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The Effect of Pollution Represented by Polycyclic Aromatic Hydrocarbons on the Levels of p53 and Some Antioxidant Enzymes in Baghdad Traffic Police

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Abstract

Objectives: To ascertain the protective effect of p53 tumor protein by monitoring its levels in comparison with the levels of antioxidant enzymes, against any type of cancer that can be caused by chronic exposure of traffic policemen to air pollutants.

Methods: This study comprises 140 participants, who have been divided into two groups (Traffic police and Office police). PAHs were analyzed for each participant by GC/FID while p53 protein and antioxidant enzymes were measured by the ELISA technique.

Results: The concentrations of polycyclic aromatic hydrocarbons and p53 tumor protein were high in the blood of traffic police compared to office police, while higher levels of antioxidant enzymes (Catalase and G-Px) were observed in the blood of office police.

Conclusion: Exposure to PAHs can cause oxidative stress, which can damage DNA and lead to cancer. However, because natural endogenous biomolecules like p53 protein can neutralize PAHs' carcinogenic effects, their elevation has a beneficial anti-cancer effect by reducing oxidative stress and preventing tumorigenesis.

Keywords: PAHs, p53 tumor protein, catalase, G-Px, DNA

Introduction

All living things, including people, are subject to air pollution's multiple detrimental consequences, and because of how it affects human life and health, this problem has gained prominence on the international political agenda. Air pollution is the number one environmental killer and the fifth-highest risk factor for total all-cause mortality.[1] It's a complex chemical mixture that contains various concentrations of gases such as nitrogen dioxide (NO_2), ozone (O_3), carbon dioxide (CO_2), sulfur dioxide (SO_2), carbon monoxide (CO), and carbon dioxide (CO_2). Gaseous pollutants may have both immediate and long-term negative effects on health.[2] Many of these gases have oxidizing properties, and one way they can be harmful to human health is by causing oxidative stress.[1] Semi-volatile kinds including Benzene, Formaldehyde, Naphthalene, and polyaromatic hydrocarbons occur as liquid droplets, but they may also move between the gaseous particle phases of air pollution.[3]

Numerous cancers and air pollution are related,[4] and it is estimated that cancer causes 4.2 million early deaths worldwide and affects organs including the lung, mouth, bladder, kidney, breast, liver, prostate, and ovary. In addition, the International Agency for Research on Cancer has classed outdoor air pollution as a category 1 human carcinogen (IARC).[5] The liver is where PAHs are mostly processed and activated after being ingested through the lungs, skin, and intestines. Many polycyclic aromatic hydrocarbons are bioactivated to form phenols, epoxides, and dihydrodiol, which are mostly oxidized by cytochrome P_{450} monooxygenases (CYPs).[6] The two main mechanisms for the carcinogenicity of PAHs are the creation of reactive oxygen species and PAH-DNA asymptotics, particularly those of diolepoxides, radical cations, and o-quinones[7] (Figure 1).

The gene encoding the p53 tumor protein is known as tumor protein (TP53). It's a phosphoprotein containing 393 amino acids in its structure[9] and 'Guardian of the Genome' is another name for it.[10] The p53 tumor protein attaches to DNA in the nucleus directly and it is involved in the cell cycle, DNA repair, and apoptosis control, as well as regulating the repair process in reaction to damaging substances such as radiation, chemicals, and UV radiation from sunshine.[9,11]

This protein is crucial in deciding whether or not a damaged cell will undergo DNA repair or programmed cell death. If DNA damage can be repaired, p53 activates the genes needed to do it, while this protein inhibits the cell from proliferating and tells it to undergo programmed cell death if the DNA cannot be repaired.[12] This means TP53 controls cell division by stopping them from expanding and dividing (reproducing) in an uncontrolled manner. In vertebrates, these p53-mediated responses are critical and decisive in preventing cancer recurrence.[13] Under genotoxic stress, p53 can induce the production of p21WAF1/Cip1, a cyclin-dependent kinase inhibitor, which can briefly arrest the cell cycle at G1 or G2. This permits the cell to remove and repair damage while also preventing damaged cells from replicating. The action of p53, which causes irreversible G1 inactivation, can also cause aging. p53 may induce apoptosis in highly injured cells by increasing the transcription of genes like PUMA and NOXA[14] (Figure 2).

