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RESEARCH ARTICLE

Epidemiological studies on Petroleum toxicity

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Abstract

Gasoline or petrol is the generic term for petroleum fuel used for internal combustion of engines. Petroleum fumes are ubiquitous in our environment and the common sources of contact or exposure are petrochemical industries (refineries, oils field, and filling stations) and homes. Also the daily use of petroleum outside the industrial settings is likely to have effect on users. The present review compiles the epidemiological studies done in various parts of world on the harmful effects of petroleum products.The available studies suggest that petroleum products are more toxic to liver and kidney as compared to other organs, No conclusive studies are available to support the role of petroleum products in skin, respiratory,reproductive and neuropsychiatric disorders.

Keywords: Gasoline, Toxicity, epidemiological studies

INTRODUCTION:-

Petrol (or gasoline) is a volatile and inflammable petroleum-derived liquid mixture primarily used for internal combustion of machines. It consists of hydrocarbons (aromatic, saturated and unsaturated) and non-hydrocarbons (N, S, O_2, vanadium and nickel) [1,2]. Petrol is distilled from crude petroleum and vapour obtained as a result of its evaporation may be considered as petrol fumes. The volatile nature of petrol makes it readily available in the atmosphere any time it is dispensed, especially at petrol filling stations and depots. Petrol contains mixture of volatile hydrocarbons and so inhalation is the most common form of exposure [3]. Petrol vapour can reach supra-lethal concentrations in confined or poorly ventilated areas, although such exposures are rare [4] . The intentional inhalation of vapour ('sniffing' or 'huffing') has been extensively documented [5]. At low doses, petrol vapour is irritating to the eyes, respiratory tract and skin. Exposure to higher concentrations of vapour may produce CNS effects such as staggered gait, slurred speech and confusion. Very high concentrations may result in rapid unconsciousness and death due to respiratory failure. [6].

Motorists are exposed to gasoline fumes during fuelling at gas stations, but the gas station attendants are more at risk by virtue of their occupational exposure.[1]. Gasoline vapour is not safe when inhaled even for a brief period of time (seconds). Vapour concentrations, expressed in parts per million (ppm) or mass of total hydrocarbons per unit volume (mg/m^3) of air above open barrel in unventilated out-house on 'hot' day is 25,000, air around tanker during bulk-loading is between 50 and 320 while air around petrol pump in service station during fuelling of vehicles is between 20 and 200 ppm [1] [7]

Gasoline fumes contains aliphatic, aromatic and a variety of other branched saturated and unsaturated hydrocarbons which are a continued source of pollution in various occupational setting It has been demonstrated that after inhalation of petroleum vapour through chronic exposure, lower concentrations of saturated hydrocarbons are detected in human and animal blood than that of the unsaturated aromatic hydrocarbons [8] . Both diesel and gasoline engine exhausts are known to contain, in either the particulate or the vapour phase, a variety of mutagenic and carcinogenic agents [8]. Benzene and toluene are major monocyclic hydrocarbons present in the refined petrol. Biological monitoring of exposure to bitumen fumes during road-paving operations indicated urinary excretion of 1-hydroxypyrene and thioethers in the exposed workers [9].

Ueng et al. (1998) reported that exposure of rats to motorcycle exhaust and organic extracts of the exhaust particulate caused a dose-and time-dependent increase in cytochrome P450 dependent monoxygenasesanglutathione-S-transferase in the liver, kidney and lung microsomes. Since petrol contains some of these constituents, chronic or frequent exposure to their fumes may affect the oxidant/pro-oxidant balance in exposed individuals.[10]

Toxicity of Petroleum products on Liver

Benzene and related hydrocarbons are metabolized through an intermediate epoxide, which is highly reactive and possibly binds to hepatic microsomal proteins and nucleic acids leading to cytotoxic effects [11]. Petroleum constituents can cause liver damage and may disturb the normal biochemical process in the hepatobilliary system, this ranges from increased enzymes to hepatic failure, again adults can be affected and have neurological damage, anaemia, hypertension, impotence, sterility and miscarriage. [12]

The toxicity of xenobiotics is usually determined biochemically by the monitoring of some plasma enzymes and lipids. A rise in enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and cholesterol are indices for liver cells damage.[13].Petroleum hydrocarbons and other related carbon containing compounds are converted into free radicals or activated metabolites during their oxidation in cells especially mammalian liver and kidney cells. It is these activated metabolites that react with some cellular components such as membrane lipids to produce peroxidation products which lead to membrane change [14]. They may react with enzymes and cause inactivation through protein oxidation [15] and or DNA breakage of the strands [16].

