

Smoking habit as a synergistic factor for genotoxicity and chest infection induced by occupational exposure to cadmium

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Abstract: Several studies proved the genotoxic effect of cadmium (Cd) exposure and damaging the respiratory epithelium leading to increase the risk for respiratory infections. In addition, the impact effect of smoking was also reported. The present study aimed at finding out the genotoxicity and lung infection caused due to confounding role of smoking habit with occupationally exposure to (Cd). The study sample was 40 exposed workers (27 smokers and 13 non smokers) compared to 40 control subjects (28 smokers and 12 non smokers) comparable in their age and socioeconomic status. A cytogenetic study was performed, biological indices' of Cd(Blood Cd(B-Cd) and Urine Cd(U-Cd) levels were estimated for the two groups. Microbiological profile for the virulent pathogens causing lung infection were screened. Statistical analysis proved a significant difference between smoking index, biological indices' of Cd (B-Cd and U-Cd) on one hand and SCE on the other hand. Cytogenetic analysis revealed the mean significant cytogenetic changes for all exposed and control groups, in the form of SCE and chromosomal abnormalities were found to be significantly higher among the exposed workers compared to controls. Microbiological profile determined more implication in smokers of both groups. In conclusion, smoking habit proved to have synergistic effect on genotoxicity and lung infection with occupationally exposure to (Cd). [Researcher. 2009;1(5):37-43]. (ISSN: 1553-9865).

Keywords: cadmium, genotoxicity, smoking, chest infection, occupational exposure

1. Introduction

Cadmium (Cd) is a heavy toxic metal commonly found in industrial workplaces. It has no nutritive function in humans (Newman-Taylor 1998), and it is a probable lung carcinogen in humans according to the Agency for Toxic Substances and Disease Registry (ATSDR 1999). Non-occupational sources of cadmium exposure within the general population include ingestion of contaminated food (Järup, et al., 1998) and inhalation of cigarette smoke (Satarug et al., 2004).

High levels of cadmium exposure are known to cause emphysema in occupationally exposed workers, but little has been reported to date on the association between chronic environmental cadmium exposure and pulmonary function (Lampe, et al., 2008)

Cigarette smoking remains a major health problem causing infectious diseases, heart disease, chronic lung disease and cancer (Kirschvink et al., 2006). Smokers have higher body burdens of cadmium

than nonsmokers (Erzen and Kragelj 2006; Grasseschi et al. 2003).

Mutation and genotoxicity caused from Cd exposure in the form of chromosomal and chromatid breaks, and high frequency of sister chromatid exchange were reported by (IRAC, 1993).

Enhancing the mutagenic action of Cd and invasive lung disease caused by excessive exposure to smoking might explain the observed increases in cancer rates, which lead to consider it a confounding factors for the increase in cancer among workers exposed to Cd (IRAC, 1993).

We aimed in this study to find out the genotoxicity and lung infection caused due to confounding role of smoking habit with occupationally exposure to (Cd).

2. Materials and Methods

2.1 Subjects

The design of this study was cross sectional study:

The study subjects were as follow:

- 40 male workers from an electroplating factory exposed to Cd (27 were smokers and 13 were non smokers)
- 40 control subjects (comparable in age and socioeconomic status), who were never occupationally exposed to Cd (28 were smokers and 12 were non smokers).

An interviewing questionnaire for recording:

- 1- Personal data (duration of employment, sources of pollutants in their residential areas, smoking duration, number of cigarettes in a package).
- 2- Clinical and medical history for any previous diagnosis of bronchial asthma, cystic fibrosis, or bronchiectasis; diagnosis of neoplasia; clinical-radiologic evidence of pneumonia.

Exclusion criteria:

Those who received any type of antibiotic treatment over five days prior to sputum sampling (for microbiological culture).

2. 2 Methods

(1) Determination of cadmium level in blood and urine:

Samples were collected from the two groups, were digested with high purity nitric acid (65%) and perchloric acid (60%) by 3:1.

Cd was determined using atomic absorption spectrophotometer. The concentration of cadmium was expressed as $\mu\text{g/L}$ blood or urine (Litonjua et al., 2005). ± 1 -G-banding according to Bayani and Squire (2004), such that for each person we examined 50 metaphase. 2-SCEs analysis: according to Pendzich et al., (1997) such that 25 – 30 complete cells were analysis from each case and SCE were scored / metaphase).

(2) Microbiological Study:

Sputum samples were collected in a sterile vial and sent within 2 h to a laboratory for processing.

Sputa were processed microbiologically for semiquantitative study following accepted laboratory methods. Balows et al., (1997). Using the microbiological loop, 0.01 ml. sputa were seeded in

the following culture media: blood agar, MacConkey agar (24 hours at 37°C), chocolate agar (the atmosphere contained 5 to 7% CO_2), and Sabouraud's agar plus chloramphenicol (35 \pm 2°C in aerobic conditions). Two types of Api-technique (bioMerieux, France) as a rapid identification system were used for identification of the various bacterial isolates based on enclosed instruction:

1- Api stept.identification system for *Streptococci*.