Materials and Methods

One hundred and forty Iraqi policemen affiliated with the traffic police in the city of Baghdad within the Iraqi Ministry of Interior. Their ages range between (25–65 years), during the period from July 15, 2019 to March 25, 2020. Subjects were divided into two groups as indicated below:

Group 1: 70 policemen of those who were performing their duty in the crowded squares and intersections in Baghdad (Traffic police).
Group 2: 70 policemen of those who were serving inside the buildings of the various traffic directorates (Office police).

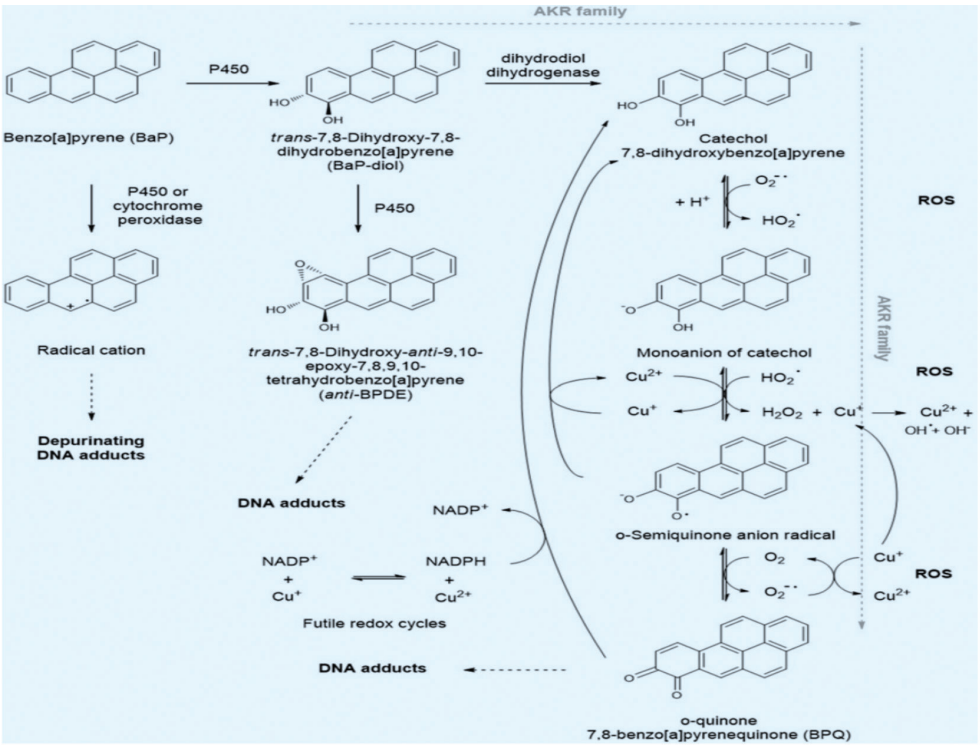

Fig. 1 **The BaP metabolites diolepoxides and o-quinones are potent reactive metabolites that can form adducts with DNA.**[8]

