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ADVERSE EFFECTS OF BENZENE EXPOSURE ON HEMATOLOGICAL AND HEPATIC BIOCHEMICAL PARAMETERS OF PETROL FILLING WORKERS IN WADI AL-HAYAH, LIBYA

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ABSTRACT

Benzene exposure is known to affect many critical organs including the hematological and hepatic functions promoting various and dangerous health problems. The primary objective of the study was to evaluate the hematological and hepatic function profiles among petrol filling workers in petrol stations located in Wadialhayah, southwest Libya. Second objective was to investigate the extent changes of hematological and hepatic biochemical parameters in accordance to the period of benzene exposure. A total of 92 adult male subjects whose ages ranged between 20-45 years were included in this study, 46 of petrol filling workers (benzene exposed group) and 46 subjects (benzene unexposed group) as a control group. Both groups were matched in ages and gender. All the results were statistically analyzed using SPSS version 20 for applying one way ANOVA test. The mean age of petrol filling workers (benzene exposed group) and non exposed group were 34.36 $\pm$ 7.26 and 33.80 $\pm$7.02 years, respectively. Length of work duration for exposed group was 7.50 $\pm$ 1.56 years. Significant decrease in the levels of RBCs, Hb, HCT, MCH, total protein and serum albumin among benzene exposed group as compared to unexposed group while MCV levels were almost the same and were not significant for both groups. On the other hand, WBCs, platelets, SGPT and SGOT levels were significantly increased among benzene exposed group as compared to unexposed group. Moreover, significant changes of hematological and hepatic biochemical parameters caused by prolonged benzene exposure. It is concluded that benzene exposure has serious health effects on hematopoietic system and hepatic functions leading to suppressed bone marrow. Moreover, long term benzene exposure causes more alterations in hematological and hepatic parameters.

KEY WORDS: hematological parameters, hepatic parameters, benzene exposure and petrol stations.

INTRODUCTION

Worldwide, a huge number of people are exposed to petrol vapor as a part of their occupation or environmentally place.[1] Petrol can be defined as volatile liquid containing mixtures of particles and gases. Typically, there are more than 150 particulate chemicals in petrol, including minor quantity of organic compounds like aromatic and aliphatic hydrocarbons, metals as lead and minute quantity of other compounds.[2] In filling stations, volatile hydrocarbons such as benzene are considered being the most dangerous.[3]

Benzene is classified as a class one carcinogen and mutagen which can contact animals and humans through several routes including inhalation, oral and dermal exposure. But, the main route of benzene exposure at work place is via inhalation.[4] Toxic effects are thought to arise from metabolism of benzene to various metabolites, especially benzoquinone and the muconaldehydes. Benzene is metabolized in the liver to its primary metabolite phenol by cytochrome P4502E1 (CYP2E1. It is subsequently metabolized to hydroquinone.[5, 6] Hydroquinone is transported to the bone marrow and oxidized to benzoquinones, which eventually release reactive oxygen species (ROS) damaging hematopoietic cells.[7, 8]

The health consequences of benzene depend on duration of exposure, in which, acute exposure to benzene causes dizziness, drowsiness, headache, fatigue, tremors and unconsciousness. Furthermore, more serious health outcomes occur on chronic benzene exposure including myeloma, myeloid leukemia and decreased production of red blood cells, weakened immunity. In addition, liver, kidney failure, central nervous system damage and cancer can be induced.[9, 10] Benzene affects many enzyme activities in the liver, tissues, and peripheral blood and this can lead to a decrease in the activity of antioxidants enzymes and may result in oxidative stress which can be defined as the unbalance between the

generation of reactive oxygen species (ROS) and the rate of their consumption by antioxidants.[11, 12]

Workers in the fuel stations are routinely exposed to benzene vapor which has been reported to increase the risks for acute and chronic health problems in motor fuel workers.[13] Activation of benzene and its reactive metabolites leads to continuous production of reactive oxygen species (ROS), which leads to lipid peroxidation and damages DNA, RNA, leading to genetic modification and alterations in the functions of important enzymes and proteins.[14] Several studies have pointed out the risk of occupational exposure to gasoline on many organs in the body leading to serious health effects on hematological and biochemical parameters.[15, 16] Since benzene filling workers have a higher body burden of benzene than others which can have serious effects on health. Therefore, the primary objective of the study was to evaluate the hematological and hepatic function profiles among petrol filling workers in benzene stations located in Wadialhayah, southwest Libya. Second objective was to investigate the extent changes of hematological and hepatic biochemical parameters in accordance to the period of benzene exposure.