Enzymes are useful bio-markers used in assessing specific functions and integrity of a cell, especially hepatocytes. An increase levels in these enzymes activities in the plasma are linked to hepatocellular damage caused by either toxins, toxins in drugs or herbs [17]. The study was conducted to assess the level exposure to this product and the possible damage caused to the liver among petrol hawkers and petrol pump attendants in Maiduguri metropolis in Nigeria..There is a significant increase in the levels of plasma liver enzyme such as *aspartate aminotransferase*, *alanine aminotransferase* and *alkaline phosphatase* in petrol hawkers when compared with control subjects. [18].Duricic *et al*;1991 reported that there are degenerative changes in hepatic and renal functions in rats exposed to petrol[19], it is also in consonant with the findings of Dede and Kagbo : 2001 reported a dose dependent hepatocytes necrosis in rat fed in diesel fuel contaminated source[20]. Shibatam reported that consumption of petroleum hydrocarbon-contaminated diets could cause liver enlargement, growth depression and histological changes [21].

In the investigation with petrol attendants exposed to petrol vapour in Owerri, the increases in the activities of serum *aspartate* and *alanine aminotransferases* and *alkaline phosphatase* for those exposed from 6 – 10 years were significantly high when compared to the control there were no significance differences (P<0.05) in the mean values of total, conjugated and unconjugated bilirubin concentrations in the test groups relative to the control [22].

There was also a significant difference noticed between the albumin concentrations of the petrol hawkers when compared to the control group[18]. Sunmonu and Oloyode reported a significant decrease in albumin and globulin concentrations of rats fed with crude oil contaminated catfish [23].

Toxicity of Petroleum products on Kidneys

The control group and the group exposed to fuel vapour from 1 – 5 years did not show proteinuria. Instead, proteinuria appeared in the subjects exposed to petrol vapour for 6 years and above. There was a significant (p<0.05) increase in the mean concentrations of urea and creatinine for the group exposed to fuel vapour for 6 – 10 years relative to the control group while no significant increase was observed for the group exposed for a maximum of five (5) years to the vapour The presence of trace protein in urine as well as the significantly increased levels of mean concentrations of creatinine and urea for attendants exposed to fuel vapour for up to 6 years indicate renal pathology [22].Artimaeus and Jacobs (2003) showed that considerable exposure to petrol or its product over a long period of time could cause nephrotoxicity in motor mechanics occupationally exposed to them[24].

In rats repeatedly exposed low dosages (0.5-2.5 ml/kg) of an Alberta crude oil (ACO) which showed no significant changes in clinical parameters of systemic impairment [25]. An earlier report (Vyskoci*et al*, 1991) showed that besides being carcinogenic or mutagenic, petroleum products can be nephrotoxic eventuating in the urinary excretion of proteins and enzymes such as *lactate dehydrogenase* and *N–acetyl –β– glucosaminidase* [26].

The study conducted at Insulaimani city assessed the effect of long-term exposure to gasoline fumes that is constantly inhaled by the workers on kidney function and on the plasma proteins profile as an aspect of general humoral immunity.Although the results indicated non-significant changes in most of the plasma proteins, gamma globulin levels are significantly decreased, which may be considered as an indication for immunotoxicity. [27] A study conducted at Nigerian petrol attendants reported an increase in IgM levels which may be attributed to inflammatory reactions [28].The exposure to gasoline fumes produced remarkable impairment in liver function, which may be a causative factor for the reported changes in certain liver-originated plasma proteins. [29] Fuel products are mixtures of aliphatic and aromatic hydrocarbons

mostly related to gasoline, most of them are toxic to many organ systems including the kidney which may be attributed to an increase in liberating toxic metabolites including reactive oxygen species. While experiments with rats indicate that exposure by inhalation to the aromatic hydrocarbons toluene, styrene, and xylene was nephrotoxic [30] Both human and experimental studies suggest that many chemicals can affect the kidney [31].The study conducted at Insulaimani city serum levels of urea and creatinine (markers of renal function) were significantly elevated in gasoline-filling workers; however, although they are within the highest accepted values, they may represent a greater tendency toward progression to renal disease. In this regard, some previous studies have shown that exposure to petrol derivatives may have detrimental effects on kidney functions[32],[33]. Stengel *et al.,* based on a case control study, did not favor an effect of solvent exposure in glomerulonephritis incidence, but rather suggested a role in the progression to ESRD [34] Using an appropriate cohort study design, Jacob *et al*., showed that long-term exposure to gasoline fumes was associated with faster progression to end-stage renal disease in patients with IgA and membranous glomerulonephritis [35] . Gasoline, however, include many chemicals and additives where anyone could be the cause for such deterioration in renal functions. Accordingly, the identification of specific solvents and exposed job categories at risk would improve intervention to prevent or delay mild renal impairment progression to end-stage renal disease in the occupational setting.In the above study, the correlation between duration of exposure and the reported changes in gamma globulin level and renal function was weak and non-significant; this might be attributed to involvement of other factors, including the constituents of the gasoline, other than the time that influence these changes. In a previous study carried out in 1995, the environmental levels of gasoline constituents were measured in the breathing zone of service station attendants during different periods.The results obtained showed that both variables could significantly increase the environmental levels of gasoline vapors and, subsequently, the risk of occupationally exposed workers [36]