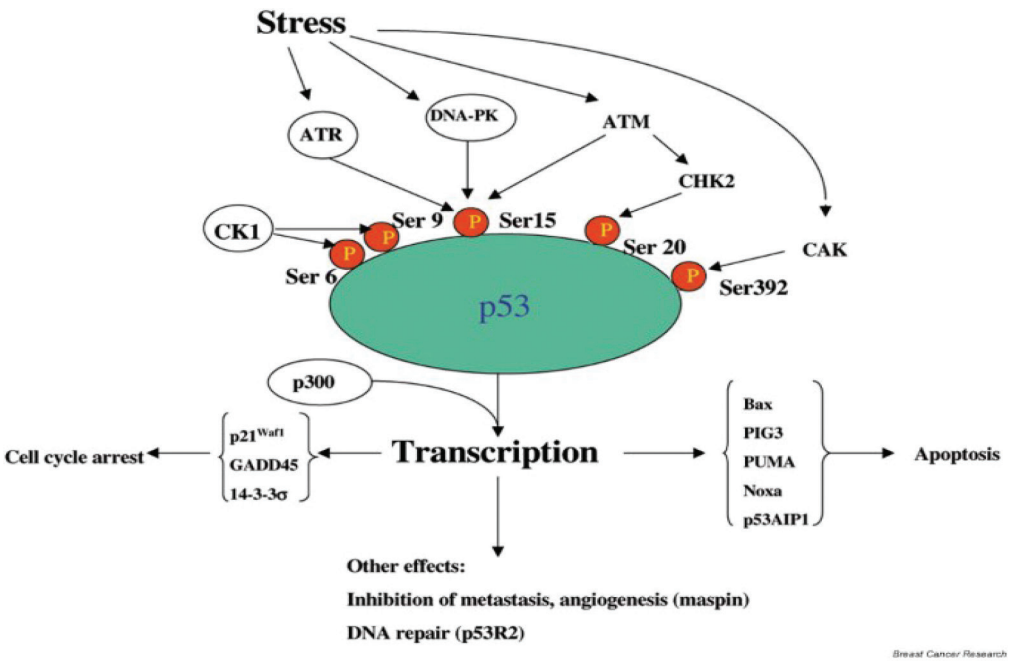

Fig. 2 **The mechanism of action of p53 protein to avoid the accumulation of genetic errors.**[15]

Six milliliters of blood were collected from each participant, and the blood samples were then centrifuged for 10 minutes at 3000 rpm to separate the serum before being aspirated, separated into aliquots, and refrigerated at 20°C until they were used for PAH.

1. Determination of PAH concentrations in serum by gas chromatography coupled with a Flame Ionization Detector (GC/FID).
2. Determination of tumor protein p53 by Enzyme-Linked Immunosorbent assay (ELISA) Kit Catalogue No. MBS2514403.
3. Determination of the serum concentration of GPX1 (Glutathione Peroxidase), by ELISA. Kit Catalog Number. E-EL-H5410.
4. Determination of the serum concentration of catalase, by ELISA Kit Catalog Number. MBS703074.

Results

The mean ± SD of age for the two groups was shown in (Table 1).

Mean concentration of PAHs, levels of human p53 protein, and two antioxidant enzymes (Catalase and G-px) for the two groups are shown in (Table 2), the effect of the exposure period to pollutants from car exhaust and diesel engines on the traffic police who are in the offices as well as the traffic police deployed in the crowded intersections of the Baghdad city are summarized in the (Table 3) and (Table 4) respectively.

Table 1. **The mean age among the groups**

Group	No.	(Mean ± SD) of Age, Year
Office police	70	38.54 ± 5.49
Traffic police	70	40.15 ± 5.7

Discussion

Exposure to these harmful substances—known as PAHs—increases the chance of developing tumors[16] because these poisons and their reactive byproducts, such as dihydrodiols and epoxides, may attach to cellular proteins and DNA causing dire consequences[17] such as mutations, developmental problems, and thus cancers that occur as a result of cell damage and biochemical disturbance.[18,19]

Table 2. **The mean concentration of PAHs, p53, Catalase and G-px among the groups**

Parameter	Group	Mean ± S.E.	*P*-value
PAHs, (ppm)	Office police	6.91 ± 0.12	0.0001
	Traffic police	8.94 ± 0.09	
p53, (pg/ml)	Office police	1070.7 ± 19.57	0.0001
	Traffic police	1431.6 ± 39.9	
Catalase activity, (pg/ml)	Office police	648.15 ± 15.3	0.0001
	Traffic police	398.52 ± 16.58	
G-Px activity, (pg/ml)	Office police	55.74 ± 2.99	0.0001
	Traffic police	34.34 ± 2.2	

P-value <0.05 is significant.

Table 3. **Comparison of studied parameters according to exposure duration for the office police group**

Parameter	Duration of exposure	Mean ± S.E.	*P*-value
PAHs, (ppm)	Less than 10 years	6.7 ± 0.31	0.599
	More than 10 years	6.97 ± 0.12	
p53, (pg/ml)	Less than 10 years	1055.4 ± 45.2	0.440
	More than 10 years	1075.64 ± 21.6	
Catalase activity, (pg/ml)	Less than 10 years	652.12 ± 43.3	0.995
	More than 10 years	646.88 ± 15	
G-px, activity (pg/ml)	Less than 10 years	59.89 ± 6.18	0.703
	More than 10 years	54.41 ± 3.44	

P-value >0.05 is non-significant.

