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Research Article

INFLAMMATORY MARKERS AND MYOCARDIAL INFARCTION AMONG INDIVIDUALS EXPOSED TO ENVIRONMENTAL TOBACCO SMOKE: HOSPITAL BASED STUDY

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ABSTRACT

Background: Various reports have indicated that inflammatory markers appear to be predictive of cardiovascular events, but most of these have focused on relatively young populations. The aim was to study changes that occur in some inflammatory markers among individuals admitted to hospital with myocardial infarction and where exposed to environmental tobacco smoke, and the correlation between different markers and individuals in the study (cases and control). **Methodology:** Hospital based case-control study. data collection was carried out during the period from the first of January 2011 to the first of July 2011. The study was conducted at AL-Diwanyiah Teaching hospital in AL-Diwanyiah governorate, the sample include eighty six participants (48 cases and 38 controls). **Results:** there was significant difference between the cases and control regarding the mean cotinine levels in their blood, the mean level of WBC, IL6 were higher among cases than among controls. There was significant difference between cases and controls when CRP level was studied, the same was for IL6. A significant Pearson's Correlation with CRP, cotinine level and IL6 among the total sample (cases and control). **Conclusion:** second hand smoke as assessed by cotinine level is associated with significant increase risk of MI, the association was also found with the studied inflammatory markers.

Keywords: Environmental tobacco smoke, inflammatory indicators and MI.

INTRODUCTION

The mechanism by which environmental tobacco smoke exposure associated with risk of CHD remain unclear, and studies results suggest that even very low level of ETS exposure are associated with changes in inflammation markers(c-reactive protein, interleukin 6, fibrinogen) , plasma viscosity and hemostatic markers (Von Will brand factor and fibrin D-dimer) were associated with significant increase risk of MI/CHD death, this effect is larger than one would expected on the basis of the risks associated with active smoking and the relative doses of tobacco smoke delivered to smokers and non-smokers[1-5]. Meta analyses and reviews have indicated that the pooled relative risk of developing coronary heart disease when exposed chronically to SHS is 1.3, interpreted as a 30% increase in risk[5-6]. Various reports have indicated that inflammatory markers appear to be predictive of cardiovascular events, but most of these have focused on relatively young populations[7-10].Moreover, few articles have explored the predictive value of inflammatory markers on cardiovascular events in cardiovascular disease–free subjects,[11, 12, 13] and even fewer have considered multiple markers, such as interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor- (TNF), simultaneously[14]. In fact, most studies have focused only on CRP[15-18].

CRP is an acute phase protein produced primarily by the liver in response to inflammatory cytokines, such as IL6[2,19,20], which has been shown in epidemiological studies to be predictive of future cardiovascular disease[18, 21].

Although elevated levels of IL-6 have been reported in some chronic inflammatory conditions, epidemiological data evaluating the potential role of IL-6 in early atherogenesis are sparse[11], prospective studies of apparently healthy[24] as well as high risk[22] individuals indicate that elevated levels of C-reactive protein, a potential surrogate for IL-6 activity are associated with first coronary and cerebrovascular events. Finally, elevated levels of IL-6 and other acute-phase proteins have been reported among patients with acute coronary syndromes[23] even among those without overt plaque rupture or acute tissue trauma[24].

Patients with elevated white blood cell (WBC) counts have been shown to have a higher risk of developing an acute myocardial infarction (AMI)[25] and to be at higher risk for adverse events during the acute setting[26] Although the mechanism responsible for these associations is unknown, several hypotheses have been postulated, including a leukocyte-mediated hypercoagulable state[27] leukocyte-mediated no-reflow[28], and indirect cardiotoxicity mediated through proinflammatory cytokines[29].

MATERIAL AND METHODS

Hospital based case-control study. data collection was carried out during the period from the first of January 2011 to the first of July 2011. The study was conducted at AL-Diwanyiah Teaching hospital in AL-Diwanyiah governorate, the sample include eighty six participants (48 cases and 38 controls).

Approval and official permission: The study design and the questionnaire were reviewed and agreed upon by the local committee of the College of Medicine, Al-Nahrain University, Baghdad,

Iraq. Ethical Approval was obtained from the Iraqi scientific council of community and family medicine to conduct the study and it was handed to the manager of the AL-Diwaniya Teaching hospital with explanation of the study's aim.

