

RESEARCH ARTICLE

Non-Hodgkin Lymphoma and Pesticide Exposure in Turkey

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Abstract

Background: Non-Hodgkin lymphoma (NHL) is a solid tumour of lymphocytes, important elements in the immune system. According to 2006 data, in Turkey the incidence was 6.5 per 100,000 in males, and 4.4 in females. The relationship between the use of pesticides and development of NHL has been extensively investigated in many studies, and it has been demonstrated that the risk of NHL is increased by exposure to such compounds. Antalya is a region of intensive agricultural activity. In this study, the relationship between the incidence of lymphoma in Antalya and the amount of pesticides employed was investigated. **Materials and Methods:** The study used data from 1995 to 2010 on the patients from the databank of TR Ministry of Health, Antalya Provincial Health Directorate, Cancer Registration Center and the patients who were histopathologically diagnosed with NHL during these years. **Results:** The relationship between the amount of pesticide used and the incidence was studied with the Spearman correlation analysis and the p value was found as 0.05. The correlation coefficient was 0.497. An increase in the NHL incidence over the years was identified, with a 2.42-fold increment found from 1995 to 2005 and a 2.77 fold elevation from 1995 to 2010. The use of pesticides increased 1.89 fold over the same period. **Conclusions:** Our study investigated the relationship of the pesticides used with NHL patients diagnosed during the same year. Since the time elapsing after exposure to pesticides until the development of cancer is not clear, no comparison can be made at present. We believe that the increase in use of pesticides since 1995 may be associated with the increase in the incidence of NHL and therefore that further studies on the issue including measurements of serum pesticide levels, are required.,

Keywords: Non-Hodgkin lymphoma - pesticides - agriculture - cancer

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Introduction

Non-Hodgkin lymphoma (NHL) is a solid tumour of lymphocytes, which is an important element of the immune system. It occurs as the 6th most common type in men and 5th most common type in women in the US, and it comprises 4-5% of all cancers (American Cancer Society 2005; Eser et al., 2010).

In the US, the incidence of NHL increased by 3-4% per year between 1970 and 1980, and the increment slowed down during 1990s. Although the increase was associated with the widespread use of HIV and immune-suppressing drugs, various environmental factors are also believed to be responsible for the increase (Clarke et al., 2004; Howlader et al., 2012). These environmental factors include occupational exposure to chemical agents as well as factors related to diet (Hardell et al., 1981).

Pesticides are chemical agents used to suppress harmful effects of pests, such as insects, rodents, weeds and fungi, which nest on or around animals and plants

and decrease nutritive value of food during storage or consumption. Pesticides are available in numerous forms. The relationship between use of pesticides and development of prostate cancer, non-Hodgkin lymphoma, leukemia, multiple myeloma, and breast cancer has been investigated in various studies (Shakeel et al., 2010; Alavanja et al., 2013). It has been demonstrated that the risk of NHL is increased by use of pesticides (Miligi et al., 2003; Richardson et al., 2008).

Antalya is a region of intensive agricultural activity in the south-west of Turkey. In this study, the relationship between the incidence of lymphoma in Antalya and the amount of pesticides used is investigated.

Materials and Methods

The data used for the present study were obtained from the patients' databank of the Turkish Ministry of Health, Antalya Provincial Health Directorate, Cancer Registration Center and the patients who were

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Table 1. Amount of Pesticides Used

Year	Amount of pesticides (kg)	Population	New NHL Diagnosis	Rough incidence (%)
1995	3190384.00	1182438	33	0.0028
1996	3291296.00	1226608	54	0.0044
1997	2582611.00	1262909	53	0.0042
1998	3316141.00	1307830	62	0.0047
1999	2440470.00	1350434	65	0.0048
2000	4086824.00	1392172	60	0.0043
2001	1998509.00	1431273	76	0.0053
2002	2387979.00	1483855	91	0.0061
2003	3287328.00	1508087	84	0.0056
2004	3104433.00	1558344	122	0.0078
2005	3692854.00	1613692	109	0.0067
2006	4685082.00	1673219	119	0.0071
2007	4791427.00	1789295	150	0.0084
2008	5871076.00	1859275	141	0.0076
2009	5725853.00	1919729	142	0.0074
2010	6045826.00	1978333	153	0.0077

histopathologically diagnosed with NHL between 1995 to 2010 were included in the study. The patients whose histopathological diagnosis was not confirmed were not included. The data were reviewed to exclude the duplicated data.

