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The Effect of Benzene Exposure in Kidney Dysfunction and Glutathione Depletion in Fuel Station Workers

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Abstract

Benzene and its derivatives are major global energy sources due to their widespread industrial and transportation uses. However, serious health complications are connected to benzene exposure, raising concerns about environmental safety and public health. The study aims to evaluate the effect of benzene exposure on kidney function, as well as the effect on the level of the vital antioxidant glutathione, due to its crucial role in cellular protection from oxidative stress. The present study was performed on fuel stations workers in Baghdad from February to June 2024. Blood serum samples were collected from 40 workers at benzene stations and 40 non-exposed persons as control. Urea concentration, creatinine concentration, uric acid, and blood urea nitrogen (BUN) were all estimated, as well as glutathione (GSH) concentration was determined. The result illustrates that the urea concentration increased significantly in benzene station workers (26.00 ± 1.53 mg/dL), compared to the individual control (19.10 ± 1.12 mg/dL). As well as a significant decrease in serum glutathione in benzene station workers (349.08 ± 9.69 µmol/L) compared to the control (574.60 ± 15.37 µmol/L). While there were no differences in creatinine concentration and uric acid. That indicates a higher likelihood of developing kidney disease and a few other health problems associated with oxidative stress. The study found that fuel station workers' benzene exposure alters several biochemical parameters. These changes may indicate a higher risk of health issues, such as disruptions in kidney function, and an imbalance between oxidants and antioxidants.

Keywords: Fuel stations workers, Creatinine, Uric acid.

1. Introduction

The exposure risk to hazardous chemicals has increased because of the intricacy of the industrial manufacturing process [1]. Benzene is a well-known volatile organic compound widely used in industrial processes and commonly present in gasoline. Chronic exposure to benzene, particularly in occupational settings such as fuel stations, has shown a correlation to a variety of detrimental health effects, among which are hematotoxicity, immunotoxicity, and organ damage [2, 3]. Among the target organs, the kidneys are especially vulnerable due to their critical role in filtering blood and eliminating toxins [4].

The main human exposure route to benzene is inhalation, but ingestion and dermal absorption exposure are also important. After intake, benzene is spread across the human body [5]. Cox *et al.*, [6] revealed the benzene undergoes metabolized in the liver into reactive types including ring-opened, conjugated, and ring-hydroxylated metabolite. The unmetabolized benzene is excreted by exhalation and its excretion rate is relying on the amount and way of exposure, while the metabolized benzene is eliminated by urine [2]. These metabolites can cause benzene toxicity, leading to chromosomal aberrations [7], cytogenetic modifications [8], neural damage and kidney cancer [9].

Recent studies have suggested that benzene exposure may contribute to renal dysfunction through mechanisms involving oxidative stress, mitochondrial damage, and inflammation [10]. Among the important impacts resulting from benzene exposure is generation of oxygen free radicals in various body tissues causes an increase in the concentration of free radicals (Oxidant) compared to the antioxidants, known as oxidative stress [11]. In kidneys, oxidant/antioxidant imbalance leading to harmful consequences such as fibrosis, autophagy, and inflammation. These processes showed signs of structural and functional impairments in the kidneys [12].

Acidosis is a primary factor causing inflammation in kidney, which ultimately increases production of intrarenal ammonia [13]. A high ROS concentration facilitates the development of body's inflammatory reaction [14]. One key biomarker of high ROS affected by benzene is glutathione (GSH), a major intracellular antioxidant responsible for maintaining redox balance and detoxification harmful substances. Depletion of glutathione not only compromises the antioxidant defense system but may also exacerbate tissue damage,

particularly in high-risk populations such as gas station workers who are frequently exposed to benzene vapor [15].

This study aims to investigate possible involvement of benzene exposure in the development of kidney dysfunction and glutathione depletion among benzene station workers. Understanding this relationship may offer insights into occupational risk assessment and preventive strategies to protect vulnerable worker populations.

2. Materials and Methods

Study participants were selected from 40 benzene exposed individuals who did not suffer from any chronic diseases and were non-smokers. Also, 40 healthy non-exposed vulnerable as a control.

2.1 Urea Test

Serum urea concentration was measured using the urease method. Samples were analyzed using a spectrophotometer using commercially available reagents. The method relies on the enzymatic decomposition of urea into ammonia and carbon dioxide by the enzyme urease, followed by measuring the resulting light output at a specific wavelength. Results are expressed in mg/dL.

2.2 Creatinine Test

Serum creatinine concentration was determined photometrically, a process in which creatinine reacts with picric acid in an alkaline condition to produce an orange-colored compound that is measured photometrically at a wavelength of 520 nm. A semi-automated chemical analyzer was used. Values are expressed in mg/dL.

2.3 Uric Acid Test

Uric acid was measured using the enzymatic method (Uricase method), which relies on the oxidation of uric acid by uricase enzyme to form allantoin, followed by measuring the light absorbance at the appropriate wavelength. Commercially available reagents were used, according to the manufacturer's guidelines.

2.4 Blood Urea Nitrogen (BUN) Analysis

Blood urea nitrogen (BUN) concentration was calculated indirectly by analyzing urea using the enzymatic method (urease method). The following equation was used to convert values.

BUN (mg / dL) = 2.14 Urea (mg / dL)

Optical absorbance was measured using a chemical analyzer according to standard laboratory procedures.

2.5Glutathione Determination

Ellman methods were used to determine glutathione (GSH) [16]. Method include reduction of GSH with Elman,s reagent (5,5` dithiobis(2-nitrobenzoic acid) "DTNB") and generate yellow substance. The intensity of chromogen formed was directly related to the level of GSH, whose absorbance was detected at 405 nm.

