International Journal of Engineering & Scientific Research
Vol. 7 Issue 7, July 2019,
ISSN: 2347-6532 Impact Factor: 6.660
Journal Homepage: http://ijmra.us, Email: esrjeditor@gmail.com
Double-Blind Peer Reviewed Refereed Open Access International Journal - Included in the International Serial Directories Indexed & Listed at: Ulrich's Periodicals Directory ©, U.S.A., Open J-Gage as well as in Cabell's Directories of Publishing Opportunities, U.S.A

A preliminary report of organochlorine pesticides (OCPs) in thehuman milk samples of preterm and full-term cases.

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ABSTRACT:

It is now a well-accepted fact that only organochlorine pesticides (OCPs) especially DDT, HCH and to some extent Aldrin / dieldrin and heptachlor play a vital role in the tissue accumulation of pesticides.It has been well established that pesticides, particularly the chlorinated hydrocarbons directly affect the fetuses and neonates as they get transferred through placenta and mother milk respectively. Nothing can cause greater fear in an expectant mother than the prospect of her unborn child being defective or intoxicated and nothing touches a man or woman more closely or personally than their reproductive capacity. In recent years, the public has become alarmed that inadvertent or careless exposure to chemicals in the environment might result in unwanted accumulation of chemicals not only in foodresidue but also in human tissues, and cause various types of harms to them. A wide scale employment of organochlorine pesticides has resulted in the incidental exposure of many non-target species, including man. This has been confirmed in all the mammalian species that have been examined including humans.Taking above points into consideration, a continued surveillance on the levels of pesticide pollutants in human population is an important task to ensure the well-being of the human pregnancy. It was, therefore, planned to conduct such as a study in Jaipur, the capital of Rajasthan and the pink city of India. The study is mainly concerned with the pesticides burden in the pregnant women and its transfer to neonates, so it will require the analysis of pesticide residues in the mother's milkusing gas liquid chromatography.The results revealed the presence of isomers of HCH, heptachlor, DDT and its metabolites and Aldrin in almost all the samples analyzed. Thirty women are included in the present study. In this study, milk ofthe women was collectedon the third day of the parturition and OCPs were estimatedusing Gas Liquid Chromatography (GLC). The data obtained was stratified and compared between Full Term Normal Deliveries (FTND) and Premature Deliveries (PD).A general trend oflow residue levels was found in the mother's milk who had Full Term Normal Deliveries (FTND) and higher levels were found in the women who had Premature Deliveries (PD). Findings of this research work may provide base line data of the extent of pesticide contamination/exposure in women body and its relation to preterm labor. The data obtained from the above work may also provide some clues, possible reasons for abortions, premature deliveries, still births, some infant diseases andmortalities. The OCPs residues present in the mother's milk indicate the pesticide burden in the human population, which in turn is a risk to human health. Secondly, this may be considered as an indication of the transfer of these chemicals from mothers to their babies through mothers' milk which may pose various problems of management of prenatal health.

KEY WORDS:
Mother's Milk, Organochlorine pesticides, Contamination, Residues, Gas Liquid Chromatograph, Full Term Normal Deliveries, Premature Deliveries (PD).

INTRODUCTION

Pesticides promote health directly through control of insect-vector-borne diseases andindirectly through increased and improved agricultural production of food and fibre.These, include insecticides, rodenticides, fungicides, herbicides and plant growthregulators. The more widely used of the modern synthetic insecticides are the chlorinatedhydrocarbons, organic phosphorous and carbamate groups of compounds. Although,there is considerable overlapping in toxicity between these groups, on average, the acutetoxicity of the organic phosphorous groups is somewhat greater than that of thechlorinated hydrocarbon compounds. However, the chlorinated hydrocarbon compounds, due to their greater stability, are considerably more of a residue problem thanare the other materials. It is therefore ironic that organochlorine compounds havepossibly been the target of more emotional criticism as well as learned controversy thanalmostany other biological discovery. Some are notoriously persistent in the environment and so can be a real hazard to wildlife and many believe, a potential hazard to man.

