valley

Indices	OR with 95% confidence interval (CI)
Infertility	2.14 (1.29÷3.54)
Miscarriage	1.15 (0.78÷1.67)
Premature delivery	0.97 (0.51÷1.84)
Stillbirth	1.04 (0.51÷2.12)
Birth defect	0.60 (0.18÷1.97)

Thus, the effect of DDT on the ability of human organism to impregnate and conceive was found as the most expressed one. In this case the infertility risk increased more than twice (OR=2.14; 95% CI 1.29÷3.54).

Conclusion

The obtained research data and analysis of existing situation on issues relevant to pesticides application are the evidence of unfavourable situation, as well as the indication that issues on ensuring the safety for wider application of chemicals in agriculture are of high priority in Armenia. Pesticides application is carried out inappropriately, in unversed way without observing agricultural, agrotechnical and economic aspects for implementation of protective measures. Their usage is also done without keeping any hygienic norms and regulations that is fraught with unfavourable, adverse consequences from both public health and ecological viewpoints. Research findings have shown that among rural population of Ararat Valley different disorders of reproductive function (increase of frequency of premature delivery, stillbirth, miscarriage, etc.) are observed. At this, organochlorine pesticides content in the group of recently confined women with complicated course of pregnancy and delivery was higher (from 29 to 75%) than in group with normal course of pregnancy and delivery, thus indicating that their presence in the organism may be a risk factor for human health.

The organochlorine pesticides application in agriculture may be explained by a number of reasons: by their low prices because selling is illegal, high efficacy, as well as by low cultural level of consumers involved in agricultural production characterized by prevalent old-fashioned mentality on "non-dangerous"' properties of pesticides. Moreover, organochlorine pesticides application may be also explained by the fact that farmers are very poorly aware or even unaware about their hazardous properties for environment and human health. They are not familiar with issues on normative-legislative regulation in the sphere of plant protection chemicals application. Because of such professional ignorance and lack of efficient

control system, the pesticides application in most cases is carried out without observation of any hygienic norms and regulations.

Thus, summarizing aforementioned it might be concluded that issues on pesticides application need further strengthening since research results confirm circulation of organochlorine pesticides in human biomedia, environment and agricultural production that is undoubtedly the consequence of their continued usage. The determined levels of environmental contamination by persistent organic pollutants may pose an additional risk for population health. In this connection, implementation of effective measures elaborated by joint efforts of concerned structures to strengthen the issues on safe application of plant protection chemicals will certainly facilitate risk reduction and ensure healthy environment. In conclusion, the close attention and efforts should be focused on issues relevant to organization and implementation of measures aimed at prevention of pesticides adverse effects on human health, particularly at prevention of possible delayed outcomes.

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