The data on the amount of agricultural pesticides used each year between 1995 and 2010 was obtained from Antalya Provincial Directorate of Agriculture. Annual population data was gathered from the household identification sheets of village clinics for the years from 1998 to 2006, and from the population data and address-based registry records of the Turkish Statistics Institute for the years from 2007 to 2010. The rough incidence was calculated by dividing the number of new cases by total population.

Statistical analysis was conducted by the SPSS 13.0 software. The significant p value was considered as <0.05. The relationship between the amount of pesticides and the rough incidence was investigated by Spearman correlation analysis, which is a non-parametric test.

Results

A total of 1514 patients were evaluated in the study, of whom 897 (59.2%) were male and 617 (40.8%) were female patients. The rough incidence rates by year of diagnosis and the amount of pesticides used in these years are given in Table 1.

The relationship between the amount of pesticides used and the incidence was studied with the Spearman correlation analysis and the p value was found as 0.05. The correlation coefficient was found as 0.497. An increase in the NHL incidence over the years was identified, while a 2.42-fold increase was found from 1995 to 2005. The increase was by 2.77 folds from 1995 to 2010. The use of pesticides was increased by 1.89 folds in the same period.

Discussion

Since the p value of the relationship between the total level of pesticides used and the NHL incidence was identified as 0.05, it was considered as a borderline

relationship. Pesticides is a generic name of a group of chemicals which contain various chemical agents. They are referred to as insecticides, fungicides and herbicides according to the pests they are used against. These chemicals also have groups, such as organochlorines, carbamates and triazines (Zahm et al., 1997).

Use of pesticides and development of cancer has been investigated in numerous studies. Pesticides may exhibit their carcinogenic effects via various mechanisms such as genotoxicity, hormonal effects or immunotoxicity. Genotoxic effects of certain pesticides on hemopoietic cells have been demonstrated (Parent-Masin et al., 1993). It has been demonstrated that use of pesticides may be associated with chromosomal changes and it may affect the NHL subtypes (Chiu et al., 2009).

Various viral and environmental factors are held responsible for the development of NHL (Barista et al., 1994; Paydas et al., 2004). Spinelli et al. investigated the relationship between the serum organochlorine levels and NHL. The serum organochlorine levels prior to treatment of 422 NHL patients were compared with those of 460 control group patients, and the levels were found higher among the NHL patients. They suggested that, exposure to organochlorines may play a role in the development of NHL (Spinelli et al., 2007). In their study, Laden et al. did not determine any relationship between serum organochlorine levels and NHL (Laden et al., 2010). Cocco et al. (2008) studied the relationship between the major types of lymphoma and organochlorine levels and could not demonstrate a relationship. In another study, a relationship between the serum organochlorine levels of male patients and NHL was demonstrated (Bertrand et al., 2010).

There have been case control studies investigating the relationship between exposure to pesticides and NHL development in Europe, the US, Canada and Australia, and most of these studies have identified an increased risk. The risk increase ratios vary between 0.9 and 4.7 (Hardell et al., 1981; Pearce et al., 1986, Woods et al., 1987; Olsson et al., 1988; Kogevinas et al., 1995; Pahwa et al., 2012). The relationship between the use of pesticides and development of NHL has also been investigated in two cohort studies, which identified a borderline increase in risk (Kogevinas et al., 1997; Bertazzi et al., 2001). On contrary to these studies, Cocco et al have demonstrated in their Epilymph study, in which 2348 patients and 2462 healthy controls were evaluated, that NHL development risk was not increased with exposure to pesticides, but nonetheless the risk of chronic leukaemia was increased (Cocco et al., 2012).

The epidemiological studies in the US have demonstrated an increase in NHL incidence in the intensive agricultural regions from 1950 to 1994. This was associated with the chemicals used in the agricultural activities. Most of the studies on the relationship between the use of pesticides and NHL have investigated whether farm life increases the risk of NHL (Pearce et al., 1987). These studies are usually retrospective cohort and case control studies and they include sampling, selection and recollection biases (Berz et al., 2011).

The first cancer registration center of Turkey was

founded in 1992. Antalya Cancer Registration Center has been recording cancer cases since 1995. The increasing number of patients over the years may be due to better recording of cancer cases. Also, the fact that the health care services provided in the fields of hematology and oncology are continuously becoming more widespread in Antalya may be a cause of this increase. These are the most significant restrictions of our study.

In our study, the relationship of the pesticides used with the NHL patients diagnosed during the same year was investigated. Since the time elapsed after the use of pesticides until the development of cancer was not known, this comparison was made. We believe that the increase in use of pesticides since 1995 can be associated with the increase in the incidence of NHL, therefore further studies on the issue covering the measurements of serum pesticide levels are required.

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