The new born which are not simply adults as they differ morphologically, physiologically and biochemically from adults, may also get exposed to pesticides via three routes, the two most important of which require exposure of the mother. Thus, a very important mode of exposure occurs, while the neonate is in utero, by the transplacental passage of the pesticides from maternal to fetal circulation. Transplacental migration of toxic chemical to the growing fetus causes a prenatal exposure, and subsequent burden of maternally carried chemicals. Confirmation of this has been done in all the mammalian species that have been examined including man. Also important is the oral exposure to the pesticide residues secreted in the mother's milk. Third is the direct or accidental exposure of the new born to the toxic chemical which is very rare. First ever report as per our knowledge related to transplacental movement of pesticides came in 1968 by Rappolt and his colleague Hale (1968) [1] who carried out a survey study in California, U.S.A in which they determined the residue levels of p, p’-DDE and p, p’ DDT in the human placenta and cord blood to assess the qualitative and quantitative deposits in the population. They concluded that the use of human obstetrical material as a source of detectable hydrocarbon residues appears to be greatly limited. Limitation was caused at least in part by the low-fat content of the tissue resulting in pesticide levels generally below the level of sensitivity of the gas chromatograph. Only in the case of placenta reportable levels of p, p’ DDE were found, with the mean level of 4.8 mg/g [1].

Humans and animals are constantly exposed in their environment to a vast array of chemicals that are foreign to their bodies. These foreign chemicals or xenobiotics can be of natural origin or they can be man-made. In general, the more lipophilic compounds are readily absorbed through the skin, across the lungs, or through the gastrointestinal tract. Constant or even intermittent exposure to these lipophilic chemicals could result in their accumulation within the organism, unless effective means of elimination are present. Lipophilic chemicals are readily absorbed into the blood, while water soluble substances are less rapidly absorbed. Similarly, the ease with which a compound crosses the cell membrane to reach the active sites of intracellular enzymes is governed by its lipid solubility. Another factor controlling the absorption and penetration of xenobiotics to the intracellular biotransformation enzymes is protein binding Intra and extracellular proteins have the capacity to bind foreign compounds and to reduce the concentration of these compounds at the active sites of enzymes, involved in their biotransformation. This capacity to bind foreign compounds results from the presence of proteins of hydrophobic regions that will bind lipid soluble compounds and hydrophilic regions that contain polar side chains of amino acids capable of forming hydrogen and electrostatic bonds with polar groups in water soluble foreign compounds. Thus, proteins and particularly serum proteins (albumin) have a capacity for nonspecific binding of foreign compounds. This binding reduces the availability of these compounds for biotransformation and has a definite effect or the intrinsic clearance of a xenobiotic by the biotransformation enzymes. Indeed, chemicals can be excreted unchanged into urine, bile, feces, expired air, and perspiration. Except for exhalation, the ease with which compounds are eliminated from the body largely depends on their water solubility. This is particularly true for nonvolatile chemicals that are eliminated in urine and feces, the predominant routes of elimination. Lipophilic compounds that are present in these excretory fluids tend to diffuse into cellular membranes and are reabsorbed whereas water soluble compounds are excreted. Therefore, it is apparent why lipophilic xenobiotics could accumulate within the body; they are readily absorbed, but poorly excreted.

Fortunately, animal organisms have developed a number of biochemical processes that convert lipophilic compounds to more hydrophilic metabolites. These biochemical processes are termed as biotransformation and are usually enzymatic in nature. It should be stressed that biotransformation is the sum of the processes by which a foreign chemical is subjected to chemical change by living organisms. It may mean that the parent molecule is chemically modified at a number of positions or that a particular metabolite of the parent compound may undergo additional modification. The end result of the biotransformation reaction(s) is that the metabolite is chemically distinct from the parent compound Metabolites are usually more hydrophilic than the parent compound. Thus, enhanced water solubility reduces the ability of the metabolites to partition into biologic membranes and thus restricts the distribution of the metabolites into various tissues, decreases the renal tubular and intestinal reabsorption of the metabolite (s) and ultimately promotes the excretion of the chemical by the urinary and biliary fecal routes. In few cases, the metabolites are more lipophilic than the parent compound and tend to accumulate in higher concentration in the body tissues e g DDE, a metabolic product of DDT, is more lipid soluble in comparison of the parent compound DDT. Sometimes biotransformation enzymes even result in the chemical species or intermediates, which are more reactive than the parent compound, this process is termed as Bioactivation [2].

There are three types of human exposure to pesticides. Acute exposure which is usually, the result of accidental contamination by excessive amounts of pesticides, chronic exposure which most frequently occurs in pesticide workers by virtue of their occupation, and incidental exposure which is the consequence of the ubiquity of pesticides and their presence in trace amounts in air, water, food and dust. The former exposure results in typical acute symptoms and signs, reflective of the toxicological properties of the material, chronic exposure of pesticides results in patterns of illness which are usually less well defined, and often consequences of multiplicity of chemical insults. Incidental exposure, the exposure to which the population at large is experiencing is ever less well documented, and with the persistent pesticide like organochlorine pesticides, the only certain effect is the acquisition of their residues in human tissues and fluids.