Oxidatitive damage due to petrol products

Xenobiotics within the organism undergo a series of reactions and biotransformation to facilitate their excretion. Oxyradicals are continually produced in eukaryotes as unwanted byproducts of normal oxidative metabolism and their production can be increased by conditions such as hypoxia/hyperoxia, redox cycling xenobiotics like metals, quinones, nitroaromatic compounds and induction of enzymes, such as cytochrome P450 and P450 reductase [37]. Consequently, aerobic organisms have developed defence systems against oxidative damage [38] , consisting of antioxidant scavengers (glutathione, vitamin C, vitamin E, carotenoid pigments) and specific antioxidant enzymes: *catalase*, *superoxide dismutase* and *glutathione peroxidase.* These enzymes participate in the removal of reactive oxygen species. The results of study conducted at petroleum attendants at Nigeria indicate significant elevation of lipid peroxidation in these subjects when compared with the control [39]. Environmental pollutants and petrol fumes have been reported to enhance peroxidative processes and oxidative stress within cells [40]. Elevated levels of the thiobarbituric acid reactive substance, malondialdehyde, reveal peroxidative damage to cell membranes and other lipid-derived macromolecules. Lipid peroxidation results from release of free radicals that can cause tissue damage by reacting with polyunsaturated fatty acids in cellular membranes to form malondialdehyde (MDA). This oxidative stress may have resulted from the build-up of ROS such as O_2-and H_2O_2 following the decrease in the activities of the enzymatic antioxidants. The increased generation of O_2-and H_2O_2 leads to increase production of the more reactive hydroxyl (OH.) radicals via Fenton and Haber-Weiss reactions [41]. OH.Radicals react at nearly diffusion-limited rates with any component of the cell including lipids, DNA and proteins[41]. The net result of this non-specific free radical attack is a loss of cell integrity, enzyme function and genomic stability [42]. The enhanced lipid peroxidation observed in the petrol attendants when compared with control subjects correlates with decrease in the antioxidant defense system in their blood. This is evident in the significant decrease in the enzymatic antioxidants-*superoxide dismutase* (SOD) and *catalase* (CAT)-as well as the non-enzymatic redox sensitive thiol compound, reduced glutathione (GSH). SOD and CAT enzymes are major primary antioxidant defense components that primarily catalyze the dimutation of superoxide radical (O_2-) to H_2O_2 and decomposition of H_2O_2 to H_2O, respectively [43],[44]. The decreased SOD and CAT activities induced by exposure to petroleum fumes probably results in accumulation of O_2-and H_2O_2 which react with metal ions to promote additional radical generation, with release of the particularly reactive hydroxyl radicals (OH-) [41]. OH-reacts at nearly diffusion-limited rates with any component of the cell including lipids, DNA and proteins. The net result of this non-specific free radical attack is a loss of cell integrity, enzyme function and genomic stability [45]. The involvement of these Reactive Oxygen Species (ROS) in inflammatory responses has been reported [46].A significant decrease in the level of glutathione was accompanied by a significant increase in MDA level in this study. This observation is in agreement with the reports that inverse relationship exists between lipid peroxidation and glutathione status [47,48]. Glutathione depletion impairs the cell defense against the toxic action of xenobiotic which

could lead to cell injury or death. Under acute oxidative stress, the toxic effects of the pollutants may overwhelm the antioxidant defenses [49]. Furthermore, the apparent decrease in glutathione detoxification system as a result of environmental xenobiotics indicates that this system is a sensitive biochemical indicator of environmental pollution[50].

