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Research Article

Chromosomal Aberrations in agricultural farmers exposed to pesticides

Abstract

Pesticides which constitute a group of environmental pollutants are commonly used in agriculture to protect crops. Pesticide exposure may be associated with increased risk of genotoxicity and carcinogenesis. Therefore, they pose a potential risk to farmers and environment. The aim of the present study is to investigate whether occupational exposure to various pesticides causes Chromosomal Aberrations (CAs) in agricultural farmers. The frequency of CAs in peripheral blood lymphocytes were evaluated in 35 Agricultural Farmers (AFs) and 40 control subjects living in Çukurova Region. The results showed that farmers exposed to pesticides had significantly increased frequencies of CAs when compared with controls ($P < 0.05$). Age-adjusted group comparisons showed that the frequency of CAs in the pesticide exposed AFs were 2,3 times higher than in the control group (OR: 2,3, 95% wald confidence limits: 1,9-2,9). The confounding factors such as variable duration of pesticide exposure, age, smoking, alcohol consumption had no significant effect on cytogenetic damage ($P > 0.05$). Fragile sites (FSs) on the 1(q21-24), 1(q31-32), 2(q31-34), 2(q21-23), 3(p21), 3(p25) and 5(q31-q34) chromosomal regions were significantly overexpressed in AFs, when compared to the control group (in 12.6% versus 4.3% of cells) ($P < 0.05$). Our findings indicate that occupational exposure to pesticides could cause cytogenetic damage in somatic cells of AFs. It is known that accumulation of CAs is a crucial step for initiation of many cancers. Therefore, it is suggested that the exposed workers should be warned about the potential harmful effects of pesticides and relevant authorities should safeguard that protective measures are taken by farmers while working in agricultural fields.

Introduction

Each year, nearly 3 million tons of pesticides are used in the World [1]. On a yearly basis, the total amount of pesticide consumption in Turkey reaches 30.000 tons in Turkey. The pesticides used in Turkey are very heterogeneous [2]. Among agricultural chemicals currently used throughout the world, pesticides have most harmful effects on natural ecosystems and biodiversity [3]. The general population is exposed to pesticides by their use in agriculture to protect crops, and in urban activities such as gardening in Turkey. AFs are occupationally exposed to mixtures of pesticides. According to the information available, 40% of the annual consumption of pesticides in our country is concentrated in the Mediterranean region [3,4]. Therefore, AFs and their families, peoples in workplace, family members (in the case of domestic use) and indirectly general population are at risk of toxicity caused by pesticide exposure in our country. Therefore, everyone is affected. For instance, Organophosphorous (OP) insecticides have been extensively used for agriculture in Turkey, and it poses a potential risk to farmers and environment. Pesticide exposure is now known to be associated with genotoxicity and increased carcinogenic risk. Genotoxicity testing plays an important role in the biomonitoring and assessment of the

carcinogenic risks associated with pesticide exposure. Several different genotoxicity end-points, single/double breaks, chromosomal aberrations, micronuclei, sister chromatid exchanges and mutations screening methods were used to examine the extent of genetic damage caused by pesticide exposure. The primary advantages of the cytogenetic analysis are related to precocious detection before clinical or histological premalignant abnormalities [5,6].

Several cytogenetic assays have been used to evaluate the potential genotoxicity of pesticide exposures in occupationally exposed populations. Populations and some studies have reported an association between occupational exposure to pesticides and increased levels of CAs and/or Sister Chromatid Exchange (SCE) in peripheral blood lymphocytes. However, high levels of SCE and CAs frequency have been observed in persons at higher cancer risk due to occupational or environmental exposure to a wide variety of carcinogens [7,8]. However, there are reports on positive genotoxic effects in populations exposed to pesticides [9-11], as well as negative findings [12,13]. However, authors found significant SCE differences in exposed workers compared to non-exposed workers and a three times increase in the Micronucleus (MN) frequency. Similar effects on SCE and MN were observed in agricultural



workers (25 women and 45 men) from Mexico who mainly used OP [14]. At the same time, the role of genetic polymorphisms as modifiers of human diseases has attracted attention in last decade, and polymorphisms in different genes involved in OP metabolism are candidates to affect susceptibility to OP-induced toxicity. Therefore, these results increase information about potential adverse effect of OP exposure that may lead to cancer development. Thus, this study aim is to investigate the chromosomal damages in pesticide-exposed AFs from cukurova region in south Turkey.

