ABSTRACT

**Background:** Exposure to gasoline and other fuels are associated with deleterious health effects to the kidneys, lungs and the liver. **Objective:** This study was conducted to investigate the effects of gasoline vapors and vehicular exhaust fumes on the kidney and liver function, and on the hematological parameters of gasoline fuel station workers. **Methods:** Blood analysis for kidney function and hematological indices were performed on gasoline station workers. Family drivers were also invited to participate to serve as control subjects. **Results:** Thirty-three participants (28 study subjects and 5 controls) joined the study. Mean serum LDH, serum creatinine and serum urea level concentrations were significantly higher in the study group compared to the controls. Mean serum urea and mean serum creatinine concentration levels were higher among study participants who were exposed to gasoline and diesel fumes for more than 5 years. There were no significant increases in the mean serum concentrations of ALP, ALT, AST and GGT between study subjects and in between study participants working less than 5 years and those working more than 5 years. **Conclusion:** Serum creatinine and urea concentration significantly increase for a longer period of time and so with a decrease in the hematological indices in people exposed to toxic fumes of gasoline and diesel fuels.

**KEYWORDS:** fuel inhalation; kidney function; liver function; gasoline; workers

INTRODUCTION

Volatile organic compounds (VOC) such as gasoline and other fuels are associated with a wide variety of deleterious health effects including respiratory diseases, liver and kidney diseases and cancer [1]. Acute and chronic exposure to vapors of VOCs were reported to cause respiratory diseases including lung edema and hemorrhage [2] and hematological malignancies [3]. Occupational exposure to solvents and gasoline increases the risk of bladder cancer in a study conducted in Finland [4]. Acute lethal poisoning resulting from massive accidental inhalation of gasoline vapors were reported with respiratory, hematological and kidney damages [5]. Red cell indices, white blood cell counts, hematocrit, hemoglobin concentration and mean corpuscular hemoglobin concentration significantly decreased among patients who were exposed to petroleum fumes for at least 2 years in duration, and was significantly correlated with prolonged exposure to toxic fumes [6]. Life time cancer risk among diesel service station workers was estimated to be 3.78 x 104 cancer risk [7]. Death from petrol inhalation may be due to myocardial sensitization to endogenous catecholamines after exposure to petroleum fuel [8]. There are scanty literatures published on the toxic effects of inhalation of...
Participants were recruited from fuel stations in Riyadh, Saudi Arabia between March and May 2015. All the participants were informed about the aim and objectives of the study and approval forms were obtained. The study protocol was reviewed by the Princess Nourah bint Abdulrahman University Research Ethics Committee.

Ten ml. of blood samples were obtained from all participants. Another five participants working as private drivers were also recruited to act as controls for the study. Blood samples were sent to the laboratory for analysis of serum LDH concentration, blood urea nitrogen (BUN) concentration, serum creatinine, alkaline phosphatase, serum alanine transaminase, serum aspartate transaminase and gamma glutamyl transferase (GGT) concentration. Blood indices for WBC count, RBC count, Hemoglobin, Hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and platelet count were also analyzed. All participants were advised to fast for at least 10 hours prior to blood extraction for the liver function tests.

All results of the laboratory tests were encoded and analyzed statistically using the Predictive Analysis Software (PASW) version 19 (SPSS Inc, IBM, Chicago, Illinois, USA). Data is presented in numbers and percentages. Independent T-test was used to determine statistical difference in the mean values between study and control participants. A p value of < 0.05 was considered statistically significant.

**Results:**

There were a total of 33 participants (28 study and 5 control participants), all males aged between 28 and 50 years old (mean: 35 years old). The study participants were gasoline station workers aged between 28 and 50 years old. The control participants were family drivers, aged between 29 and 47 years old (mean: 37.4 years old).

The metabolism of benzene in humans has been extensively studied an archived by the Toxic Substances and Disease Registry [9,10,11]. Metabolism of benzene occurs in other organs besides the liver which is its primary site of metabolism following oral absorption [12].

Table 1 shows the mean results of the laboratory tests for all patients. The table also shows the difference of the laboratory results between the study and the control participants. Study participants had significantly higher serum LDH compared to the control group (251.10 ± 27.69 U/L versus 186.69 ± 43.10 U/L, 95% CI of -98.68 to -30.29, p=0.002). Study participants also had a significantly higher serum urea concentration (3.96 ± 0.95 mg/dL versus 2.14 ± 0.06 mg/dL, 95% CI of 1.44 to 2.19, p=0.001), and a significantly higher serum creatinine concentration than the control group (7.96 ± 6.65 umol/L versus 67.60 ± 1.82 umol/L, 95% CI of 0.28 to 6.45, p=0.034). There were no statistically significant differences in the serum concentrations of ALP, ALT, AST and GGT.

