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Investigation of Biochemical and Hematological Parameters of Workers Exposed to Benzene

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***Abstract*—**Benzene is the basic member of organic compounds classified as aromatic hydrocarbons. In many studies, it is determined that the risk of acute myeloid leukaemia (AML) or other leukaemias increase in conditions of recurrent exposure of benzene and products containing benzene. Benzene exposure can be determined by the analysis of phenol in urine. The aim of this study is to assess retrospectively the biochemical and hematological markers of workers who exposed to benzene.

189 patients were included in this study who referred to Ankara Occupational Diseases Hospital for periodical examination that had exposed to benzene. 151 persons were included as control group. Phenol analysis was made by Agilent Gas Chromatography device, biochemical parameters by Konelab Prime 60i device, whole blood analysis by Beckman Coulter LH780 device and sedimentation measurement by Alifax device.

While there were not a significant difference between benzene exposed workers and control group in aspartate aminotranspherase (AST), alanine aminotranspherase (ALT), creatinine, C-reactive protein, sedimentation and lymphocyte levels (p values; 0.935, 0.576, 0.673, 0.110, 0.171, 0.157 respectively), there were a significant difference in erithrocyte, leukocyte, hemoglobine, neutrophil and blood urea nitrogen levels (p values; 0.021, 0.045, 0.001, 0.018, 0.017 respectively). The mean erythrocyte and hemoglobine values were lower in benzene exposed workers according to control group, but the mean leukocyte, neutrophil and blood urea nitrogen values were higher in benzene exposed workers according to control group.

As a result, although hematological effects of benzene and the relation between benzene and AML or other leukaemias were retained, we think that it should be investigated in more detail the effects on other systems in case of chronic exposure.

***Key words*—**Benzene, biochemical parameters, hematological parameters.

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I. INTRODUCTION

Benzene is the basic member of organic compounds classified as aromatic hydrocarbons. It is a good solvent and is used as an initiative compound in the synhesis of styrene and phenol which are used in production of plastics in industry, in compounds of nylon, in production of synthetic detergent. Benzene is used in aviation gasoline, as initiative compound of anylin which is used in dye production and as insectisid [1]. Workers, especially in dyeing and industry of shoe are continous exposed to aerosols, thinner, toluene and benzene.

Benzene has quite many effects on health. High levels of benzene exposure via respiration air can be resulted by death, low levels of exposure can cause lethargy, vertigo, tachycardia, headache, tremble, confusion and blackout. In long term exposure, haematopoetic system can be affected and anemia can occur. Benzene is a ubiquitous environmental pollutant that is known to cause hematotoxicity and leukaemia in humans. In many studies, it is determined that the risk of acute myeloid leukaemia (AML) or other leukaemias are increased in conditions of recurrent exposures to benzene and products containing benzene [2,3].

It has been well documented that at high exposure, benzene causes progressive degeneration of the bone marrow, aplastic anemia, and leukemia [World Health Organization, 1993]. Lymphocytes have been demonstrated to be more sensitive to benzene exposure than other types of white blood cells (WBC) in animal studies, however, results obtained from human populations regarding this selective effect on lymphocytes have been contradictory [4,5].

Even benzene can be urinary excreted without metabolizing, it can be also urinary excreted by being converted to primary or secondary metabolites (benzene oxide, benzene dihydrodiol, phenol, benzoquinon, sphenilmercapturic acid, muconic acid and catechol) [6].

The effects of benzene on health have been investigated in many studies until today [7,8]. The aim of this study is to assess retrospectively the biochemical and hematological markers of workers who referred to our hospital for periodical examination that had exposed to benzene.

The most common exposures occur through auto exhaust, industrial emissions and cigarette smoke [9]. A large section of population is occupationally exposed to benzene through work environment [10]. Several reports available suggest that exposure to benzene is a serious health problem. Benzene toxicity is related to the ability of its reactive intermediates to bind to DNA and proteins [11,12]. A causal relationship between benzene exposure and lung cancer has also been suggested [13,14]. It has been shown that benzene induces oxidative

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stress, cell cycle alterations, and programmed cell death in cultured cells [15,16]. Metabolites derived from this pollutant have also been shown to cause blood disorders and cancer in several animal models [17,18].

Chronic exposure to benzene can result in anemia, thrombocytopenia, leukopenia or aplastic anemia [19].