The human pesticide accumulation in the form of their residues which may be the parent compound or its metabolite is a biological index of pesticide exposure which may be acute, occupational or incidental. In acute intoxication, the residue level provides diagnostic information, in the occupationally exposed; the residue is a surveillance tool reflective of industrial exposure. In the general population pesticide residues is a measure of incidental exposure. The average level of pesticide residues in the cord blood and placental tissue may be considered as an indication of the transfer of these toxic chemicals from the maternal to fetal circulation across the placenta which may shatter the concept of “placental barrier". The residues of pesticides present in the maternal blood indicate the pesticide burden in the human population which in turn is a risk to the human health. Secondly, pesticides excreted in the mother's milk and their consumption by the neonate pose various problem of neonatal health and nutrition.The occurrence of DDT in the human milk was first noted by Laug et al. (1951) [3]andsubsequently, data on organochlorine pesticide concentration in human milk samplesfrom several countries was reported from all over the world.It is of great interest that human milk contains more DDT than does cow’s milk [4] and that the mother is apparently in negative DDTbalance during lactation [5].

More petrifying studies have indicated that we have largely over looked the darker side of these chemicals as OCPs are reported to be carcinogenic [6], [7] mutagenic [7],[8] teratogenic [8],[9] immunosuppressive [10],[11] create endocrine dysfunction such as hypothyroidism or high estrogenic activity [12],[13] disturb reproductive processes [14],[15] growth depressants [16],[17] induces several psychogenic and neurogenic abnormalities in adult stages [18],[19], and are associated with abortions, premature deliveries, still births and infants with low birth weights [20]-[23]. OCPs have been in use in India nearly for a half century now. Even after having clear cut evidence suggesting that these chemicals have the ability to eliminate entire species from the planet, the annual consumption of pesticides in India is about 85,000 tons of which OCPs comprise the bulk [24]. Therefore, today OCPs are perhaps the most ubiquitous of the potentially harmful chemicals encountered in the environment and are still widely detected in humans despite the considerable decline in environmental concentrations [25-30].

The study is mainly concerned with the pesticides burden in the pregnant women and its transfer to neonates, so it will require the analysis of pesticide residues in the mother’s milkusing gas liquid chromatography.The results revealed the presence of isomers of HCH, heptachlor, DDT and its metabolites and Aldrin in almost all the samples analyzed. Thirty women are included in the present study. In this study, milk ofthe women was collectedon the third day of the parturition and OCPs were estimated using Gas Liquid Chromatography (GLC). The data obtained was stratified and compared between Full Term Normal Deliveries (FTND) and Premature Deliveries (PD).A general trend oflow residue levels was found in the mother’s milk who had Full Term Normal Deliveries (FTND) and higher levels were found in the women who had Premature Deliveries (PD). Findings of this research work may provide base line data of the extent of pesticide contamination/exposure in women body and its relation to preterm labor. The data obtained from the above work may also provide some clues, possible reasons for abortions, premature deliveries, still births, some infant diseases andmortalities. The OCPs residues present in the mother’s milk indicate the pesticide burden in the human population, which in turn is a risk to human health. Secondly, this may be considered as an indication of the transfer of these chemicals from mothers to their babies through mother’s milk which may pose various problems of management of prenatal health.

MATERIALS AND METHODS

Since, organochlorine pesticides are lipophilic in nature they may accumulate in human milk in alarming concentrations. During the lactation mother may reduce body burden of these pesticides.In this study, milk ofthe thirty women was collectedon the third day of the parturition and OCPs were estimated using Gas Liquid Chromatography (GLC). The data obtained was stratified and compared between Full Term Normal Deliveries (FTND) and Premature Deliveries (PD). A private clinic "Sanjeevini hospital Bani Park, Jaipur has been identified for the proposed work. In general, they had no history of any occupational or accidental exposure to pesticides. However, they were asked to fill up a questionnaire giving information about their health and relevant to the pesticide residue accumulation such as age, dietary habits, area of residence, parity, social status, accidental or occupational exposure to pesticides etc. according to WHO methodology [31] by interviewing the subjects at the time of collection of samples.

Sample Collection

Mother's milk

The breast milk, approximately 5 ml, from all the subjects were collected at the third day of parturition directly by the manual expression of the breast into cleaned, pesticide free, 50 ml wide mouthed glass tube with a cap lined with aluminium foil. No breast pumps or other devices were allowed to be used for the collection of milk samples Immediately after the milk samples were collected the containers were capped and kept in deep freeze, till analysed, generally within 48 hours.

