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Original Research Article

Assessment of Pesticide Burden and its Association with Occurrence of Leukemia

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Abstract

Background: Uncontrolled use of these chemical pesticides in animal husbandry, agriculture and public health operations has emerged as a long-term irreparable environmental damage, throughout the world. Besides causing acute and chronic toxicity, pesticides are also known to enhance the risk of cancers by acting as carcinogens themselves and by suppressing the immune system which has the ability to destroy the process of tumor formation in the body.

Methodology: A total of 150 leukemia patients were recruited into this case-control study and 80 were taken as control. Pesticides were extracted and separated from the samples by liquid partition and column chromatography so they may be analyzed by gas chromatograph. The qualitative and quantitative estimations of organochlorine pesticides were carried out by gas chromatograph.

Results: organochlorine pesticide levels in control subjects were 0.3456 ± 0.017mg/L and in Leukemia patients were 0.4772 ± 0.048mg/L (P value > 0.05). Pesticide burden in CML patients was 0.5087 ± 0.058mg/L, in CLL patients was 0.3519 ± 0.044mg/L, 0.4331 ± 0.127mg/L observed in ALL patients followed by AML with a total pesticide burden of 0.3358 ± 0.027mg/L.

Conclusion: Training and extension programs by the Ministry of Agriculture for safe pesticide usage should be improved and expanded. Occupational exposures can be reduced through changes in application methodology.

Keywords: Pesticides, Leukemia, Organochlorines.

Introduction

Agriculture is the basis of India's economic development as well as of food production therefore; greater attention has been paid to sustaining agricultural growth. Introduction of high-yielding varieties, adoption of new agricultural technology along with pesticide use has all contributed to its successful take off. [1] the relatively large amount of synthetic chemicals (mainly pesticides) have been introduced and used by farmers during the last four decades, which are posing a potential hazard to

human and its environment. Reckless use of these chemical pesticides in animal husbandry, agriculture and public health operations has emerged as a long-term irreparable environmental damage, throughout the world. Pesticides are chemicals whose toxic effects may extend far beyond their aim of killing and eliminating agricultural pests. [2] Genotoxicity is another serious possible harmful effect caused by these compounds and calls for special attention in view of the irreversible nature of its manifestation. Besides causing acute and chronic toxicity pesticides are also known to enhance the risk of cancer in two ways: the direct way- by acting as carcinogens themselves; and, the indirect way- by suppressing the immune system which has the ability to destroy the process of tumor formation in the body. Most tumors associated with immune suppression have been lymphomas and leukemias. [3]

The organochlorine pesticides being lipophilic are sequestered by lipid-rich tissues in all organisms. From adipose tissue, they are distributed to all parts of the organisms according to the equilibrium mediated by blood transport. The partitioning of organochlorine pesticides from adipose tissue to blood serum is related to the lipid content of serum because they are bound to lipids, phospholipids, albumin and macromolecular components of serum. Thus, the blood serum can constitute a good indicator of body burden, especially when the pesticide residue levels are expressed at the lipid base. For the monitoring surveys, human tissues in-vivo are difficult to access but the blood samples provide easy resolution therefore, in this study, blood samples were collected from patients to find out the body burden of pesticides. [4]

So the main objective of this study was to monitor the pesticide burden in the body of Leukaemia patients and then find out any association between the blood level of pesticides and the development of Leukaemia.

Materials & Methods

The present study was a case-control study carried out in the outdoor/ indoor department of S.M.S. Medical College, Jaipur, India. The ethical approval was taken from the institutional review board of the hospital, and written informed consent was obtained from all the enrolled subjects. A total of 150 leukemia patients were prospectively recruited into this study and 80 were taken as a control, as they did not have any cancer. Thus 80 subjects serve as control against 150 cancer cases. The preformed and pretested questionnaire included a detail information regarding family history of any major disease (particularly cancer), health status, age, economic status, religion, dietary habits and also the use and accidental exposure to the pesticides either at home or at work place. Samples were taken by venipuncture method using a 2ml syringe and stored in EDTA vials at 4^{o}C. Pesticides were extracted and separated from the samples by liquid partition and column chromatography so they may be analyzed by gas chromatograph. Extraction was done by the method given by Bush et al (1984) with little modification according to the laboratory conditions [5]. The qualitative and quantitative estimations of organochlorine pesticides were carried out by gas chromatograph. The differences in the pesticide residue level between different groups were analyzed with the help of the student's'‘t’ test. The data were analyzed using MS Excel 2010, Epi Info v7 and SPSS v22.

