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Original Research Article

Burden of Organochlorine Pesticides and Their Association with Occurrence of Lymphomas

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Abstract

Background: Unheeding use of these chemical pesticides in farming, animal husbandry, factories and public health operations has emerged as a long-term irreversible environmental damage, throughout the globe. Apart from causing acute and chronic toxicity, organochlorine pesticides are also known to increase the risk of carcinogenesis by acting as carcinogens themselves and also by suppressing the immune system which has the ability to destroy the process of carcinogenesis in the body.

Material & Methods: A total of 135 study subjects were recruited, out of them 55 lymphoma patients were recruited into this case-control study and 80 patients were taken as control. Organochlorine 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 Lymphoma patients were 0.4874 ± 0.069 mg/L (P value > 0.05). The pesticide burden in observed NHL patients was 0.5253 ± 0.103mg/L and followed by a total pesticide burden in HL patients was observed at 0.4482 ± 0.092mg/L. This difference between lymphoma and mean pesticide levels was not found statistically significant (P value > 0.05).

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: Lymphoma, organochlorines, Non-Hodgkin's Lymphoma, Hodgkin's Lymphoma.

Introduction

Farming is the main basis of India's economic evolution as well as for food production therefore; greater concentration has been paid to sustain agricultural growth. The Introduction of high- yielding crops, the adoption of new agricultural technology along with massive pesticide use have all contributed to its successful journey. [1] A relatively large amounts of synthetic chemical agents (mainly pesticides) have been introduced into farming and used by farmers during the last few decades, which are posing a serious hazard to humans and the surrounding environment. Incautious use of these chemical agents (pesticides) in farming, animal husbandry and public health operations has emerged as a long-term irreversible environmental damage, throughout the globe. Pesticides are chemical agents whose toxic effects may extend far beyond their target of killing and eliminating agricultural pests. [2] Genotoxicity is another potential possible harmful adverse effect caused by these pesticides and calls for special attention in view of the irreversible nature of its outcome. Besides causing acute and chronic toxicity pesticides are also known to increase the risk of carcinogenesis in two ways: the direct way- by acting as carcinogens themselves and secondly as the indirect way- by suppressing the immune system which has the ability to destroy the process of carcinogenesis in the body. Most cancers associated with immune suppression have been leukemia and lymphomas. [3]

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

Hence the main objective of the present study was to monitor the organochlorine pesticide level in the body of Lymphoma patients and then find out any association in blood level of organochlorine pesticides and the development of lymphoma.

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 institutional review board of the hospital, and written informed consent was obtained from all the enrolled subjects. A total of 135 patients were prospectively recruited into this study and 80 were taken as control, as they did not have any cancer and 55 patients of lymphoma were recruited for the study. Thus 80 subjects serve as control against 55 cancer cases. The preformed and pretested questionnaire included a detail information regarding family history of any major disease (particularly lymphoma), health status, age, economic status, religion, dietary habits and also the regarding use and accidental exposure to the organochlorine pesticides either at farm, home or at work place. Samples were taken by venipuncture method using 2ml syringe and stored in EDTA vials at 4^{o}C. organochlorines 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 student's 't' test. The data were analyzed using MS Excel 2010, Epi Info v7 and SPSS v22.

Results

In present study the out of total 135 study patients 55 had lymphoma and 80 patients were act as controls organochlorine pesticide level in control subjects were 0.3456 ± 0.017mg/L and in lymphoma patients were 0.4874 ± 0.069mg/L (P value > 0.05). In case of Lymphoma out of 55 patients 50.90% were the patients of Non-Hodgkin's Lymphoma (NHL) and the remaining 49.10% subjects suffered from Hodgkin's Lymphoma (HL). The total pesticide burden in NHL patients was 0.5253 ± 0.103mg/L and in HL patients was 0.4482 ± 0.092mg lit. All the pesticides analyzed were found higher in patients than control. (Table-1) This difference between lymphoma and mean pesticide levels was not found statistically significant (P value > 0.05).

Table 1: Mean pesticides levels among lymphoma patients and study controls.