MATERIALS AND METHODS

STUDY POPULATION

Retrospective cohort study was conducted during the period from January to June 2022 at Albalsam clinic, Garma, Obary, southwest Libya. A total of 92 male subjects whose ages ranged between 20-45 years were included in this study, 46 of petrol filling workers (benzene exposed group) and 46 subjects (benzene unexposed group) as a control group. Both groups were matched in ages and gender. Information was obtained by face-to-face interviews by using structured questionnaire including age, sex and general demographic details, occupational background, work-history records with the duration of work, education, using protective equipments at work, smoking status, dietary intake habits, drugs taken, prevailing diseases and symptoms. All participants were informed of the purpose of the study, were free to ask questions throughout the study and signed an informed consent form.

INCLUSION CRITERIA

• Healthy adult male subjects working in petrol filling stations (benzene exposed group) aged between 20-45 years.
• Healthy male subjects who have not worked in petrol filling stations (unexposed group) aged between 20-45 years.

EXCLUSION CRITERIA

• Subjects aged less 20 and above 45 years.
• Smoking subjects.
• Subjects suffering from diarrhea.
• Kidney, heart, liver, respiratory and blood diseases.

SAMPLE COLLECTION

Subjects were made to relax and comfortably seated. Venous blood sample (5ml) was collected aseptically by using heparinized disposable syringes from a peripheral vein on arm of each subject. 2 ml of blood was delivered into tubes contain ethylene diamine tetraacetic acid (EDTA) as anticoagulant used for determination and hematological parameters which include red blood cells (RBCs), white blood cells (WBCs), platelets, hemoglobin (Hb), hematocrit (HCT), mean corpuscle volume (MCV) and mean corpuscle hemoglobin (MCH),. The remaining blood were used for measuring hepatic function parameters including serum glutamic pyruvate aminotransaminase (SGPT), serum glutamic oxaloacetate aminotransaminase (SGOT), total protein and serum albumin. The parameters were analyzed by 200 Mindray chemistry analyzer and photometer 4040.

STATISTICAL ANALYSIS

All the results were tabulated and analyzed using Statistical Package for Social Sciences (SPSS) version 20 to apply one way ANOVA test to compare the means and standard deviations of hematological parameters (RBCs, WBCs, platelets, HB, HCT, MCV and MCH) and liver function parameters (SGPT, SGOT, Total protein and serum albumin). The results were considered statistically significant at p. value < 0.01.

RESULTS

The results of the study have been presented and summarized in the form of tables. A total of 46 male subjects whose ages ranged between 20-45 years were included in this study. 46 of petrol filling workers (benzene exposed group) and 46 non benzene exposed group (control group). All the results analyzed using Statistical Package for Social Sciences (SPSS) version 20 for applying one way ANOVA test to compare the means and standard deviations of the variables of exposed and unexposed group. The results were considered statistically significance at p. value< 0.01.

Table 1 illustrates the demographic characteristics of benzene exposed and unexposed group. The mean age of petrol filling workers (benzene exposed group) and non exposed group were 34.36 $\pm$ 7.26 years and 33.80 $\pm$7.02 years, respectively. Both groups were matched in ages and not statistically significance (P. value= 0.70). Length of duration work for exposed group was 7.50 $\pm$ 1.56 years.

Table 2 reveals a comparison of hematological parameters which include RBCs, WBCs, platelets, HB, HCT, MCV and MCH between benzene exposed and unexposed group. RBC's, HB, HCT, and MCH were significantly decreased among exposed group. WBCs and platelets were significantly increased among exposed group. There were no significant changes in MCV between the two groups.

