Variability in cardiovascular functions and baroflex sensitivity following inhalation of petroleum hydrocarbons

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ABSTRACT

Objective: Although petroleum products are useful chemical compounds which form an integral part of our modern technology, they have been reported to cause deleterious effect on health following their inhalation. Petroleum hydrocarbons-dependent health hazards and their mechanisms have been associated with the routes of administration. This study, therefore, aimed at the isolation and chemical characterization of various petroleum products, and also investigating in rat model of Sprague dawley strain, the variability in cardiovascular functions and possible mechanism following inhalation of petroleum products. **Materials and Methods:** Control rats were not exposed to any form of petroleum products, while the petrol-exposed, diesel-exposed, and kerosene-exposed were exposed to petrol, diesel, and kerosene respectively. **Results:** When compared with the controls, all exposed groups showed a significant ($P<0.05$) increase in the systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP), and heart rate (HR). In comparison with the control, exposure to petroleum products also led to significant ($P<0.05$) increase in baroreflex sensitivity in the diesel- and kerosene-exposed rats. Baroreflex sensitivity was comparable in the control and petrol-exposed rats ($P>0.05$). Body weight gain was significantly ($P<0.05$) reduced in petroleum products exposed rats. **Conclusion:** These results suggest that the variability of cardiovascular functions associated with inhalation of petroleum products is in attendant to baroreflex sensitivity and resetting of arterial pressure.

Key words: Body weight, baroreflex sensitivity, heart rate, mean arterial pressure, petroleum hydrocarbons

INTRODUCTION

The adverse health implications of exposure to petroleum products (crude oil) remain a public health concern since these compounds form a basic part of our lives. Human exposure to the hydrocarbons contained in these products can occur through ingestion of contaminated food, drinking water and soil residues, contact of contaminants with skin (dermal exposures), or inhalation of vapours and air borne soils[1] by consumers or refinery workers. Inhalation of the hydrocarbons can be accidental or intentional. Inhalant abuse, the deliberate inhalation of hydrocarbons as a form of recreational drug use, has become a significant health issue affecting children and adolescents.[2] Their low cost, ready availability and ease of use contribute to this problem. Inhalation is most commonly achieved by sniffing, huffing or bagging.[3]

Interest on the adverse effects of petroleum hydrocarbons has grown in recent years, and focus has been on the deleterious effects of these products on various systems in the body. Sudden death from inhalation of petroleum

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products is well recognized in misusers of volatile substances.[2,4] Over the years, there have been various concerns about both, acute exposure as a result of daily use of petroleum products, and exposures from spillage, blowout vandalization and tanker accidents, and the chronic exposure by drinking contaminated water. It has been shown that petroleum products cause tachycardia, dysarrhythmias, dizziness, pulmonary hypertension,[2] pulmonary aspiration, severe respiratory and cardiac failure, impaired regulation of vascular tone and endogenous fibrinolysis.[5,6]

Studies have suggested that these effects are dependent on the route of administration.[2,4] The proposed mechanisms, however, are myocardial sensitization to catecholamine, vasovagal events, respiratory depression, hypoxia and hypercapnia.[2,4] This study, therefore, sought to investigate in rat model, changes in cardiovascular functions associated with exposure to petroleum products and possible role of the baroreflex activities.

MATERIALS AND METHODS

Animal and treatments

Sprague-Dawley rats weighing between 130-150 g were obtained from the animal house of the Physiology Department, Ladoke Akintola University of Technology, Ogbomoso, Nigeria. They were housed in well- ventilated cages maintained at 25 ± 2°C, on a 12-hour light-dark cycle. Rats were on standard rat chow and tap water *ad' libitum*. They were acclimatized for 2 weeks before the experimental period.[7,8] Procedures in involving animals and their care were performed in accordance with the National Institutes of Health (NIH) guideline for the care and use of animals. Rats were assigned to one of the four experimental groups of comparable body weight. Control group was not exposed to any form of petroleum products. Petrol-exposed, diesel-exposed and kerosene-exposed groups were exposed to petrol, diesel and kerosene respectively, by placing them in an exposure chamber over wire gauze with the appropriate petroleum products under the gauze. A modified nose-inhalation exposure method was used as previously described.[9,10] The cages housing the animals were placed in respective exposure chambers with calibrated beakers of 1000 cm^3 containing 500 cm^3 of petrol, diesel, and kerosene respectively. The petroleum fractionated products were allowed to freely evaporate within the respective exposure chambers at ambient humidity and temperature, and animals were exposed to vapors (0.5 ± 0.08 cm^3/min/kg/m^3/day) generated from direct evaporation of the petroleum products. The animals were exposed for 5 minutes daily. At the end of exposure, animals were transferred to petroleum-free section of the animal house. The initial and final volumes of petroleum products in the beaker before and after exposure were respectively recorded. The differences in volume per day were used as estimate relative concentrations of vapors used.