Results

In the present study the total organochlorine pesticide level in control subjects was 0.3456 ± 0.017mg/L and in Leukemia patients was 0.4772 ± 0.048mg/L (P value > 0.05). Among the 150 patients, suffering from Leukemia, 69.33% were patients of Chronic Myelocytic Leukemia (CML),

8.66% were Chronic Lymphocytic Leukemia (CLL) patients, 20.66% were Acute Lymphocytic Leukemia (ALL) and the remaining 1.33% subjects suffered from Acute Myelocytic Leukemia (AML). The total pesticide burden in CML patients was 0.5087 ± 0.058mg/L, in CLL patients, was 0.3519 ± 0.044mg/L, 0.4331 ± 0.127mg/L observed in ALL patients followed by AML with a total pesticide burden of 0.3358 ± 0.027mg/L. All the pesticides analyzed were found high in patients as compared to the control. (Table-1) This difference between leukemia and mean pesticide levels was not found statistically significant (P value > 0.05).

Table 1: mean pesticide levels among leukemia patients and study controls.

Leukemia types	No. of patients	Mean pesticide levels (mg/L)	P Value
CML	104	0.5087 ± 0.058	0.568
CLL	13	0.3519 ± 0.044	1.00
AML	31	0.4331 ± 0.127	1.00
ALL	2	0.3358 ± 0.027	1.00
Total	**150**	**0.4722 ± 0.048**	**1.00**
Control	80	0.3456 ± 0.017	

All the blood samples that were analyzed for pesticide residues by Gas Chromatograph were found laced with organochlorine pesticides viz. DDT & its metabolite, HCH & its isomers (α, β, γ, δ), aldrin, dieldrin, endrin, heptachlor, and endosulfan. Patients suffering from CML had a significantly higher amounts of residues of total HCH along with δ isomer, aldrin, dieldrin, heptachlor epoxide, endrin and total endosulfan in comparison with controls. Total HCH along with γ, δ isomer, dieldrin, and heptachlor epoxide were found to be significantly high in CLL patients than in control. Only δ-HCH and aldrin were found significantly high in the case of ALL patients while in case of AML patients δ-HCH, heptachlor epoxide and endosulfan sulfate were found significantly high when compared with control. When all the Leukemia patients were taken collectively, all the pesticide residues were found significantly high in their blood except total DDT, total endosulfan and heptachlor. (Fig -1)

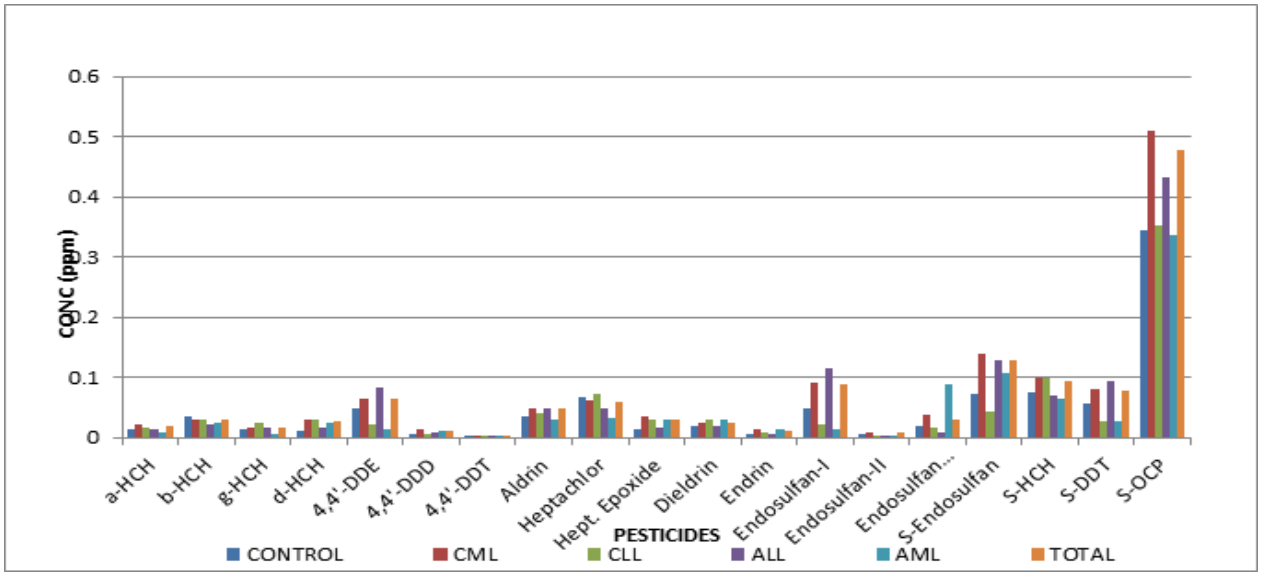

Figure1: Comparison of pesticide residues in blood of control subjects and subjects with different leukemia cancer

Discussion

Persistent organochlorine pesticides (POPs) are problematic environmental contaminants because of their widespread use and their risk to every form of life. Due to their lipophilic and persistent nature, they have high bio-accumulating potential and they bio-magnify at higher trophic levels in the food web. They are, therefore, widely found in all human tissues including blood, placenta, developing fetus and mother's milk {Voorspoels 2002 [6]; Nebile *et al* 2010 [7]; Fukata et al 2005 [8]. It was shown that POPs are equally partitioned in the lipid compartments of different human tissues, such as liver, muscles, adipose tissue and blood {Haddad *et al* 2000 [9]. However, blood plasma is the most convenient matrix for the monitoring of occupational or background exposure to these chemicals. Therefore, in the present investigation, human blood was used as an exposure indicator of pesticides.