Materials and Methods

Study population

AFs in our study are exposed to pesticides such as organophosphorus, carbamates, pyrethroids and plant growth regulators. The study was carried out on a group of 35 AFs exposed to a mixture of pesticides in Çukurova region (southern region) of Turkey between October 2016 and December 2018. Age interval of AFs exposed to pesticides was 23–57 years (the overall average age was 37.6 ± 9.7). Fourty controls that were not exposed to pesticides were included in the this study. The age range of the control group was 18–65 (the average age was 39.3 ± 12.9). Both, the exposed farmers and unexposed subjects were selected from the same region. Prior to the study, all groups were informed about the study and signed a written consent before sampling. Complete information regarding sex, age, marital status, medical history, life style (smoking, drinking, etc.) along with the occupational history regarding various aspects of pesticides, duration of exposure, working hours/day, name and class of pesticides, protective measures used etc. was enquired from the workers and recorded in the questionnaire. A wide range of products can be cultivated in Cukurova region due to the favorable ecological conditions (wheat, cotton, corn, sunflower, soy, peanut, citrus, palm, pomegranate, watermelon, and vegetables ...). AFs have direct contact with pesticides through manual application and exposure to aerial spraying in the regions near their homes and in their workplaces. Moreover, they show scarce and inadequate use of personal protective equipment, i.e. gloves, boots, masks, longsleeved shirts, and hats. When planning the study, the necessary consultations were made with the ethics committee of the Çukurova University Medical Faculty (2016–BAP 4527).

Cytogenetic analysis

Five milliliters of peripheral blood was collected into heparinised tubes from each subject for culture. Each sample was examined for expression of CAs in the Genetics Laboratory of the Department of Medical Biology and Genetics, Faculty of Medicine, Cukurova University. Lymphocyte cultures were set up by mixing 0,5ml of whole blood samples, with 4.5 ml of RPMI-1640 medium containing 15% foetal calf serum, antibiotics (5 UI/ml penicillin and 5mg/ml streptomycin), and phytohaemagglutinin (PHA, 1.5% of the final culturemedium) (all reagents from Gibco, Life Technologies, Italy) according to standard cytogenetic techniques. Standard cytogenetic techniques were used for harvesting and slide preparation.

Three slides were prepared for each subject. The slides were prepared by trypsin G-banding and 50 metaphases/individuals were analysed on coded slides for structural CA, such as chromatid and chromosome breaks, fragile sites, gaps, deletions, translocations, di-centric chromosomes and aneuploidy. FSs and gaps were also scored, but excluded from the final percentage of cells with CA. All gaps and breaks were recorded according to the ISCN (1985). The classification of FS was done according to the nomenclature established in human gene mapping HGM 11 [15].

Stastical analysis

In the statistical analysis of the data, SPSS 20 and SAS university edition programs were used. Descriptive statistics were used for all the parameters studied. The comparison of continuous variables between groups was evaluated using non-parametric tests (as between the duration of spraying activity, total number of CAs/cell, smoking history, tobacco chewing, alcohol consumption, and pesticide residues). Chi-square, independent two-group t-test, and logistic regression analysis were used to demonstrate the age-related effect of pesticides on frequency of CAs. $P < 0.05$ was considered significant.

Results

A complete history including age, the duration of spraying activity, total number of CAs/cell, smoking history, tobacco chewing, alcohol consumption, and the results of the farmer and control groups studied is given in Tables 1,2.

In AFs, The average ages, the average working-years, the average of spraying year and the average number of spraying done in one year was shown in Table 3.