Body weight gain and cardiovascular variables

The body weights of rats were determined before and after the experiment. The body weight gains were deduced by subtracting the initial body weights from the final body weights. At the end of the experimental period, the animals were anesthetized with 25% urethane and 1% chloralose, and placed on the dissecting board. The femoral artery was isolated and cannulated, and blood pressure was recorded using the pressure transducer (P23LD Statham Hato Rey, Inc) of the grass 7D polygraph (Grass Instruments ltd, QuinincyMassachusetts,) and the heart rate (HR) was obtained from the blood pressure recording. The mean arterial pressure was obtained using the following formula:

$$MAP=DP+1/3(SP– DP)$$

Where, MAP=mean arterial pressure
DP=diastolic pressure
SP=systolic pressure.[11]

After a stable blood pressure recording, the right and left internal carotid arteries were isolated, raised and occluded with a bulldog clip below the carotid sinus for 30 seconds, and the blood pressure of the animals were recorded during the occlusion. The clip was removed after 30 seconds to normalize the system. The peak changes in heart rate (HR) and MAP were obtained. Baroreflex sensitivity was calculated from the ratio $\Delta HR/\Delta MAP$.[12]

Statistical analysis

Data are expressed as mean+standard error of mean (SEM) of 10 rats per group. Statistical analyses were done by analysis of variance (ANOVA). Unpaired student *t* – test was used to analyze the level of significance between the control and treated groups. $P<0.05$ was considered to be significant. All analyses were done using Graph Pad Prism 5.

RESULTS

Table 1 shows the composition of various petroleum products used as separated by gas chromatography. Petrol has the least aliphatic constituents by proportion; however,

the highest aromatic compositions when compared with diesel and kerosene. Diesel contains more aliphatic and aromatic constituents than kerosene. Figure 1 shows significant (P<0.05) reductions in the mean body weight gain of exposed rats when compared with the controls. The least weight gain was seen in petrol-exposure, followed by diesel-exposure. In comparison with control rats, exposure to petroleum products led to significant (P<0.05) increase in systolic pressure (SP), diastolic pressure (DP), mean arterial pressure (MAP)and HR [Table 2]. Similarly, diesel- and kerosene-exposed rats showed a significant (P<0.05) increase in baroreflex sensitivity when compared to control rates [Figure 2]. Baroreflex sensitivity was comparable in the control and petrol-exposed rats (P>0.05). Petrol exposure led to more increase in MAP and heart rate when compared with rats exposed to other hydrocarbons. Control rats showed comparable baroreflex sensitivity throughout the intervals of observation. The baroreflex response peaked at the 5th second of exposure in the petrol- and kerosene-exposed rats, followed by a gradual resetting. However, diesel-exposed rats showed a gradual increase in baroreflex sensitivity throughout, though with a fluctuation at the 25th second. Nevertheless, the baroreflex sensitivity was highest in the kerosene-exposed rats until the 30th second.

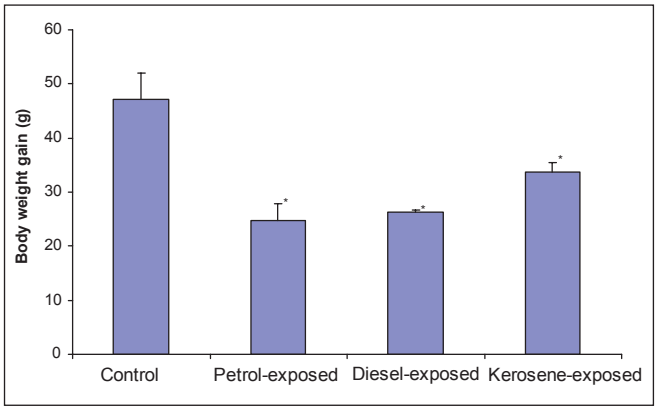

Figure 1: Effect of various petroleum products on body weight gain. *P<0.05 vs control

Table 1: Hydrocarbon compositions of petrol, diesel, and kerosene as isolated by gas chromatography

Hydrocarbons (%)	Petrol	Diesel	Kerosene
Aliphatic	9.3966665	69.276666	64.649999
Aromatic	88.46334	22.826666	6.4266666
Fatty acids	-	0.8833333	-
Polar	2.14	6.7099998	28.593333

DISCUSSION

This study seems to be the first to report the effect of inhalation of various petroleum products hydrocarbons on body weight gain. The results from the present study demonstrate that petroleum hydrocarbons impaired body weight gain in experimental animals exposed to various petroleum products. This finding agrees with previous studies[3,13] that showed that petroleum solvents dissolve fat and lipids in the body with resultant degeneration of fat store in the body. It is also in agreement with the results of Uboh *et al*.[14] that showed that petrol vapors induced growth suppression and weight loss. The least weight gain seen was in the petrol-exposed rats followed by the diesel-exposed and kerosene-exposed rats. The discrepancy seen in the weight gains in rats exposed to various forms of petroleum products could be associated with their aromatic compositions. Petrol with the highest aromatic content showed the least weight gain, while kerosene with the least aromatic composition showed the highest weight gain among the exposed rats.