Table 3 shows comparison of hepatic biochemical parameters which include ALT, AST, Total protein and serum albumin between exposed and unexposed group. ALT, AST were significantly increased among benzene exposed group as compared to unexposed group, whereas, total protein and serum albumin were significantly decreased among exposed group as compared to unexposed group.

In the **table 4 and 5**, the results were divided into three groups in accordance to the duration of work in years. First group < 5 years, the second group was between 5-10 years and the third group was > 10 years. All hematological parameters and hepatic biochemical parameters were significantly changes among the three groups (p. value < 0.01).

Table 1: Demographic characteristics of benzene exposed and unexposed groups.

Characteristics	Exposed group Mean±SD	Unexposed group Mean±SD	P. values
Age (years)	34.36 ±7.26	33.80 ± 7.02	0.70
work duration in years	7.50 ± 1.56	……	…..

SD, standard deviation

Table 2: Comparison of hematological parameters between benzene exposed and unexposed groups.

Parameters	Benzene exposed group Mean±SD	Benzene unexposed group Mean±SD	P. value
RBCs x 10^6 µl	3.41±0.92	4.36 ±1.06	< 0.01
WBCs x 10^3 µl	9.21±2.81	6.33 ±1.99	< 0.01
Platelets x 10^3 µl	362.84 ± 84.87	307.34 ± 78.77	< 0.01
Hb g/ dl	12.48 ±1.83	14.59 ±2.03	< 0.01
MCV fL	83.54 ±5.21	85.60 ±5.66	0.07
HCT %	36.34 ±7.15	40.82 ±5.91	< 0.01
MCH pg	24.48 ±3.33	30.67 ±3.98	< 0.01

The results were analyzed using Statistical Package for Social Sciences (SPSS) version 20 for applying one way ANOVA test to compare the means and standard deviations of parameters of exposed and unexposed group. The results were expressed as means and standard deviations (SD). The results were considered statistically significance at P. value <0.01.

Table 3: Comparison of hepatic biochemical parameters between benzene exposed and unexposed groups.

Parameters	Benzene exposed group Mean±SD	Benzene unexposed group Mean±SD	P. value
SGPT	39.54 ±11.65	31.15 ±10.03	< 0.01
SGOT	38.91 ±11.36	25.36 ±8.13	< 0.01
Total protein	6.70 ±1.39	8.11 ± 0.90	< 0.01
Serum albumin	4.48 ±2.22	6.68 ±1.13	< 0.01

Differences between benzene exposed and unexposed group are significant by using one way ANOVA test (p value < 0.01)

Table 4: Distribution of hematological parameters of benzene exposed group in accordance to work duration.

	Work duration			
Parameters	**< 5 years N = 10 2.3 ±1.15**	**5-10 years N = 23 7.21 ±1.50**	**> 10 years N = 13 13 ±2.04**	**P. value**
RBCs x 10^6 µl	4.7±0.46	3.25±0.61	2.86±0.66	< 0.01
WBCs x 10^3 µl	5.5±1.46	9.13±1.74	11.62 ±1.82	< 0.01
Platelets x 10^3 µ	279.1±95.19	368.26±67.38	417.69±52.30	< 0.01
Hb g/ dl	14.58 ±0.91	12.48±1.40	10.88±1.39	< 0.01

MCV fL	88.4±5.46	82.60±3.86	81.46±5.12	< 0.01
HCT %	45.7±5.22	36.13± 4.23	29.53±3.90	< 0.01
MCH pg	27.8±4.02	23.78±2.15	23.15±3.02	< 0.01

Differences of hematological parameters among the three groups of benzene exposed subjects were significant by using one way ANOVA test (p value < 0.01).

Table 5: Distribution of hepatic biochemical parameters of benzene exposed group in accordance to work duration.

	Work duration			
Parameters	**< 5 years N = 10 2.3 ±1.15**	**5-10 years N = 23 7.21 ±1.50**	**> 10 years N = 13 13 ±2.04**	**P. value**
SGPT	27.3 ±1.68	36.87 ±6.54	53.69 ±8.53	< 0.01
SGOT	26.4 ±4.27	41.13 ±8.68	44.61 ±12.52	< 0.01
Total protein	5.11 ±0.77	4.29 ±1.02	3.73 ±1.11	< 0.01
Serum albumin	3.87 ±0.81	2.90 ±0.33	3.2 ±0.59	< 0.01

Differences of hepatic biochemical parameters among the three groups of benzene exposed subjects were significant by using one way ANOVA test (p value < 0.01.