2- Api 20 E: identification system for *Enterobacteriaceae* and other Gram –negative rods.

Bacterial agents recovered were classified into three groups:

1- Group (1): *Pseudomonas aeruginosa*, *Enterobacteriaceae* spp. (e.g. *Proteus* spp, *Citrobacter freundii*, *Escherichia coli*, *Serratia marcescens*).

2- Group (2): *Streptococcus pneumonia* and other Gram-positive cocci, e.g. *Staphylococcus aureus*.

3- Group (3): Gram-negative cocci, e.g. *Moraxella catarrhalis*.

(3) Statistical Analysis

The collected data were statistically analyzed using SPSS. χ^2 was used for the statistical analysis of the qualitative data and t-test, as well as analysis of variance (ANOVA). The difference was considered significant at P- value ≤ 0.05 levels.

3. Results

Table (1) showed no statistically significant difference between both exposed and control regarding smoking habits.

Table (2) demonstrated that the biological indices of Cd of the exposed group were significantly higher than that of the control group.

Table (3) demonstrated that there were significant difference between smoking index, biological indices' of Cd (B-Cd and U-Cd) on one hand and SCE on the other hand while no significant difference in comparison to chromosomal aberration.

From Table (4) the mean significant cytogenetic changes for all exposed and control groups, in the form of SCE and chromosomal abnormalities were found to be significantly higher among the exposed workers compared to controls, with exception of chromatid and chromosome gaps.

Semiquantitative bacterial cultures were performed on all samples. Bacterial numbers less than (10^3) colony-forming units (cfu) x ml(-1) were found only in the two smoker workers & two non-smokers in both groups. Colonization with $10(3)$ cfu x ml(-1), was present in 1/13 and 3/27 in the worker (nS, S), and 2/28 of S. A higher cfu $>10^4$ colonized 1/13& 3/27 in the workers (nS, S), and 1/28 of S. Whereas, $>10^5$ colonized only smokers of both group. It was noticed

from table (6) that the most frequently isolated bacteria were group 2 organisms (53.9%), followed by the other two groups which were isolated nearly by the same percentage (18.2% and 18.6%). In addition, 37% and 23% of smoker & non smoker exposed group of workers were infected with different kinds of bacteria. Whereas, the percentage were 21.4% and 8.3% among Smoker and non smoker controls.

Table 1. Distribution of smoking habits among studied groups

Variables	Exposed (40)		Control (40)		χ^2	P value
	No.	%	No.	%		
Smoking habit						
Smokers	27	67.5	28	70	0.058	NS
Non-smokers	13	32.5	12	30		

NS= non significant.

Table 2. Blood and urine cadmium level among the studied groups

Variables	Exposed (40)	Control (40)	Statistical Analysis	
	Mean±SD	Mean±SD	Independent t-test	P>value
B-Cd µg/liter	18.66±9.61	2.48±1.23	10.56	0.0005*
U-Cd µg/liter	18.47±4.84	4.16±2.32	5.06	0.0005*

Table 3. Statistical variations between smoking index, (B-Cd), U- Cd levels and SCE, chromosomal abnormalities among exposed group

Variables	SCE	Chromosomal abnormalities
B-Cd µg/liter	0.7*	0.1
P-value	0.0005	NS
U-Cd µg/liter	0.5*	0.2
P-value	0.0005	NS
Smoking index	0.75*	0.15
P-value	0.0005	NS

*= significant. NS=non-significant

Table 4. Mean of all Chromosomal abnormalities for all the exposed and control groups (metaphases were 100/person)

Parameters Mean±SD	Exposed(40)		Control(40)		Statistical analysis	
	Mean±S D	Mean± SD	Mean±S D	Mean± SD	Independent t-test	P>value
		9.453±1.6		5.643±0.9		13.29
Chromosomal abnormalities	No.	%	No.	%	χ^2	P-value
Cromatid gap With*	16	40	14	35	0.213	NS
Without**	24	60	26	65		
Chromatid break With*	18	45	0	0	23.226	P<0.0001
Without**	22	55	40	100		
Chromosome gap With*	18	45	12	30	1.92	NS

Without**		22	55	28	70		
Chromosome break	With*	27	67.5	7	17.5	20.46	P=0.0001
	Without**	13	35.5	33	82.5		
A centric fragment	With*	8	20	0	0	8.889	P<0.005
	Without**	32	80	40	100		
Tetraploidy	With*	9	22.5	2	5	5.165	P<0.05
	Without**	31	77.5	38	95		
Dicentric	With*	11	27.5	1	2.5	9.804	P<0.005
	Without**	29	72.5	39	97.5		

With* = had Chromosomal abnormalities

Without**= had no Chromosomal abnormalities

Table 5. Distribution of the semiquantitative bacterial culture among studies groups

	Control		Occupational workers	
	Smokers (s) (n=28)	Non smokers (ns) (n=12)	Smokers(s) (n=27)	Non smokers (ns) (n=13)
<10 ³ cfu/ml	0	1	2	1
10 ³ -10 ⁴	2	0	3	1
10 ⁴ -10 ⁵	1	0	3	1
10 ⁵ -10 ⁶	1	0	2	0
>10 ⁶	0	0	0	0