Extraction of Pesticide from Samples

Pesticides were extracted and separated from samples by liquid partition and column chromatography so that they could be analyzed by Gas Liquid Chromatography (GLC) and Thin Layer Chromatography (TLC) procedures. All reagents and chemicals used were of analytical grade and checked for any pesticide contamination. Specimens of milk were extracted by the methodology given by Takie and his coworkers in 1983 with little modifications according to the prevailing laboratory conditions [32].

Quantitative Estimation

Quantitative estimation of pesticide residues in all the extracts was done by HP 5890 series II gas chromatograph (GC) equipped with Ni 63 Electron capture detector (ECD) coupled to HP 3396A integrator. Glass coiled column (1.43 m x 4 mm L x I. D) was packed with Solid Support, Chromosorb 100/120 mesh size along with the Liquid phase: 1.5% OV - 14±1.95% OV-210. Purified nitrogen (IOLAR-1) gas was used as the carrier gas and a known volume of sample was injected in the column with the help of the 10 µl Hamilton syringe. Different peaks of the samples were identified by comparing their retention times with those of standards. Quantitation of the samples were done by the data obtained from the integrator and were based on peak areas. Standards were obtained from Environmental Protection agency (EPA) U.S.A.

Recovery Analysis and Confirmation of Pesticide residues

Recovery analysis was done by fortification experiments and the percentage recovery was 95–98%.TLC was used for confirming the identity of the OCPs already detected by the GC. The pesticides for which the GC was standardized and were estimated were Aldrin, isomers of HCH (α, β & γ), metabolites of heptachlor (Heptachlor & Heptachlor epoxide) and DDT (DDE, DDD and DDT).

Statistical Analysis

The calculations are based on biological statistics and values are expressed as mean± standard error (S.E.). The difference in the pesticide residue levels between different groups was analyzed with the help of student t test. Significance between the residue levels of different groups was judged at 5 % and 1% levels.

OBSERVATIONS

Table 1: Concentration of organochlorine pesticides (OCPs) in human milk samples (30 Subjects) of preterm and full-term cases (ppm).

S.No.	Organochlorine Pesticides	FTND cases	Preterm cases
		22 Cases Mean±S.E.	**8 Cases Mean±S.E.**
1.	∝-HCH	0.1345±0.0299 (n=22)	0.1202±0.0145 (n=8)
2.	γ-HCH	0.0206±0.0067 (n=17)	0.0464±0.0206* (n=6)
3.	β-HCH	0.1412±0.0245 (n=17)	0.0584±0.0150 (n=5)
4.	Heptachlor	1.5814±0.2992 (n=120	1.2185±0.3276 (n=8)
5.	Aldrin	0.0538±0.0065 (n=180	0.2572±0.0510# (n=17)
6.	Heptachlor epoxide	1.1718±0.2842 (n=13)	0.7216±0.1325 (n=6)
7.	DDE	0.1831±0.0234 (n=21)	0.3031±0.1016* (n=7)
8.	DDD	0.0078±0.0038 (n=8)	0.0303±030151 (n=60
9.	DDT	0.1238±0.0800 (n=16)	0.0366±0.0170 (n=16)
10.	Σ HCH	0.2792±0.0551 (n=22)	0.2972±0.1148 (n=8)
11.	Σ Heptachlor	1.858±0.4045 (n=18)	1.7587±0.3524 (n=8)
12.	Σ DDT	0.2374±0.0309 (n=22)	0.2823±0.0753 (n=7)
13.	Σ OCI	2.3056±0.478 (n=22)	2.3117±0.3777 (n=8)

*Statistically Significant (P<.01)
Statistically Significant (P<.05)
Σ HCH-total HCH
Σ Heptachlor-Total Heptachlor
Σ DDT-Total DDT
n-no of positive samples
ND-not detected

As its clear from the Table:1. That a general trend oflow residue levels was found in the mother's milk who had Full Term Normal Deliveries (FTND) and higher levels were found in the women who had Premature Deliveries (PD). Findings of this research work may provide base line data of the extent of pesticide contamination/exposure in women body and its relation to preterm labor. The values are expressed as mean plus minus standard error and Statistically Significant at (P<.01) and (P<.05).