Inclusion criteria[9]

All participants should have the following criteria

1. Not smoking (No current smoking in past 5 years if they are ex-smokers).
2. Had history of previous exposure to tobacco smoke in last 3 days (Not related to cigarettes only but cigar, pipes, smokeless tobacco, Nergella or any other product containing nicotine) Cases: Include all patients admitted to (CCU) for chest pain and diagnosed as myocardial infarction (MI) by physicians and available investigation Controls: They were taken from the same hospital and from persons who are attending for causes other than chest pain.

Exclusion criteria for cases and control[9]

1. Those reported using some of nicotine in previous 3 days other than exposure to tobacco smoke.
2. Pregnant women (physiological increase in hemodynamic state).
3. Previous history of kidney disease due to its effect on elimination of cotinine.
4. Use of anticonvulsant drugs, disulfiram or rifampicin because they increased the liver enzymes so it effect on metabolism of cotinine.

Questionnaire form was used to obtain information regarding some sociodemographic characteristics

Blood sample was taken by the researcher herself from all participants and left 20 minutes then centrifuged in a speed 1000-2000 cycle/min for 10 min the separated serum was stored at -5c° until analysis, serum cotinine was analyzed at AL-Nahrain medical college by using the Calbiotech [Inc. (U.S.A)] Cotinine Direct ELISA Kit which designed for the detection cotinine in serum and urine.

Data analysis

The collected data (88 participants) were analyzed using SPSS (Statistical Package for Social Science) at version (18.0); the data was applied to find out any significant relation between the exposure to secondhand smoke and risk of myocardial infarction , P value ≤ 0.05 or less considered as significant.

Descriptive analysis for each variable including frequencies, percent, mean, range and standard deviation were computed.

Then analysis done by t-test (for quantitative variable) and chi-square test (qualitative variable).

RESULTS

Table (1) shows that there were 48 cases &38 controls in the sample, with 27.1% of cases & 2.6% of control had previous history of MI, and 72.9%, 31.6% of cases and controls respectively had history of chest pain.

In table (2) there was significant difference between the two groups regarding the mean cotinine levels in their blood, while the mean level of WBC, IL6 were higher but not

significant among cases than controls. There was significant difference between cases and controls when CRP level was studied (χ^2 =36.82 P=<0.001), the same was for IL6 with χ^2 =9.72 P=0.05 (table 3).

Table (4) showed significant Pearson's Correlation when type of individuals included in the study (whether they were cases or controls) with CRP (P=0.001), cotinine level (P=0.001) and IL6 (P=0.002), also CRP showed significant correlation with cotinine level (P=0.005) table (4).

Discussion:

In order to examine potential pathways linking SHS exposure to CHD risk, we examine the epidemiological associations between SHS exposure, assessed by serum cotinine, and some inflammatory markers (WBC, CRP and IL6) among cases of MI admitted to CCU and diagnosed by specialist and group of controls taken from the same hospitals, both groups were exposed to ETS during the last 3 days and were nonsmokers.

The highly significant and higher level of serum cotininine was demonstrated among cases of MI, the same result was obtained by Whincup et al[30], also it is estimated that exposure to ETS increases the risk of cardiovascular diseases by 25% for a non-smoker compared with that of the unexposed, these findings are particularly alarming in view of the huge economic burden imposed on public health systems by CVD[31]. Vardavas 2000[2] concluded that SHS is a mixture of volatile chemicals, carcinogens and toxins, it is likely that it would have a multiple pathways of interference within the human body that, either on their own or in synergy, promote a causal interaction between exposure and coronary heart disease.

In a study by Ridker[11] They found that mean concentration of IL6 was higher among participants who developed MI than those participants who did not, this result was similar to the present study. Moreover, in analyses limited to nonsmokers, the relationship between baseline level of IL6 and subsequent risk remained highly significant such that the relative risks of future myocardial infarction from lower to highest quartiles of IL6 among nonsmokers were 1.0.1.4, and 2.6 (P 0.001)[11].

In the present study IL6 was significantly correlated with cases of MI, this agreed with other studies[11, 23,24,32] they showed that IL6 levels increases with the acute phase response of MI and that these elevation may be a marker for plaque instability. However because blood samples in the present study were collected on admission to CCU with MI, we cannot exclude the possibility that acute ischemia was a cause of IL6 elevation in these data or that those patients had already a high levels of IL6 before the attack. In another study done by Balbay et al 2001[33] they found that the serum concentration of IL6 was more than twice as high in the AMI group as compared to control group.