2.6 Statistical Analysis

For examine the impact of the differential parameters, The Statistical Analysis System [17] was utilized to analyze the study data. Additionally, Mean values were statistically compared using the T-test.

3. Results and Discussion

Benzene effects on kidney functions, including blood urea nitrogen (BUN), uric acid, creatinine, and urea, along with antioxidant glutathione are illustrated in (table 1).

Table 1: The serum level of some kidney functions tests parameters among fuel workers and control individuals.

Parameters	Mean ± SE		T-test	P-value
	Exposure	Control Exposure		
Blood Urea nitrogen (BUN) (mg/dl)	0.260 ±0.04	0.290 ±0.03	0.112 NS	0.578
Uric Acid (mg/dl)	0.990 ±0.09	0.750 ±0.11	0.293 NS	0.103
Creatinine (mg/dl)	0.900 ±0.15	0.836 ±0.07	0.358 NS	0.711
Urea (mg/dl)	26.00 ±1.53	19.10 ±1.12	3.991 **	0.0019
* (P ≤ 0.05), ** (P ≤ 0.01), NS: Non-Significant.				

Benzene is one of the main organic compounds found in crude oil and fuels and is classified as a toxic pollutant in the atmosphere. It has been recognized that exposure to benzene vapor contributes to carcinogenic effects on humans [18].

Occupational exposure to benzene may also cause health effects not related to cancer, such as disturbances in blood, liver, kidney, nervous, and immune system functions [19]. Therefore, a comprehensive knowledge of the health effects resulting from contact to benzene is essential for initiating effective risk assessment strategies, which contribute to the early

diagnosis of pathological changes associated with this exposure.

Results indicate clear differences between individuals exposed to benzene and those not exposed, in terms of kidney function and antioxidant parameters. The exposed group showed elevated urea levels, indicating a decline in kidney efficiency [20]. While there are no differences in blood urea nitrogen (BUN), uric acid and Creatinine. Additionally, significantly lower concentrations of antioxidants were observed. In contrast, the unexposed group showed normal kidney function parameters and a balanced antioxidant system.

These observed changes could suggest an early sign of renal dysfunction. The weakness of the renal function means that benzene metabolites may include more renal toxic substance [21]. This agrees with the investigation of earlier study of Tarhuni *et al*., [22] and El-Shakour *et al*., [23] on the crude oil and its processed derivative toxicity.

The studies have shown a significant elevation in creatinine, urea, and uric acid levels in petrol station workers in comparison with individuals in the control [24-26]. In parallel, results of Neghab *et al*., [9] showed that occupational exposure to volatile aromatic hydrocarbons (VAHs) in refinery workers is associated with significant changes in kidney function markers. While data of Mark and Reddy showed a significant increase in creatinine concentrations in individuals in the group exposed to benzene, compared to individuals in the unexposed group. Furthermore, study conducted by Owagboriaye *et al*., [27] revealed some histological alterations in the kidneys of mice exposed to gasoline vapors.

The retention of hydrocarbons in the kidneys of these mice may contribute to oxidative stress and impaired kidney function. Like other known foreign substances, the chemical components in gasoline vapor undergo metabolic transformations within the body, triggering the formation of various metabolites. Some of these metabolites may exhibit diverse biological interactions, which may lead to harmful effects when they interact with organs responsible for excretion and metabolism, such as the kidneys and liver [27].

Benzene vapor inhalation could lead to dysfunction in many organ systems. The adsorption of many solvents from blood stream into lipid-rich tissue occurs easily, leading to widespread disorder. The increased urea levels indicate a reduced ability of the kidneys to eliminate

nitrogenous wastes, which may be attributed to a decreased glomerular filtration rate as stated by Roy *et al*., [28].

Finding in (table 2) indicate a significant decrease in glutathione levels. Several previous studies conducted on gas station workers in Nigeria reported similar results, they revealed that the exposed group of workers showed a significant decrease in glutathione levels [29, 30].

Table 2: The serum level of Glutathione (µmol/L) among fuel worker and control individuals

Parameters	Mean ± SE		T-test	P-value
	Exposure	Control exposure		
GSH (µmol/L)	349.08 ± 9.69	574.60 ± 15.37	52.499 **	0.0001
* (P≤0.05), ** (P≤0.01), NS: Non-Significant.				

Environmental contaminants and benzene fumes have been observed to contribute to the activation of peroxidation processes and oxidative stress at the cellular level [31]. Lipid peroxidation occurs because of the release of free radicals, which undergo a reaction with unsaturated fatty acids molecules within the cell membrane, leading to tissue damage and the production of malondialdehyde (MDA) as a product of this reaction. This oxidative stress may be attributed to the accumulation of reactive oxygen species, such as $O2^{-}$ and H2O2, resulting from decreased activity of antioxidant enzymes. This process leads to the accumulation of (OH.) radicals. These free radicals exhibit a high capacity to interact with various cell components, such as lipids, proteins, and DNA [32]. This indiscriminate attack of free radicals ultimately leads to damage to cell integrity, disruption of enzyme functions, and genomic instability [33].

The significantly higher level of lipid peroxide in gas station workers, compared to the control individuals, indicates a defect in the efficiency of the antioxidant defense system in their blood. Reactive oxygen species (ROS) have been reported to contribute to stimulating inflammatory responses [29].

4. Conclusion

Results of the current study investigation indicate that occupational exposure to benzene at fuel stations is correlated with marked changes in some certain biochemical parameters, which may reflect an increased risk of health problems, including disturbances in kidney function and oxidant / antioxidant balance among workers in this environment.

5. References

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