There have been many studies reporting the carcinogenicity and hematotoxicity of benzene at high exposures, both in animal and epidemiological studies [20,21]. Benzene has been associated with leukopenia, thrombocytopenia, and aplastic anaemia [22.23]. The association of leukaemia with high exposures to benzene has also been reported, with acute myeloid leukaemia being most commonly described [22,23,24].

Smokers are thought to be at an increased risk of leukaemia, in particular myeloid [25]. Cigarette smoke contains measurable quantities of benzene. Wallace [26] found smoking to be the most important source of benzene exposure in a general population, with the average smoker (32 cigarettes a day) taking in about 1.8 mg benzene a day.

II. MATERIALS AND METHODS

189 workers were included in this study who referred to Ankara Occupational Diseases Hospital for periodical examination that had exposed to benzene. 151 persons who had not exposed to benzene were included as control group. The mean age of workers were 39.74±7.97. Benzene exposure was determined by detecting phenol levels in spot urine sample with Agilent Gas Chromatography device. Analysis were made by FID detector. Biochemical parameters were analyzed by Konelab Prime 60i device, whole blood analysis were made by Beckman Coulter LH780 device, sedimentation measurement were made by Alifax device.

Statistical analysis

Analysis of normality of the continuous variables was performed with the Kolmogorov-Smirnov test. Data were expressed as mean±Standard Deviation (SD), unless indicated otherwise. Significance between two groups was determined by unpaired Student's t test for continuous variables and by chi-square test for discrete variables. Pearson's correlation coefficients were used to evaluate the relationships between variables. Linear regression analyses were used. P values <0.05 were considered significant. Statistical analysis was performed using the SPSS software package (SPSS 16.0; SPSS Inc., Chicago, IL, USA).

III. RESULTS

While there were not a significant difference between benzene exposed workers and control group in aspartate aminotranspherase (AST), alanine aminotranspherase (ALT), creatinine, C-reactive protein, sedimentation and

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lymphocyte levels (p values; 0.935, 0.576, 0.673, 0.110, 0.171, 0.157 respectively), there were a significant difference in erithrocyte, leukocyte, hemoglobine, neutrophil and blood urea nitrogen levels (p values; 0.021, 0.045, 0.001, 0.018, 0.017 respectively). The mean erythrocyte and hemoglobine values were lower in benzene exposed workers according to control group, but the mean leukocyte, neutrophil and blood urea nitrogen values were higher in benzene exposed workers according to control group.

IV. DISCUSSION

Benzene is an aromatic hydrocarbon that is used widely in industry. Although it has effects particularly on hematopoetic system, it affects other systems as well. Benzene levels can be monitored by urine phenol analysis [1-6].

In many studies that were investigated hematological effects of benzene [5,6], there were mentioned about substantial decreases of erithrocyte, hemoglobine and leukocyte levels. Qu et al. found in their study that RBC, WBC and neutrophil counts decreased in 130 Chinese workers who exposed to benzene according to control group [7]. Also in our study, erythrocyte and hemoglobin levels were determined lower in benzene exposed workers according to control group (p values; 0.021, 0.001 respectively). While in some of the studies there were suggested that there were decreases in neutrophil and lymphocyte levels, in some of them there were found elevations in neutrophils. In our study there were not a significant difference in terms of lymphocyte levels between control group and exposed group, but leukocyte and neutrophil levels were significantly high in exposed group (p values; 0.157, 0.045, 0.018 respectively). In other studies which AST, ALT or blood urea nitrogen were assessed except blood cells [27,28], AST and/or ALT levels were found increased in exposed groups. In our study we didn't found a significant difference in AST and ALT levels between groups, but there were a significant difference in blood urea nitrogen levels (p values; 0.935, 0.576, 0.017 respectively). Blood urea nitrogen levels were found significantly high in exposed group.

In many studies it has been reported that exposure to high levels of benzene can result in a depression of blood cell counts [29,30,31,32,33]. Significant decreases of WBC, RBC, and platelet counts have been observed in human populations exposed to relatively high levels of benzene [34,35,36]. However, there are few studies that have attempted to examine the relationship between benzene exposure and hematological response, over a broad and well characterized range of benzene exposures. There are limited published data on relationship between benzene exposure and response to exposure. Ward et al. indicated that blood cell depression was unlikely to occur at low levels [5]. However, Khuder et al. reported that the decreases in absolute RBC and

platelet counts were observed in workers followed longitudinally, while exposed to relatively low levels of benzene [33].