Considering the clinical and demographic characteristics of the agricultural farmers shown in Table 1; as a protecting measure, 54.3% of farmers have hand-face washing habit, but the 62.9% of them do not take a shower after spraying and 51.4% of them smoke during the application. Bonnet, overalls and boots are not used by any AFs. The rate of those with health complaints was 54.3%. The rate of coughing and eye burning was 54.3% and 45.7%, respectively. No significant correlations were found between AFs-agriculturing/spraying years, the number of pesticides they used in a year and the percentage of CAs ($p=0.25$, $r=-0.19$; $p=0.32$, $r=-0.17$; $p=0.98$, $r=-0.00$). Regression analysis indicates that the data were not influenced by age, cigarette smoking, or alcohol consumption ($P > 0.005$). It was shown that the exposure conditions among AFs have not caused detectable increases of CAs. In AFs-group, 1642 metaphases were analyzed. A total of 273(16.8%) CAs were observed in 252(15.4%) metaphases that including one or more various CAs. It was found that 96,7% and 3,3% of these CAs were structural and 3,3% numerical ones, respectively. Among the structural CAs; 20(7.3%) deletions, 6(2.2%) translocations, 31(11.4%) chromatid breaks, 1(0.4%) chromosome breaks, 207(75.8%) fragile regions (FS) were found in the analyzed cells. In the control group, 2000 metaphases were analyzed and a total of 156(7.9%) CAs were observed in 138 (6.9%) of the analyzed cells. CAs found in controls were 83% structural

**Table 1:** Clinical, demographic characteristics and number of damaged cells for the agricultural farmers.

Age	Years of farming/ many times of spraying in year	Spraying shape	Spray training	Spraying + eat/ smoking	Protection against pesticide	House spraying smoking	Health complaints	Smoking year / pack	Alcohol	X-ray	CAs/ scanned cells
57	15/7	Pump	No	No/Yes	Hand-face washing	No	Eye burn, itching, skin rash	40/2	No	No	0/50
29	5/3	Pump	No	No/No	Hand-face washing	No	-	No	once a week	No	0/50
42	30/30	Pump	No	Yes/No	Gloves,take a shower	No	Eye burn, weakness, nausea	No	no	No	3/30
25	10/10	Tractor	No	No/Yes	None	2 times in a year	Eye burn, itching	10/1	No	No	0/50
55	30/40	Pump	No	No/No	Hand-face washing	No	Eye burn, fatigue	40/0.5	No	No	4/50
32	22/10	Tractor	No	Yes/Yes	Hand-face washing	3 times in a year	Eye burn, itching	13/1	No	No	0/50
43	20/10	Tractor	No	No/No	Hand-face washing, take a shower	No	-	20/1	No	No	4/50
51	40/10	Tractor	No	No/No	Hand-face washing, take a shower	No	-	No	No	No	4/21
26	2/10	Tractor	No	No/No	Hand-face washing, take a shower	No	-	No	No	No	7/50
56	30/15	Tractor	No	No/Yes	Hand-face washing, take a shower	No	Eye burn,muscle and joint pain,weakness	23/1	No	No	10/50
30	15/30	Tractor	No	No/No	Hand-face washing	No	Eye burn,weakness	No	No	No	10/50
37	30/12	Tractor	No	No/No	Hand-face washing, take a shower	No	-	No	No	No	7/50
51	40/10	Tractor	No	No/No	Hand-face washing, take a shower	No	-	35/1	No	No	2/24
37	30/30	Tractor	No	Yes/Yes	None	Once in a year	Eye burn, weakness muscle and joint, pain	30/2	No	No	4/42
23	1/7	Tractor	No	Yes/Yes	None	No	Eye burn, itching	no	No	No	10/50
44	30/30	Pump	No	Yes/Yes	take a shower	Twice in a week	Eye burn, itching, fatigue, cough, shortness of breath blurred vision	30/2	No	No	7/50
45	20/20	Pump	No	No/No	Gloves, hand-face washing	Once in a year		5/3 piece	No	No	5/50
37	20/20	Pump	No	No/no	Gloves, hand-face washing	Once in a month	Fatigue, blurred vision	15/1	No	No	9/50
36	20/30	Pump	No	No/No	Gloves, hand-face washing	No	Eye burn, weakness	10/0.5	No	No	9/50
32	15/30	Pump	No	Yes/Yes	None	No	-	10/1	No	No	7/34
37	22/30	Pump	No	No/Yes	Hand-face washing, take a shower	No	Eye burn, itching, skin rash, fatigue, weakness	15/1	No	No	4/50
41	20/30	Pump	No	No/Yes	Gloves, hand-face washing	Once in a month	-	20/1	No	No	12/50
43	25/10	Tractor	No	Yes/Yes	Take a shower	3 times in a year	Eye burn, headache, fatigue	20/1	No	No	0/50
35	28/40	Tractor, pump	No	Yes/Yes	Gloves, take a hower	4 times in a year	-	23/1.5	No	No	14/50
53	35/50	Pump	No	Yes/Yes	Take a shower	3 times in a year	-	No	No	No	18/46
37	20/30	Pump	No	No/No	Hand-face washing, take a shower	Once in a year	Fatigue, weakness	No	No	No	6/50
39	20/10	Tractor	No	Yes/Yes	None	No	Eye burn, muscle and joint pain, weakness,	20/1	No	No	0/50
42	5/3	Tractor	No	Yes/Yes	None	No	-	3/1	No	No	20/50
28	15/10	Tractor	No	No/Yes	None	No	-	15/1	No	No	25/50