DISCUSSION

Benzene is an important component of petrol which is one of the main contributors to air pollutants and has mainly been associated with multiple toxicities affecting the hematological, hepatic, immunologic, and chromosomal functions and moreover, can increase the risk of carcinogenesis.[16, 17]

In the present study, majority of petrol filling workers didn't use any protective equipments such as protective clothes, masks, and goggles while working in petrol stations due to inadequate awareness of possible adverse health effects of benzene toxicity, as 76.08% of petrol filling workers were not educated (Elementary level). About 86.95% of workers were having their food and drinking water at workplace without any safety procedures and 84.78% of them didn't use special clothes for the work purpose. Therefore, all may contribute to the direct susceptibility of benzene toxicity at the work place which leading to serious health effects. Furthermore, the most common symptoms among benzene exposed group were Exhaustion, headache and Dizziness which count for 73.91%, 28.26% and 21.73% respectively. The symptoms were obvious in workers who had been working in period of more than 5 years.

It was obvious from the study that there was significant differences in hematological parameters including RBCs, WBCs, platelets, HB, HCT, and MCH between benzene exposed and unexposed group. RBC's, HB, HCT, and MCH were significantly decreased among exposed group whereas; WBCs and platelets were significantly increased among exposed group. There were no significant changes in MCV between the two groups. The study was in agreement with several studies conducted in the west and east of Libya.[18, 19 and 20] Other studies showed an increase in WBCs, platelets and reduction in RBCs, Hb, MCV, HCT and MCH and were negatively correlated with benzene exposure length.[21] Other studies supported our findings of WBCs increments among petrol filling workers as compared to non-workers.[22, 23] Conversely, this finding was not in agreement with other studies which showed significant increases in MCH values.[24, 25 and 26] Several studies showed a relationship between benzene exposure and leukemia.[27, 28 and 29] It is reported that benzene has a toxic effects on hematological components causing anemia, aplastic anemia, and multiple myeloma among the workers who are occupationally exposed to benzene.[30, 31 and 32] Several studies have reported that toxicity of gasoline comes mainly from benzene metabolites such as phenol and hydroquinone which are mainly formed in liver. Hydroquinone is transported to the bone marrow and oxidized to benzoquinones, which eventually release reactive oxygen species (ROS) damaging hematopoietic cells.[33, 34, 35 and 36]

The study revealed significant increase in liver enzymes (SGPT and SGOT) among benzene exposed group as compared to unexposed group whereas, there was a significant reduction in total protein and serum albumin. The findings of the study were in consistent with other studies.[37, 38 and 39] Several other reports demonstrated elevation in liver enzymes among subjects exposed to benzene or petroleum products and organic solvents.[40-41] Hepatocellular injury due to benzene exposure could be the reason of overproduction of liver enzymes in response to stimuli or cell death.[40-41] Liver is the primary organ for the transformation and metabolizing of toxins, therefore, liver injury may occur due to its susceptibility to benzene.[42] Prolonged exposure to organic solvents such as benzene, toluene and xylene is a risk factor for liver cancer.[43, 44]

CONCLUSION

It is concluded that petrol filling workers are continuously exposed to benzene at work place which is considered as a leading cause of hematopoietic suppression and liver injury. Exposure to benzene causes a reduction in RBCs, Hb, HCT and MCH and on the other hand, elevation in WBCs and platelets. In addition, increment in SGPT, SGOT and reduction in total protein, serum albumin occurred due to benzene exposure. Anemia, leukemia and liver injury could be occurred due to benzene exposure.

RECOMMENDATION: Personal protective equipments such as protective clothes, masks, and goggles at work place to reduce workplace petrol exposure should be encouraged. Taking the necessary precautions during having food or drinking water at the work place. Regular measurements of hematological and hepatic biochemical markers could be useful for avoiding the effects of long term benzene exposure. Further studies on petrol filling workers are needed to understand the other serious health effects.

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