It has been reported in some animal and human studies that within the WBCs, lymphocytes appear to be more sensitive than other cell types. However, the selective effect of benzene on lymphocytes has not been as clearly documented in humans [5]. Rothman et al. compared hematological outcomes in a cross-sectional study of 44 workers heavily exposed to benzene and unexposed controls from a Chinese occupational population. They observed that all hematological parameters, including WBCs, absolute lymphocyte count, platelets, and RBCs were significantly decreased among exposed workers compared to controls. In a subgroup of workers who were not exposed to higher than 31 ppm benzene on any of five sampling days, only the absolute lymphocyte count was significantly different between exposed workers and control group. Therefore, they concluded that the absolute lymphocyte count is the most sensitive indicator of benzene associated hematotoxicity [4]. But Qu et al. suggested in their study within 130 Chinese workers that lymphocytes might not be more sensitive to chronic benzene exposure than neutrophils [7]. Ward et al. analyzed hematological screening data collected over a 35-year period at a rubber hydrochloride manufacturing plant to examine the relationship between benzene exposure and hematological parameters. They observed that both WBCs and RBCs significantly decreased with elevated levels of benzene exposures. Their data also showed a stronger effect of benzene on WBCs than on RBCs, but did not provide evidence that low WBC count was due to selective depletion of lymphocytes. Methodological differences in counting lymphocytes may have contributed to the differences in the findings of benzene associated lymphocyte depression reported among different studies [5].

Rushton et al. in their study suggested that there was no evidence of association between exposure to benzene and lymphoid leukaemia, either acute or chronic. There was some suggestion of a relation between exposure to benzene and myeloid leukaemia, in particular for acute myeloid and monocytic leukaemia [3].

Just as benzene can show effect of its own directly, it or its metabolites can do so by binding to tissue protein, DNA and RNA. Previous studies showed that the toxic metabolites of benzene formed covalent bonds on the proteins of liver, kidney and stomach organs, as well as binding with DNA and RNA [37,38]. Turhan and Dere observed in their study that benzene caused a significant increase in the LDH, AST and ALP activities and slightly increased the levels of ALT activity ($p > 0.05$) in benzene-treated rats in comparison to those of controls [39]. In another study, Kang et al. were found that exposure to polycyclic aromatic hydrocarbons such as benzo(a)pyrene, phenanthrene and pyrene in rats results with increases in ALT, AST and ALP activities [40]. Also, Dere et al. were shown that a significant increase in ALT in the liver and in LDH, AST and ALT in the kidney occurs after exposure to benzene. The increase in the activity of these enzymes in the serum may result

consequent to impairment of the function of tissues with subsequent liberation of the enzymes into the circulation from the damaged tissue [41]. In another study Dere et al. showed that benzene had affected four important hepatic marker enzyme activities in serum (LDH, ALP, ALT and AST). Their findings indicate that the liver damage may occur in the rats exposed to benzene. They found significant increases in serum LDH, ALP and AST activities in rats [28].

As a result, both biochemical and hematological effects of benzene and the relation between benzene and AML or other leukaemias were retained. We think that it should be investigated in more detail the effects of benzene on other systems in case of chronic exposure.

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TABLE 1. Comparison between worker group who exposed to benzene and control group.

Parameters	**Workers who exposed to benzene (n=189)**	**Control group (n=151)**	**P values**
Phenol	66,20(781)	4,5(40,10)	0,000
RBC	5,07(4,13)	5,15(1,93)	0,021
WBC	7,5(37,5)	7,10(10)	0,045
Hb	15,30(7,30)	15,7(4,80)	0,001
Neutrophil	4,5(30,90)	4(8,40)	0,018
Lymphocyte	2,20(4,30)	2,20(4)	0,157
ALT	23(88)	23(60)	0,576
AST	21(56)	22(40)	0,935
Blood urea nitrogen	15,10(37)	14(27)	0,017
Creatinine	0,82(0,61)	0,80(0,73)	0,673
CRP	2,11(32)	2,10(19)	0,110
Sedimentation	3(75)	2(41)	0,171