29	15/40	Tractor, pump	No	No/No	None	No	-	16/2	No	No	7/47
23	2/4	Tractor, pump	No	No/No	None	No	Itching	No	No	No	8/48
29	3/12	Tractor, pump	No	No/No	None	No	Eye burn, cough, shortness of breath blurred vision	No	No	No	6/50
39	17/12	Tractor	No	No/No	v	No	-	20/0.5	No	No	8/50
32	15/15	Tractor, pump	Yes	No/No	Mask, gloves	No	-	15/1	Once a month	No	12/50
23	5/9	Pump	No	No/No	None	No	Eye burn, fatigue	No	No	No	30/50

Table 2: Demographic characteristics and CAs/cells of control group.

Age	Job	Smoking years/ pack number	alcohol	X-ray	CAs
27	Student	16/1	No	No	4/50
37	Advisor	No	No	No	3/50
34	Builder	20/1	No	No	2/50
43	Builder	No	No	No	0/50
20	Student	No	No	No	6/50
28	Builder	10/1	No	No	5/50
36	Attendant	No	No	No	7/50
39	Farming	No	No	No	4/50
45	Electrician	No	No	No	3/50
41	Artisan	20/2	No	No	7/50
56	Artisan	No	No	No	0/50
45	Worker	No	No	No	5/50
47	Artisan	No	No	yes	4/50
26	Artisan	10/1	Once in a month	No	4/50
42	Farming	No	No	No	0/50
55	Farming	No	No	No	0/50
65	farming	No	No	No	2/50
39	Paint technician	15/1	Once in a weak	No	3/50
53	Worker	No	No	No	6/50
23	Builder	5/1	No	No	0/50
30	Builder	15/1	No	No	0/50
33	Builder	20/1	No	No	0/50
26	Builder	10/1	Once in a month	No	5/50
33	Accountant	No	No	No	4/50
63	Attendant	No	No	No	1/50
37	Artisan	No	No	No	2/50
53	Accountant	20/0.5	No	No	0/50
40	Baker	17/1	No	No	4/50
54	Baker	40/1	No	No	2/50
43	Baker	15/1	No	No	6/50
22	Baker	7/2	Once in a month	No	4/50
18	Baker	5/0.5	No	No	5/50
23	Baker	No	-	-	0/50
62	Attendant	No	No	No	26/50
42	Baker	30/1	No	No	8/50
34	Baker	10/0.5	No	No	6/50

47	Baker	7/1	No	No	4/50
65	Baker	no	No	No	7/50
26	Baker	6/0.5	No	No	2/50
29	Baker	14/0.5	No	No	4/50

Table 3: Physical characteristic, personal habits and exposure period of agricultural farmers.