DISCUSSION

It is well known that the females significantly reduce their body burden of pesticidesduring lactation [33]. Therefore, the neonate would get exposed to them orallyeven if there is no immediate exposure of the mothers to these toxic compounds Humanmilk is a primary and the potent source of the infant nutrition It is rich in fat and standsat the end of the food chain Since the lipid content of the milk is high and organochlorinepesticides are lipophilic in nature, therefore, they can accumulate in human milk inalarming concentrations. Therefore, human milk can be used as an evaluation index ofenvironmental contamination by these noxious chemicals, although the main objective ofits analysis is to determine the amounts ingested by children, who without a doubt, willhave to face other sources of contamination during their lives. Therefore, average levelsof organochlorine pesticides in the mother's milk may be counted as an index for theirdaily intake by the neonates, which may in turn pose various problems of managementof neonatal health and nutrition

In the present study concentration of organochlorine pesticides were found to be higher in milk of mothers undergoing premature labour in comparison of women who had full term labour deliveries (Table:1.). Concentration ofa-HCH, Aldrin, and DDE were statistically higher in the milk ofthe women who had premature deliveries. In the other pesticides such as total DDT, total HCH, DDD and total OCPs concentration, a general trend of greater accumulation in the milk of preterm mothers were found whereas concentration of total heptachlor, a-HCH, ß-HCH, heptachlor, heptachlor epoxide and DDT were found to be higher in the mothers with full term normal delivery. Therefore, females with preterm labour accumulated more pesticides in comparison ofmothers with full term labour. This could suggest some role oforganochlorine pesticides in the preterm deliveries.

Our findings are contradictory to the results of a survey study conducted by Siddiqui (1982) from Lucknow in which he reported that HCH levels in the milk of mothers undergoing full term normal delivery were, same as obtained in mothers undergoing premature delivery and showing still births [34].

Whatever the infant’s chemical exposure from maternal milk, it is superimposed on an existing neonatal body burden. Transplacental migration of toxic chemicals to the growing fetus causes a prenatal exposure and subsequently burden of maternally carried chemicals. But whereas prenatal exposure cannot at present be avoided in the course of childbearing, breast feeding has an acceptable alternative. The question that parent and their physicians must address is whether or not to nurse, and it is one that cannot be answered with any clear substantiating evidence. For most chemicals, level in milk cannot be assigned. Even more equivocal is the choice between avoiding exposure to chemicals in breast milk and obtaining the "beneficial factors" in human milk.

CONCLUSION

Since our food articles contain excessive DDT and HCH residues [35] it is only imperative that Indian population contain highest amount ofthese insecticides’other sources such as air, water, contact with contaminated surfaceetc contribute only small portion of DDT or HCH residues found in human Body. Adosage response relationship has been established in case of DDT, i.e. storage of DDTin human body increases with increase in dosage of DDT, though at a progressivelydeclining rate [36] That means the amount of residues present in humanbody is directly co-related with residues present in the environment.

It can be concluded that the magnitude of pesticide pollution is quite high to contaminate the food and environment and as a result toxicant reach the human body through various sources mainly through the absorption from the gastrointestinal tract via contaminated food chain. From there, they are further circulated in maternal blood, cord blood stored in milk and placental tissue of the women. Since, the pesticides are reported to be carcinogenic, mutagenic, teratogenic, immunosuppressive, induces endocrine dysfunction and high estrogenic activity, disturb the reproductive processes, growth depressants, induces several psychogenic and neurogenic abnormalities in adult stages and are also reported to be associated with abortions, premature deliveries, still births, low birth weight consequences are obvious on the mother and the developing baby. It poses various problems of management of neonatal nutrition and health. It calls for suggestions like special care in nutrition and in the environment of mother throughout the life and especially during pregnancy and lactation. It would be advisable for a woman to avoid the consumption of fatty food stuffs and heavily polluted working environment. In the light of our findings stricter regulations may be discussed and such measures have to be weighed against the benefits of the use of pesticides. Present findings on obstetric toxicology of pesticides particularly in relation to distribution of pesticidal pollutants in pregnant women may finally lead to a better understanding of the influence of chemicals on fetal development and provide grounds for further studies on placental toxicology as related to pesticide pollution in India. In the end, it must be emphasized that there is a rising protest that pesticides are destroying harmless wild life and endangering the health of man himself. The battle against the harmful insects would be much less costly and more efficient, and the problem of contamination of the environment by toxic materials would be vastly reduced, if insect activities are controlled by natural means. The use of pest-specific predators; parasites or pathogens; sterilization of insects with the help of radiations; trapping insects using insect attractants like pheromones; use of juvenile hormones or hormone inhibitors may therefore be suggested as alternate ways of pest control.

ACKNOWLEDGEMENTS

Financial Assistance provided by Indian Council of Medical Research is gratefully acknowledged.

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