Mean duration of work for all participants was 5.76 ± 3.36 years (range of 1 - 15 years). Mean duration of work for the study group was 5.46 ± 3.0 years, and was 7.40 ± 5.03 years for the control group (p=0.242). The mean serum concentrations of urea and creatinine were significantly higher among workers who were exposed to gasoline and fuel fumes for more than 5 years. Mean serum urea concentration in patients working for less than 5 years was 3.85 ± 0.77 mg/dL, whereas the mean serum urea concentration in patients working for more than 5 years was 4.63 ± 0.91 mg/dL (95% CI of -1.44 to -0.13, p=0.021). The mean serum concentration of creatinine in patients working for less than 5 years was 69.71 ± 5.91 umol/L, whereas the mean serum concentration of creatinine in patients working for more than 5 years was 75.79 ± 7.52 umol/L (95% CI of -11.326 to -0.817, p=0.025). There were no significant differences in the mean serum concentrations of ALP, ALT, AST and GGT between participants working less than 5 years and those working more than 5 years.

Table 2 shows the blood indices results for both study and controls. WBC count was significantly higher among gasoline fuel station workers than the controls (7.82 ± 1.41 versus 6.08 ± 1.33, p=0.039). The mean MCH of study participants was significantly lower than the control group (25.10 ± 2.13 versus 30.04 ±0.82, p=0.012). The mean MCHC of the study group was significantly lower than the control group (32.29 ± 5.80 versus 35.80 ± 0.60, p=0.040). All other blood indices were not significantly different between the study and the control group.

**Discussion:**

The association between fuel inhalation exposure and the effect of toxic fumes on individuals particularly those working in gasoline and fuel stations have been studied and a report by Lohi et al found that occupational exposures to solvents and gasoline increases the risk of bladder cancer this has been verified by Papi et al. in which respiratory, hematological and kidney damage were reported after acute lethal poisoning resulting from massive accidental inhalation of gasoline vapors [13,14]. Our study reports a novel account of the toxic effects...
of chronic gasoline and fuel vapor inhalation on renal and hematological parameters, with special emphasis on the effects of the duration of exposure to gasoline and fuel fumes.

In this paper, we found out that the serum urea and serum creatinine concentration were significantly higher amongst individuals who were exposed to gasoline and fuel. Mean urea concentration in our control subjects was 2.14, and mean urea concentration in our study subjects was 3.96. That is a staggering 85% higher concentration among our study subjects compared to our control subject. On the other hand, the mean serum creatinine concentration in our control subjects was 67.60, and the mean serum concentration in our study subjects was 70.96, which is around 5% higher than in control subjects. Our results show that indeed, there is a considerable and significant effect of gasoline and fuel exposure to the kidney function of individuals, particularly those working in gasoline and fuel refilling stations, and is in accordance with the report conducted [15]. It is too presumptuous at this point of time to conclude if our patients are at greater risk of developing bladder cancer, to refute or second the report conducted by Lohi et al, unless we follow up our patients for a considerable amount of time [13,15].

Both serum urea and serum creatinine reflect the function of the kidney. Blood urea nitrogen is a normal waste product of protein metabolism. In normal individuals where the kidneys are functioning well, urea is excreted or removed from the body through the kidneys. When the kidney function slows down due to a disease or an abnormality, blood urea level rises. The normal level of blood urea in adults is 3.5 to 6.5 mmol/L (roughly 20 to 30 mg/dL). In our study, three study patients had serum urea concentration above 6.5 mmol/L, and 11 other study patients had serum urea concentration above 4.0 mmol/L. The three study patients who had elevated serum urea concentration were those who were working for more than 5 years in a gasoline and fuel refilling station, whereas 5 of the 11 study patients who had serum urea concentration between 4.0 and 6.5 mmol/dL also worked for more than 5 years in a gasoline and fuel refilling station. The association between the higher levels of serum urea concentration in these patients and duration of exposure was also shown in our results wherein serum urea concentration was significantly higher among those subjects who were working in gasoline stations for more than 5 years. In fact, our study patients had serum urea concentration 85% higher than the controls. This is something to ponder on.

Serum creatinine on the other hand is regarded as a more accurate marker of kidney function compared to serum urea. Similarly however, serum creatinine levels also increase when the kidneys are not functioning properly, although in certain cases, serum creatinine is somehow affected by muscle mass. The normal levels of serum creatinine varies from laboratory to laboratory, but is usually between 50 and 120 umol/L. In our study however, all of our study patients had serum creatinine levels below 120 umol/L. Despite these, our study showed significantly higher serum creatinine levels among those working in gasoline and fuel refilling stations than our control patients. Sugie et al reported sudden death due to liquefied petroleum gas (LPG) inhalation, and showed that the liver and kidney were among the major organs where high concentrations of LPG accumulated [16]. Abnormal liver functions alongside neurological symptoms were reported in a case report of a male, following accidental inhalation of natural gas containing propane and Butane [17].