	Agriculture farmers (n=35)	Controls (n:40)
Age (yrs) [Mean±SD]	37.6±9.7	39.3±12.9
Smoking year [Mean±SD]	19.4±10	14.8±8.5
Smoking piece (day) [Mean±SD]	21.8±10.0	19.5±8.0
Alcohol quantity (weekly) [Mean±SD]	2.5±2.1	1.7±1.5
Years of farming [Mean±SD]	19.2±10	-
Years of spraying [Mean±SD]	15.4±9.7	-
Spraying in year [Mean±SD]	19.1±12.6	-

and 16.7% numerical ones. The chromosome breaks were more frequent than the chromatid-type breaks. Among the structural CAs; 6(3.8%) deletions, 11 (7.1%) translocations, 2(1.3%) duplications, 12(7.7%) chromatid breaks, 11(7.1%) chromosome breaks, 2(1.3%) dicentric chromosomes and 86(55.1%) FS were found in the analyzed cells. There was a significant difference between the results of the percentage of CAs/number of cells scanned between AFs (Ort±ss:16.5±13.8) and control groups (Ort±ss:7.8±8.6), and CAs were found significantly more in AFs (p=0.002). The effect of pesticide application and age factors on chromosomal disorders was examined (OR:1, 95% wald confidence limits: 0.9-1.009). Chromosomal damage was not affected by age in control subjects (P>0.05). When examined by age, the CAs were 2,3 times higher in the pesticide exposed AFs than in the control group (OR:2,3, 95% wald confidence limits: 1.9-2.9).

In AFs-group, from the CA analysis it was obvious that the overwhelming majority of aberrations were fragilities. Deletions and translocations were counted as two breaks each and chromatid breaks as one in calculating the total chromatid break frequencies. FS was found in 12.6% of the AF's cells and in 4.3% of control cells. These findings clearly show that pesticides increase FSs on chromosomes. These FSs also cause chromatid and chromosome breaks. In AFs, most frequent FS expression was observed on chromosome 1 and less frequent on chromosome 2, 3. These FSs were located on 1(q21-24) and 1(q31-32), 2(q31-34), 2(q21-23), 3(p21), 3(p25) and 5(q31-q34)



regions and significantly overexpressed in AFs. Chromosomes 2 and 3 were more susceptible to breakage in those individuals.

Discussion

Pesticides constitute a heterogeneous category of chemicals specifically designed for the control of pests, weeds or plant diseases. Their application is still the most effective and accepted means for the protection of plants from pests. But, the use of pesticides for agricultural purposes has been reported to be associated with many deleterious health effects in personnel involved in their regular and extensive use. Because, pesticides contain numerous genotoxic compounds, farmers occupationally exposed to pesticides during spraying activities are more prone to genotoxicity than unexposed. Occupational exposure is often the best source of information about the health risks associated with pesticides. The effects of chronic exposure to pesticides can lead to the development of several diseases, including different types of cancer, since the genotoxic and mutagenic capacity of these substances are high. A recent study in our region has shown that the cukurova region is the most important agricultural area and is responsible for 32% pesticide use in Turkey [16]. As a consequence of this wide pesticide use, acute pesticide poisoning cases are quite common in this region. Exposure to pesticides might occur via oral intake within the home environment while occupational exposure occurs via dermal contact and inhalation.

In the present study, the pesticide-exposed farmers showed significant increase in CAs when compared to unexposed controls. So, the occupational exposure increases cytogenetic damage induced by pesticides exposure. Researches on pesticide-exposed workers from all over the world in the last decade also demonstrated statistically significant DNA damage, MN and CAs [17-30]. In a recent study, it was found an increased frequency of MN and CAs in pesticide-exposed agricultural workers from northeastern Brazil [25]. By the other hand, other studies have indicated that pesticide exposure caused no significant genotoxic effect in agricultural workers, when compared to the control population [31,32]. Furthermore, polymorphisms in metabolism and DNA-repair genes may modulate the extent of DNA damage in pesticide-exposed workers [33]. Since the AFs are frequently exposed to mixture of pesticides, it is difficult to attribute the genotoxic damage to any chemical class or compound. Genotoxicity observed in the AFs of the present study may be due to lack of proper protective measures while spraying or storing pesticides. DNA damage is an important intermediate step in cascade of events leading to cancer development. The frequency of CAs is often used to evaluate chromosomal instability that correlates with a high risk of several cancers [34]. These findings suggest that we should consider the potential carcinogenic risk for farmers exposed to pesticides.