The present study showed a highly significant positive finding of CRP among cases of MI, Recent epidemiological evidence has indicated an association between exposure to SHS and CRP both in adults and in youth and through both biomarker and self reported assessment of exposure[34,35]. Ridker et al, proposed that men with elevated levels of CRP were at a greater risk for myocardial infarction compared to men with normal levels, independently of all other factors known to predict clinical coronary outcomes, including lipid levels. Furthermore, it has been hypothesized that elevated CRP levels in themselves may have a direct effect on the development and aggravation of atherosclerosis [36].

The mean WBC was higher (not significant) among cases than controls, this result agreed with other studies, . Barron H V 2000[37] in their study confirm previous observations that relate elevated WBC count to adverse clinical outcomes in patients with acute MI and also an elevated WBC count was associated with reduced epicardial patency and greater thrombus formation at the site of the ruptured plaque, suggesting that an elevated WBC count may be a marker of a hypercoagulable or thromboresistant state. Sadovsky 2001[38] mention that the white blood cell (WBC) count is a simple and more readily available marker of inflammation and Patients with acute myocardial infarction who have elevated WBC counts appear to be at higher risk of mortality and recurrent acute myocardial infarction (AMI), he concluded that a WBC count above 10,000 per mm3, even on the second hospital day, is a potent predictor of adverse outcomes of mortality or nonfatal events in patients with acute myocardial infarction and unstable angina.

In conclusion second hand smoke as assessed by cotinine level is associated with significant increase risk of MI, the association was also found with the studied inflammatory markers, these result would require larger studies to be done to answer many questions which are raised regarding type of association and its consequence on the treatment of MI.

Table 1: Distribution of cases and controls in the sample according to different variables

Variables	Cases(n=48)		Controls (n=38)	
Age \years	**Freq**	**Percent**	**Freq**	**Percent**
<50	13	27.1	8	21.1
50-59	18	37.5	16	42.1
≥ 60	17	35.4	14	36.8
Sex				
Males	25	52.1	20	52.6
Females	23	47.9	18	47.4
History of Previous MI				
Yes	13	27.1	1	2.6
No	35	72.9	37	97.4
History of previous chest pain				
Yes	35	72.9	12	31.6
No	13	27.1	26	68.4
Hypertension				
Yes	34	70.8	31	81.6
No	14	29.2	7	18.4
Diabetes mellitus				
Yes	18	37.5	17	44.7
No	30	62.5	21	55.3

Table 2: Level of some inflammatory markers and serum cotinine among cases and controls in the studied sample

Variables	Cases (n-48) mean±SE	Controls (n=38) Mean±SE	Significant (t-test)
WBC	12.467±0.941	10.982±0.469	t-test=1.053 P= >0.05
IL6	27.081±7.857	10.815±2.968	t-test=1.503 P= >0.05
Cotinine	5.319±0.789	2.018±0.358	t-test=2.878 P= <0.05

Table 3: Level of some inflammatory markers among cases and controls in the studied sample

Variables	Cases		Controls		Significant
	Freq	**Percent**	**Freq**	**Percent**	
CRP					χ^2 =36.82
Positive	29	80.5	4	10.5	P=< 0.0001
Negative	7	19.5	34	89.5	
Total	36	100	38	100	
IL6(New)					χ^2 =9.72
<12.5pg\ml	22	45.8	30	78.9	P=<0.05
≥12.5pg\ml	26	54.2	8	21.1	
Total	48	100	38	100	

Table 4: Correlation between different variables among total sample Cases & Controls)

		Type^	wbc	CRP	cotinine	Newinterlukin^^
Type (cases or control)	Pearson Correlation	1	-.141-	.700**	-.357**	-.336**
	Sig. (2-tailed)		.196	.000	.001	.002
	N	86	86	86	86	86
wbc	Pearson Correlation	-.141-	1	.036	.070	.142
	Sig. (2-tailed)	.196		.742	.522	.194
	N	86	86	86	86	86
CRP	Pearson Correlation	.700**	.036	1	-.303**	-.183-
	Sig. (2-tailed)	.000	.742		.005	.091
	N	86	86	86	86	86
cotinine	Pearson Correlation	-.357**	.070	-.303**	1	.078
	Sig. (2-tailed)	.001	.522	.005		.473
	N	86	86	86	86	86
newinterlukin	Pearson Correlation	-.336**	.142	-.183-	.078	1
	Sig. (2-tailed)	.002	.194	.091	.473	
	N	86	86	86	86	86

**. Correlation is significant at the 0.01 level (2-tailed).
^. Cases=1 Control=2
^^. IL6 <12.5Pg\ml =1 ≥ 12.5 Pg\ml =2

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