Serum LDH on the other hand was also found significantly higher among our study patients who were working as gasoline and fuel refilling stations. Serum LDH, though not a specific test, may reflect tissue or cellular damage. Whether this higher degree of serum LDH levels among fuel station workers is an effect of some kidney tissue damage, it may also reflect other possible causation such as the presence of anemia. In such case, if we consider anemia as the probable cause of this elevated serum LDH levels, the mean MCH and MCHC levels in our study patients were significantly lower in gasoline station workers compared to family drivers. (refer to Table 2) We all well know that MCV reflects the red cell size and MCHC as the amount of hemoglobin inside the red blood cell. Thus, a low MCV and low MCHC reflects microcytic anemia. This is supported by a lower hemoglobin count in our study patients compared to controls, although the difference did not reach statistical significance. (Table 2) Our results of WBC count was significantly higher among gasoline fuel station workers than the controls disagree with to the results from found the mean WBC was significantly lower in workers compared with controls of WBC [9].

The low number of subjects in our study, itself serves as the limitation. However, despite the small number of our participants, this study was still able to show the significant effects of toxic fumes from gasoline and diesel fuels to the kidney and hematological parameters. Furthermore, this study will serve as a jumpstart to conduct further studies to verify our results and confirm the effects of gasoline and diesel fumes inhalation. There is also a need to quantify the effects of these toxic fumes on the kidney function tests and hematological parameters in relation to time and duration of exposure, with follow-ups over a longer duration of exposure to account the detrimental effects of such exposure. Another important limitation of this study arises due to the nature of benzene as a molecule which has a relatively short half-life making it hard to isolate its effects on the biomarkers of exposure. Typically biomarkers reflect only very recent exposure and variability has been reported with serial sampling in day-today and week-to-week sampling [18,19].
Table 1: Blood chemistry indices of participants (study versus control)

<table>
<thead>
<tr>
<th>Laboratory tests</th>
<th>All</th>
<th>Study</th>
<th>Controls</th>
<th>P values (study vs. control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean LDH, U/L</td>
<td>33.96 ± 7.33</td>
<td>25.10 ± 7.69</td>
<td>186.59 ± 43.10</td>
<td>0.002</td>
</tr>
<tr>
<td>Mean creatinine, umol/L</td>
<td>7.05 ± 2.66</td>
<td>7.90 ± 2.66</td>
<td>67.60 ± 1.82</td>
<td>0.034</td>
</tr>
<tr>
<td>ALP, U/L</td>
<td>80.97 ± 17.60</td>
<td>85.40 ± 23.73</td>
<td>80.18 ± 16.72</td>
<td>0.550</td>
</tr>
<tr>
<td>ALT, U/L</td>
<td>73.73 ± 25.89</td>
<td>61.60 ± 27.1</td>
<td>40.54 ± 24.82</td>
<td>0.094</td>
</tr>
<tr>
<td>AST, U/L</td>
<td>26.73 ± 8.29</td>
<td>31.0 ± 8.09</td>
<td>25.96 ± 8.23</td>
<td>0.216</td>
</tr>
<tr>
<td>GGT, U/L</td>
<td>39.42 ± 20.59</td>
<td>51.8 ± 13.46</td>
<td>37.21 ± 21.03</td>
<td>0.147</td>
</tr>
<tr>
<td>LDH = Lactic Dehydrogenase, ALP = Alkaline Phosphatase</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>WBC = white blood cells</td>
<td>5.63 ± 0.34</td>
<td>5.64 ± 0.33</td>
<td>5.55 ± 0.44</td>
<td>0.688</td>
</tr>
<tr>
<td>RBC count</td>
<td>7.56 ± 1.52</td>
<td>7.82 ± 1.41</td>
<td>6.08 ± 1.33</td>
<td>0.039</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>16.17 ± 1.08</td>
<td>16.09 ± 1.09</td>
<td>16.62 ± 1.01</td>
<td>0.327</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>47.85 ± 2.61</td>
<td>47.92 ± 2.55</td>
<td>47.30 ± 3.42</td>
<td>0.745</td>
</tr>
<tr>
<td>MCV</td>
<td>85.06 ± 4.01</td>
<td>85.37 ± 4.24</td>
<td>83.36 ± 1.98</td>
<td>0.119</td>
</tr>
<tr>
<td>MCH</td>
<td>89.39 ± 1.78</td>
<td>88.56 ± 1.83</td>
<td>90.04 ± 0.82</td>
<td>0.012</td>
</tr>
<tr>
<td>MCHC</td>
<td>32.31 ± 5.48</td>
<td>32.29 ± 5.80</td>
<td>35.80 ± 0.60</td>
<td>0.040</td>
</tr>
<tr>
<td>Platelets</td>
<td>274.52 ± 72.91</td>
<td>271.43 ± 71.75</td>
<td>291.80 ± 85.71</td>
<td>0.637</td>
</tr>
</tbody>
</table>

WBC = white blood cells
RBC = red blood cells
MCV = mean corpuscular volume
MCH = mean corpuscular haemoglobin
MCHC = mean corpuscular haemoglobin concentration
PLT = platelet count.

Conclusion:

Serum creatinine and urea concentration significantly increase for a longer period of time and so with a decrease in the hematological indices in people exposed to toxic fumes of gasoline and diesel fuels. Results from the present analysis suggest future work is needed to examine adverse health effects related for close monitoring of fuel station workers health not only for environmental exposures but also for their kidney and general health that may find them susceptible because of the environmental exposures in their workplace.

REFERENCES