High CAs may be associated with the risk factors such as smoking, drug use, hypertension, diabetes, stress and age. Thus, factors such as age, sex, lifestyle, smoking habits, alcohol consumption and history of recent illnesses can influence the frequency of genotoxic effects [35]. The age of the individuals demonstrated to have influence in the increase

of CAs, and being verified a positive correlation between them [31,36,37]. A progressive increase in spontaneous chromosome instability/chromosomal loss due to the aging process is associated with the accumulation of DNA damage which is caused by age-related decline in DNA repair capacity [38]. In the present study, the effects of personal habits such as the time of exposure to pesticides, the use of personal protection equipment, smoking habits and alcohol consumption were also evaluated. But, it was shown that these factors did not have any effect on markers of genetic damage (Table 1). Although Fenech et al., [39], questioned gender, advanced age, malnutrition and other individual conditions lead to an increase in the amount of DNA damage, a large part of the studies with rural workers do not observe such correlations [12,31,40,41]. Smoking and alcohol consumption are the major confounding factors effecting genotoxicity. Smoking is a well-documented source of a variety of potentially mutagenic and carcinogenic compounds. Although the exposure to pesticides, smoking and alcohol consumption are important factors effecting general health, no significant correlation was observed between this parameters and the CAs in the present study ($p>0.05$). Other studies also reported no differences in DNA damage between smoker and non-smoker workers occupationally exposed to pesticides [42-44].

The chromosome fragilities in FSs may be resulted from single-strand DNA breaks, which if not repaired, may lead to chromosome damage such as deletions, translocations or other rearrangements [45]. We also observed a greater number of chromosome and chromatid breaks, deletions and translocations in AFs. We also observed significantly greater number of FSs. The increase in fragility may increase the risk for breakage or deletion in AFs. In the present study, chromosomal breaks in AFs were found to be greater than the control (in 3.5% versus 2.0% of cells). This also shows that AFs in the present study were occupationally exposed to pesticides for a long period of time. It is known that pesticides play an important role in the production of DNA single-strand breaks [46]. However, some pesticides may induce oxidative stress that leads to increased DNA damage, and act as clastogenic agents causing DNA damage resulting in chromosomal breaks. Over time, these breaks can be repaired by DNA repair enzymes. As it is known DNA repair mechanism protects cells against genotoxicity, repairs DNA strand-breaks and preserves genetic stability [47].

Identification of the basis of instability at FS and the related genes provides an entree to understanding the important aspects of chromosomal instability, which is a prominent effect that pesticides cause. However, the FS is a very interesting subject for the study of clinical disorders, which can lead to the formation of deletions and translocations. At the same time, the characterization of FS has demonstrated that they are associated with genes that relate to tumorigenesis and behavioural disorders [48,49]. In the present study, FSs were significantly overexpressed in AFs ($P<0.05$), when compared to the control group (in 12.6% versus 4.3% of cells). It may be considered that the expression of FS could be an indicator of chromosomal instability within the genome of AFs. In the



present study, we found significantly overexpressed FSs at the chromosomal regions of 1(q21-24), (1q31-32), 2(q31-34), 2(q21-23), 3(p21), 3(p25) and 5(q31-34) in the AFs. The regions can be hot spots for AFs. Specifically, FS expression at 5(q31-34) region was observed to be most frequent. Specific studies have previously reported that in a variety of cancers, certain tumor suppressor genes were located to region 5(q31). It was reported that protocadherin genes that are located to region 5(q31) could be tumor suppressor genes in Wilms' tumor [50]. An association between the sprouty homolog 4 gene at 5(q31) and testicular cancer was shown in a earlier study [51]. Some tumor suppressor genes on 5(q31) are important in hematological transformation [52,53].