Vitamin E is a powerful chain-breaking antioxidant, primarily preventing lipid peroxidation by breaking the chain of events leading to the formation of hydroperoxides. This action should also lead to a reduction in DNA damage since the intermediate products of lipid peroxidation include lipid peroxides, which can cause strand breaks in DNA [51]. Significant decrease of vitamin E observed in petrol attendant may be attributable to its role in preventing lipid peroxidation which may cause its depletion. No significant difference was observed in vitamin C levels in petrol attendants when compared with the control. Albumin level in petrol attendants did not change significantly when compares with the controls. This study agreed with the study of Akinosun et al. (2006) [52]. Albumin transports free fatty acids in the plasma and possesses cysteine residue which enhances its capacity to neutralize peroxyl radicals. Data from this study seem to suggest that oxidative stress is associated with occupational exposure to petrol fume in these individuals. [53]

Malignant diseases due to petrol products

The numbers of epidemiological studies which have investigated the risks of malignant disease in association with the petroleum industry have burgeoned in the past few years. This mass of data has not led to any firm conclusions. However, certain statements can be made with some degree of confidence. There does not appear to be any evidence that working in the petroleum industry - particularly refining processes - leads to any dramatic excess of cancers in general and most cancer sites in particular. There is some corroborative evidence from the studies cited here that known carcinogens such as benzene and the polynuclear aromatics have resulted in some excess of leukaemia and skin cancer in limited numbers of petroleum industry workers, but these findings are not consistent across even the best designed studies. This may be due to relatively low level exposure in the past. Of the remaining cancer sites where excesses have been reported in one or more studies, the evidence of a link with kidney cancer remains weak with few cohort studies exhibiting excess and with the best case referent study showing no excess. Interestingly, some studies show a reversal of the normal bladder kidney dominance for genito-urinary cancers. For brain cancer, the highest excesses occurred in the studies weakest on methodology. Nevertheless, modest excesses are found in some well planned studies and corroborative evidence linking solvent exposure with brain cancer exists elsewhere in the literature. The excess risk for pancreatic cancer is rarely statistically significant but cannot be easily ignored with 10 cohort studies showing SMRs ranging from 1.08 to 1.38. Such relatively low excesses must be viewed in the light of low SMRs for "all causes" and "all cancers". However, the pre-eminent message to be drawn from a reading of the epidemiological literature on malignancy and petroleum industries is the methodological flaws. The main concerns must be with the almost uniform poor exposure information, the widespread practice of ignoring latency, the failure to control for confounding, and the relatively low power of many studies. If such shortcomings persist in future publications, it is unlikely that further progress will be made regarding aetiology. Further work, more carefully designed, and larger populations are needed to evaluate the significance, if any, of leukaemia and melanoma, as well as cancers of the renal tract, the brain and the pancreas.The oil refinery and distribution industries cannot be given clean bill of health on these cancer sites at present[54] .

Cardiovascular diseases due to petrol products

Cardiovascular disease remains the most important cause of death in Western society. The most rational conclusion is that refinery workers show no evidence of excess cardiovascular mortality. Where the more specific rubric is ischaemic heart disease is reviewed, a similar mortality deficit is noted - the exception being an SMR of 1.22 in one of the OCAW reports (Thomas et al;1980)[55]. One study of the Standard Oil plant in Indiana reviewed periodic health examination data on 9,955 white male workers Forty-two per cent of the workers had an excess weight (on the Quetelet index), 15% undertook inadequate exercise, 16.5% were hypertensive (diastolic blood pressure above 90 mm Hg) and 20.3% were current smokers.(Vanpeenen, P.F.D *et al*;1985)[56]. The authors do not relate this to cardiovascular morbidity nor mortality at the plant. Indeed there is little evidence to suggest that their findings are in any major way different from those that might be found in any working population. Results from the three Russian studies are hard to interpret. In one, evidence is presented of a rising blood pressure and pulse towards the end of the shift [57]. In another, 60% of the workforce are deemed to be "hypertonic" [58] whilst in a review of the Perm City complex, Lebedeva and co-workers found a blood pressure elevation in 14.3% of the 353 workers [59]. Such a prevalence of hypertension is in line with the U.S.study but evidence for increased heart size and electrocardiographic changes are difficult to interpret in the absence of any comparison group. In short, cardiovascular disease mortality and morbidity does not seem to be in excess in workers exposed to gasoline [54].

Respiratory diseases

Respiratory disease mortality is not as important a cause of death as cardiovascular diseases but disorders of the respiratory tract are one of the commonest causes of morbidity. In the occupational context, the lung is the target organ par excellence as toxic materials in the workplace usually gain entry to the body via an airborne route. Nevertheless, the petrochemical industry is not a predominant cause of occupational lung disorder the refinery workers smoke less than the average and that this is the major determinant of their favourable respiratory disease outcome rather than any direct beneficial effect of refinery work. [54].

Other diseases

Not enough literature is available to correlate the petroleum toxicity with skin disorders, reproductive disorders, neuropsychiatric disorders and other diseases.

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