The present study includes the analysis of 230 blood samples, in which 150 subjects suffered from leukemia and 80 subjects did not suffer from any cancer, thus they were taken as control group. In the present case-control study, the association between the risk of leukemia and lymphoma, and the residue level of several organochlorine pesticides (OCPs) was examined and it was observed that there is significantly high concentration of total OCPs in the blood of leukemia (0.4772 mg/L) patients in comparison to controls (0.3456 mg/L). This may indicate that pesticide residues level in the blood may increase the risk of developing leukemia in the general population of Rajasthan (table-1).

The exposure of the general population to these lipophilic OCPs is mainly through the food, dairy products and even through drinking water, which may be considered as indirect exposure. Only farmers or pesticide applicators are directly exposed to different kinds of pesticides. It was assumed that 80% of pesticide exposure to the general population is mainly through the food [10]. DDT and HCH insecticides are the major contaminants of Indian food stuff. The current intake in developing countries like India is reported to be at least 5-10 fold greater than that in the more developed nations, therefore, the population of developing countries is at higher risk from OCP exposure. Factors such as malnutrition which is quite common among the rural and poor populations in developing nations, can increase risks related to pesticide exposure. Of greatest concern is the magnitude of exposure to OCPs to which infants and children are subjected through human and dairy milk. The estimated daily intake of DDT by infants is at least 100 fold greater than the ADI (Acceptable Daily Intake) prescribed by FAO/WHO [11].

In the studies recently conducted in India by ICMR (Toteja *et al*, 2006) , it was reported that 50-80% of wheat grain and wheat flour samples were found to be contaminated with the residues of HCH and DDT [12]. Residues of α-HCH, β-HCH, heptachlor-II, aldrin, and DDT were found in wheat flour samples whereas 60% of water samples were found to contain aldrin and 50% with DDT and a few had α-BHC (Bakore *et al* 2004) [13]. Similarly, 60-75% rice samples (Toteja *et al*, 2003) collected from different geographical regions of country were found having the residues of these insecticides [14]. These studies clearly indicate that the Indian food stuff is highly contaminated with pesticides

Ahlborg *et al* (1995) also reported that food especially meat, poultry, fish and dairy products had the highest concentrations of DDT and its metabolites, BHC and its isomers, aldrin/ dieldrin and heptachlor/ heptachlor epoxide [15]. A monitoring study done by John *et al* (2004) in Jaipur city (the selected city for the present investigation), observed contamination of eggs, meat and fish with organochlorine pesticides [13]. Most of the samples, collected from different areas of the city, were found to be contaminated with

residues of DDT and its metabolites (DDD and DDE), isomers of HCH (α, β, γ), aldrin, heptachlor and heptachlor epoxide. The Magnitude of contamination indicated that the residue levels exceeded the limit of tolerance prescribed by WHO/ FAO. Similarly, Bakore *et al* (2002) analyzed vegetables like potatoes, tomatoes, cabbage, cauliflower, spinach and okra from different areas of the city [16].

A Similar association was observed by Beard *et al* (2003) who showed an increased risk of leukemia with pesticide exposure [17]. The study conducted by Abadi-Korek *et al* (2006) also indicated increased risk of childhood leukemia with parental exposure of pesticides [18]. However, study conducted by Feychting *et al* (2001) are in contradiction with this finding. They did not find any relationship between childhood leukemia and paternal exposure of pesticides [19].

Considering the type of leukemia individually, there was 0.5087 mg/L concentration of total pesticide in CML patients which is significantly high ($p>0.05$) in comparison to the controls (table-1). The total pesticide residues observed in CLL patients was 0.3519 mg/L and in AML patients was 0.3358 mg/L which shows no significant difference as compared to the control (table-1). This presumably means that there is no association between pesticides levels in blood and the occurrence of CLL and AML. This may be attributed to the small sample size analyzed, and thus, a definite conclusion could not be drawn here. [20]

Conclusion

Training and extension programs by the Ministry of Agriculture for safe pesticide usage should be improved and expanded. Occupational exposures can be reduced through changes in application methodology. Specifically, ground-based applications rather than airblast or airborne applications should be used. In addition, further advances in protective clothing and the use of closed application systems should be advocated. Major pesticide companies should join and support research programs and take steps to minimize the health risks from their products. Thorough testing for toxicity should be a condition for continued registration of products for sale.

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