We report that specific regions on long arm of chromosome 1(q21-24) and 1(q31-32) were induced in AFs. In one study, specific regions on both arms of chromosome 1(q21) and 1(q32) were induced in changes involving this chromosome in cervical carcinoma [54]. In other studies, NORE1 gene at 1(q32.1) that is homologous to the tumor suppressor gene RASSF1A was isolated [55]. Specific genes located at 1(q21) were associated with myeloproliferative neoplasms, and this region may contain oncogenes or tumor suppressor genes [56]. According to the results of the present study, the 1(q21-24) and 1(q31-32) regions may contain certain oncogenes or tumor suppressor genes. Some genes on chromosomes 2 are also known to play a role for tumor development, and may be affected by these alterations [57]. Therefore, the chromosome regions 2q could play a role in the pathogenesis of cancer. FS expression at 3(p21) and 3(p25) was observed to be most frequent in our AFs. In some studies, the GPX1 gene was reported as a selenium-dependent detoxifying enzyme gene located at chromosome 3(p21), and GPX1 Pro/Leu genotype was associated with an increased risk of breast cancer and may also be associated with the development of high-stage tumors [58]. The TU3A gene located on 3(p21.2) was reported as a candidate tumor suppressor gene in renal cell carcinoma, and is also involved in primary cancers of the bladder and testis [59]. The RASSF1 gene on 3(p21.3) is silenced in a variety of human cancers, including lung, bladder, prostate and kidney cancers [58]. In conclusion, the regions on chromosomes 1, 2, 3 and 5 contains numerous cancer-related genes, and these genes may be candidates for AFs.

In the present study, the distal deletions and FSs on chromosome 16(q22) mosaicism was found in 32% (16 cells) of 50 analyzed cells of a farmer [del(16)(q22)x10; fra(16q22)x6]. The deletion on chromosome 16q will show the breakpoint. Few cases of 16(q22) have been reported so far as rare events. It has been suggested that there are critical regions within 16(q22) [60], which produce a pattern of features including growth retardation, intellectual disability, physical anomalies, renal and musculoskeletal malformations and congenital heart defects. However, deletion of chromosome 16q is frequently associated with diverse tumors. Numerous studies strongly suggest the presence of one or more tumor suppressor genes on chromosome 16(q22-qter) including the widely studied cadherin gene family. Therefore, pesticides could play a role in formation of the chromosome 16q deletions and FSs. However,

we found a similar 16(q22) mosaicism in a control group; in 36% (18 cells) of 50 cells analyzed showed [del(16q22)x14; chrbr(16q22)x4] chromosome constitution.

Conclusion

Our findings show that there is relatively great risk of genotoxic damage for agricultural workers exposed to pesticide. This genetic damages may be caused by the direct exposure of the DNA to pesticides or by the oxidative stress generated from the exposure, since the markers of oxidative stress are also altered. Thus, it is concluded that individuals exposed to pesticides are subject to genetic damage and, consequently, more susceptible to diseases resulting from these damages. The genotoxicity revealed by exposure to pesticides may be taken as an early warning signal for future development of diseases such as cancer and congenital malformations. Accumulation of CAs is a crucial step for initiation of many cancers and assessment of chromosome damages in pesticide-exposed workers may be advisable. Further, it is understood that the exposed farmers are not fully informed about the potential harmful effects of pesticides. Thus, relevant authorities should ensure that protective measures are used by farmers while working in agricultural fields. Besides, the affected farmers need to be monitored periodically. In order to minimize or prevent pesticide exposure, it is necessary to apply stricter rules. Initiation of awareness campaigns to educate farmers about the use of personal protective equipment, precautionary measures for safe handling and spraying techniques, effective personal hygiene and post-exposure cleanliness would minimize the deleterious effects of pesticide exposure.

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