Table 6. Colonized microorganisms in different groups

Microorganisms groups	Control		Occupational workers		Total colonized from each group
	Smokers (n=28)	Non smokers (n=12)	Smokers (n=27)	Non smokers (n=13)	
Group 1 <i>Pseudomonas aeruginosa</i> & <i>Enterobacteriaceae</i>	2/28 (7.1%)	-	4/27 (11.1%)	-	18.2%
Group 2 Gram-positive cocci <i>Staphylococcus aureus</i> , <i>Streptococcus pneumoniae</i>	3/28 (10.7%)	- 1/12(8.3%)	5/27 (18.5%)	2/13 (15.4%)	52.9%
Group 3 Gram-negative cocci <i>Moraxcella catarrhalis</i>	1/28 (3.6%)	-	2/27 (7.4%)	1/13 (7.6%)	18.6%
Total	21.4%	8.3%	37%	23%	

4. Discussion

Cadmium contamination of the environment is very persistent. Thus in polluted areas cadmium is not only an occupational but also environmental and public

health problem of a large magnitude (Linshaw et al., 1996).

The mutagenic action of smoking was proved in many studies (Mili et al., (1991), Sopori et al. (1998) and Mori et al. (2003).

The present study discussed the confounding effect of smoking in mutagenicity of occupational exposure to Cd (Cadmium) levels in blood, urine, hair and other tissues reflect the degree of exposure. The average daily excretion of Cd in persons is usually below 1 µg/L creatinine, increasing with age and smoking (Allessio et al., 1993). Normal blood concentration of Cd in non – exposed persons ranges from 0.05 to 0.3 µg/dL. Occupationally exposed persons may be at range 1-10 µg/dL. A blood level of 5 µg/dL or higher is considered toxic (Grum 1990). The blood and urine Cd level of exposed workers in the present study were significantly higher compared to their controls. Our results agrees with those of Tang et al. (1990).

Our results showed a significant difference between smoking index ,biological indices' of Cd (B-Cd and U-Cd) on one hand and SCE on the other hand which results agreed with those of many studies who demonstrated a close relation between B-Cd and U-Cd and cigarette smoking (Wulf et al., 1986; Järup et al., 1998; Rowland and Harding, 1999; Mori et al., 2003 and Mannino et al., 2004). Which suggested that smoking was considered as confounding factor influencing the level of SCE.

Shiraishi et al.,(1972) reported marked increase in various chromosomal aberrations due to Cd increased exposure, also Bauchinger et al.,(1976) found a significant increase in chromatid breaks and acentric fragments but not dicentrics of 24workers at a smelting plant occupationally exposed to dust and fumes of zinc, lead and Cd. Furthermore, positive data of genotoxicity in a group of workers with the high cumulative exposure to Cd was documented (Forni, 1992).

The present study revealed a high prevalence of various chromosomal aberrations such as breaks, acentric fragments, acentric chromosome and tetraploidy with significant difference between Cd exposed workers and the control individuals.

The observed higher frequency of chromosome breaks was explained by Bui et al. (1975) to be due to a more frequent effect of Cd prior to the phase of DNA synthesis of the cell cycle.

In contrast, Tang (1991) did not found SCE among Cd exposed with increased chromosomal aberrations, which showed a significantly higher mean value for SCE of the exposed workers compared to the controls. In addition SCE was significantly correlated with B-Cd

and U-Cd levels of the exposed workers. Studies of Bilban (1998) agreed with our results.

Our results showed that 37% of smoker workers were infected with different kinds of bacteria followed by non smoker workers (23%). Whereas, infection was noticed in 21.4% of and 8.3% of Smoker and non smoker controls. Those results confirmed the synergistic effect between smoking and occupational exposure to Cd. Simpson et al. (1998) reported that people exposed to cigarette smoking have a high prevalence of work related respiratory tract symptoms which are related to dust exposures and smoking habits. Some experts believe that a low-level infection in the lungs may trigger an inflammatory reaction that continues to produce subsequent acute attack. The possible mechanisms by which smoking increases the risk of infections include structural changes in the respiratory tract and a decrease in immune response, both systemically and locally within the lungs (Lidia et al., 2004). In addition, Cigarette smoking is an important risk factor for virulent bacterial and viral infections. For example, smokers showed 2- to 4-fold increased risk of invasive pneumococcal disease. Influenza risk is seven fold higher and is much more severe in smokers than nonsmokers (Arcavi and Benowitz ,2004).

So, we recommended the cytogenetic studies to be an essential component of pre-employment evaluation of cadmium exposed workers, also to exclude susceptible individuals. In addition, regular biological indices of cadmium should be checked regularly. Also, engineering control measures exhaust ventilation and health educational courses should be implemented to highlight dangerous impact of smoking on health. This study suggests that chronic cadmium exposure is associated with reduced pulmonary function, and cigarette smoking modifies this association. These results should be interpreted with caution because the sample size is small, and further studies are needed to confirm our findings.

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