The finding in this study that inhalation of petroleum hydrocarbons resulted in increased arterial blood pressure, MAP and HR in these animals substantiate findings in previous studies[15] which reported that inhalation of hydrocarbons elicited vasoconstriction and impaired

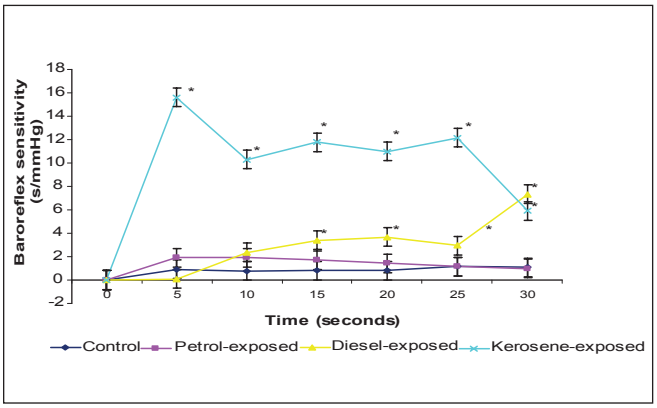

Figure 2: Variation in baroreflex sensitivity following inhalation of various petroleum products in rat model. *P<0.05 vs control

Table 2: Cardiovascular variables in rats after inhalation of petrol, diesel, and kerosene

Variables	Control	Petrol-exposed	Diesel-exposed	Kerosene-exposed
SP (mmHg)	116.0 ± 1.789	196.2 ± 1.158*	139.0 ± 1.183*	160.0 ± 3.536*
DP (mmHg)	81.60 ± 0.980	135.8 ± 1.114*	112.6 ± 0.812*	106.8 ± 1.530*
MAP (mmHg)	93.07 ± 1.221	155.9 ± 1.102*	121.4 ± 0.7339*	124.5 ± 2.181*
HR (beats/min)	382.0 ± 0.894	461.6 ± 3.326*	453.4 ± 5.913*	46.0 ± 4.301*

*SP: Systolic pressure; DP: Diastolic pressure; MAP: Mean arterial pressure; HR: Heart rate. *P<0.05 vs. control*

vascular tone. This finding suggests that petroleum hydrocarbons may have a pressor effect on cardiovascular functions. The pressor effect could be correlated to the ability of hydrocarbons to cause sensitization of myocardium to catecholamines, impairment of vasovagal event, respiratory depression, hypoxia, and hypercapnia[2,4,16] with consequent sympathetic effect and elevation of arterial blood pressure. This study revealed that inhalation of petroleum hydrocarbons led to increase baroreflex sensitivity, except in petrol-treated rats.

Baroreceptors are sensors located in the blood vessels and act as a part of the baroreflex negative feedback mechanism in the short-term regulation of arterial pressure.[17] These mechanoreceptors reset in the maintenance of a normal arterial pressure.[11] The pressor effects of the hydrocarbons observed in exposed rats could explain the variation in baroreflex sensitivity. The baroreflex sensitivity of petrol-exposed rat was near normal, compared to that seen in diesel- and kerosene-exposed rats, which showed a significant increase. The near normal baroreflex sensitivity seen in petrol-exposed rat coupled with significant rise in arterial blood pressure suggest a resetting of the arterial pressure to a new higher than normal value as though normal. On the other hand, the more sensitive baroreflex and high arterial pressure seen in diesel- and kerosene-exposed animals implies an impairment of the factors that regulate the baroreceptors to correct or adjust to the arterial blood pressure.

It is noteworthy that petroleum hydrocarbons are risk factors of cardiovascular dysfunctions,[18-22] which are major challenges among refinery workers, inhalant abusers, and the general population at large since they form an essential component of life, thus accounting for clinical complications leading to increased mortality.[16,23] The severity of cardiovascular implications associated with petroleum products inhalation may be related to the different components of the various petroleum products. The volatile aromatic hydrocarbons proportion in petrol might account for the pressor effect and rapid adjustment of the baroreflex to the increased arterial blood pressure compared to the increased baroreflex sensitivity seen in diesel- and kerosene-exposed rats, with lower aromatic hydrocarbons. Similarly, kerosene with the least aromatic hydrocarbons showed a higher increase in baroreflex sensitivity compared with diesel. However, the gradual rise in the baroreflex sensitivity noticed in the diesel-exposed rats could be associated with its aliphatic constituents. This suggests that the hydrocarbon constituents of petroleum products in entirety account for these variations.

In conclusion, we have demonstrated that the variability of cardiovascular functions seen in petroleum hydrocarbon inhalation is associated with baroreflex sensitivity and arterial pressure resetting. The study suggests that petroleum products with high aromatic hydrocarbons produced a marked pressor effect with more rapid resetting of the arterial blood pressure. The severity of cardiovascular dysfunctions is dependent on the proportion of individual hydrocarbon composition of various petroleum products. It is suggested that the cardiovascular variation and weight changes seen in petroleum products exposure should be ascribed to the combinatorial effect of hydrocarbon compositions contained therein, rather than an individual chemical substance.

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