Study patients	No. of patients	Mean pesticide levels (mg/L)	P Value
Non-Hodgkin's Lymphoma	28	0.5253 ± 0.103	0.266
Hodgkin's Lymphoma	27	0.4482 ± 0.092	1.00
Total	**55**	**0.4874 ± 0.069**	**1.00**
Control	80	0.3456 ± 0.017	

In case of NHL, α-HCH, δ-HCH, total endosulfan with endosulfan sulfate, dieldrin, heptachlor epoxide, DDD, DDT and total pesticides were found to be significantly high in patients than control. Similarly HL patients had significantly high level of total HCH along with α, δ isomer, DDD, aldrin, heptachlor epoxide, endrin and total pesticides than control. When all the Lymphoma patients were taken collectively all the pesticide residues were found significantly high in their blood except total DDT, dieldrin and heptachlor. (Fig -1)

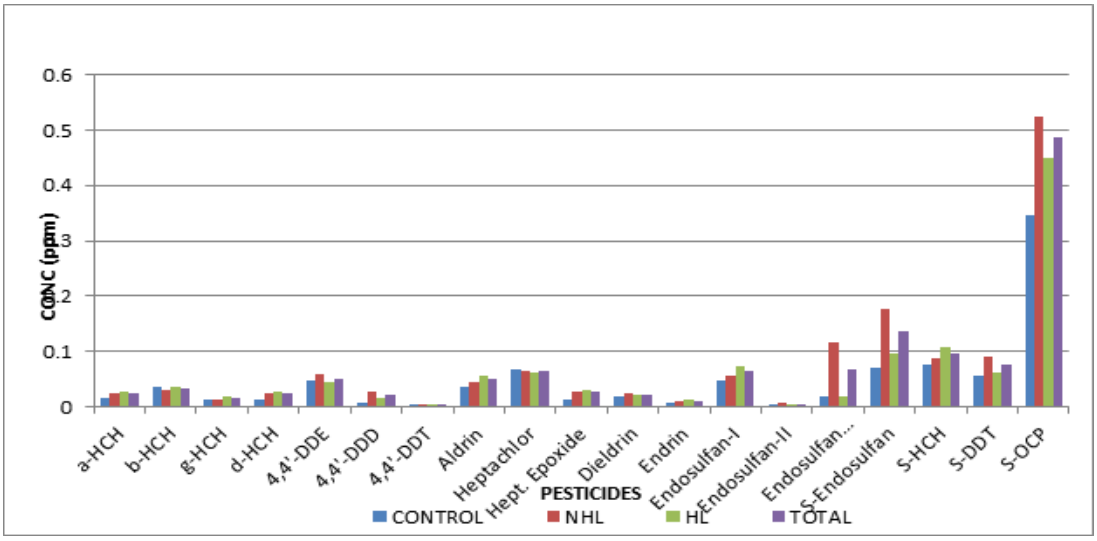

Figure 1: Comparison of pesticide residues in blood of control subjects and subjects with different lymphoma cancer

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 an exposure indicator of pesticides.

The present study includes the analysis of 135 blood samples, in which 55 subjects suffered from lymphoma 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 lymphoma and residue level of several organochlorine pesticides (OCPs) was examined and it was observed that there are a significantly high concentration of total OCPs in the blood of lymphoma (0.4874 ± 0.069mg/L) patients in comparison to controls (0.3456 ± 0.017mg/L). This may indicate that pesticide residue levels in the blood may increase the risk of developing lymphoma in the general population of Rajasthan (table-1).

The exposure of the general population to these lipophilic OCPs is mainly through 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 food [10]. DDT and HCH insecticides are the major contaminants of Indian food stuffs. 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 populations 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% of rice samples (Toteja *et al*, 2003) collected from different geographical regions of the country were found to have the residues of these insecticides [14]. These studies clearly indicate that the Indian foodstuff is highly contaminated with pesticides

Ahlborg *et al* (1995) also reported that food especially meat, poultry, fish and dairy products had 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 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 city [16].

In the present study Among the NHL patients, significantly high residues of pesticides in blood (0.5253 mg/L) were obtained as compared to that in the blood of controls (table-1). Studies conducted by Fritschi *et al* 2005 [17] and Mester *et al* 2006 have also suggested a greater incidence of lymphoma among the pesticide-exposed population [18]. But findings of Dryver *et al* (2004) do not suggest that the exposure to pesticides may cause lymphoma [19].

In present study HL patients also have significantly high residues of total OCPs in their blood that is 0.4482 mg/L, as compared to controls (0.03456 mg/L). Kristensen *et al* (1996) found a non-significant increase in the risk of having Hodgkin's Lymphoma in the children's of farmers and in population associated with poultry (chicken farming) [20].

Considering the type of lymphoma individually, there was 0.5253mg/L concentration of total organochlorine pesticides in NHL patients which is non-significantly high ($p>0.05$) in comparison to controls (table-1). The total pesticide residues observed in HL patients was 0.4482mg/L which shows no significant difference as compared to control (table-1). This presumably means that there is no significant association between pesticide levels in blood and occurrence of NHL and HL. This may be attributed to the small sample size analyzed, and thus, a definite conclusion could not be drawn here. [21]

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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