Table 4. **Comparison of studied parameters according to exposures duration for the traffic police group**

Parameter	Duration of exposure	Mean ± S.E.	*P*-value
PAHs, (ppm)	Less than 10 years	8.80 ± 0.21	0.487
	More than 10 years	9.01 ± 0.09	
p53, (pg/ml)	Less than 10 years	1353.5 ± 80.07	0.491
	More than 10 years	1467.47 ± 44.8	
Catalase activity, (pg/ml)	Less than 10 years	394.49 ± 33.7	0.947
	More than 10 years	400.36 ± 18.8	
G-px activity, (pg/ml)	Less than 10 years	35.27 ± 5.00	0.781
	More than 10 years	33.91 ± 2.28	

P-value >0.05 is non-significant.

The results of this study showed the presence of high levels of polycyclic aromatic hydrocarbons in the blood serum of the traffic police who are at the busy street intersections of the city of Baghdad, relative to the levels in the blood serum of the office police group. Since 2003, the number of passenger auto-mobiles., trucks, buses, and household generators have skyrocketed in Iraq, posing serious environmental concerns. Research was carried out by Chaichan et al.[20] on and around the Muhammad Al-Qasim roadway close to the University of Technology in Baghdad, to assess the connection between the level of activity, the movement of cars with various engines, and the pollution that comes from exhaust pipes, and its was discovered that pollutants such assulfur and Polycyclic aromatic hydrocarbons, increase during the start and end periods of the working hours of state departments. Moreover, Iraqi inhabitants employ hundreds of thousands of tiny electric generators in their houses,[21] which use heavy oil or gasoline to create electricity, resulting in large quantities of soot, carbon deposits, and sulfur oxides.[22]

A recent study that measured air pollutants around Iraq, it showed that the highest number was recorded in Al-Diwaniyah, followed by Baghdad, specifically the Dora area.[23] Our results are in agreement with several previous studies, such as[24] of PAHs released by vehicles, which found that street cops have high exposures, much higher than chefs, and their exposure levels are comparable to coke factory workers. Another study in China found that traffic cops have a higher risk of PM2.5 pollution in the workplace than office cops who are considered a control group.[25]

Among the objectives of this research is to study the impact of polycyclic aromatic hydrocarbons on the levels of p53 protein, and the results showed that the levels of this protein are affected by polycyclic aromatic hydrocarbons, as its level increased significantly in the traffic police group located in the crowded intersections of Baghdad city compared to the office police group, indicating that the amount of PAHs changed in direct proportion to the change in the concentration of p53 protein. On the other hand,[26] discovered a substantial link between plasma levels of p53 and urine 1-hydroxypyrine, which is an acceptable biomarker of Polycyclic aromatic hydrocarbons exposure. Another study conducted in Saudi Arabia on professional workers during the Hajj season to appreciate the effect of intense exposure to polycyclic aromatic hydrocarbons on the cancer biomarker proteins p53 and p21 discovered a positive engagement between short-term PAHs exposure and blood concentrations of p53 and p21.[27] In another study, carried out by Yu et al.[28] to explore the influence of prolonged exposure to PAHs on cellular processes occurring in mouse lung fibroblasts (mLFCs), this study concluded that long-term exposure to B a A and B a P increased the protein expression levels of p53 and p21. In most cell types examined, p53 is a short-lived nucleoprotein with a half-life of 5–20 minute. The half-life of p53 rises several times once the DNA is damaged.[29] The activation of p53 is caused by the generation of DNA damage by a range of factors, including polycyclic aromatic hydrocarbons and oxidative stress. This tumor suppressor gene encodes a protein that acts as a crucial mediator of cell cycle arrest, allowing DNA repair or starting an apoptotic cascade, and thereby preventing mutations from being passed on to daughter cells.[11,30] The p53 protein's activity may also be increased when healthy tissues experience pathophysiological alterations that cause oxidative or redox stress, such as damage from ischemia and reperfusion to the heart, brain, and other tissues. Thus the oxidative stress generated by hydrogen peroxide appears to be a potent stimulator of p53 activity.[29]

Many occupational persons, such as workers in coke plants and food processing plants, are exposed to contaminants, as are traffic policemen who are exposed to PAHs through vehicle exhaust and road dust.[31] PAHs activation can be categorized into 3 paths: (1) cytochrome P_{450} enzymes and epoxide hydrolase catalyzes the formation of dihydrodiol epoxides (CYP/EH pathway), (2) cytochrome P_{450} peroxidase activity generates a polycyclic aromatic hydrocarbons reactive cation in metabolic oxidization, and (3) ortho-quinones are produced by dihydrodiol dehydrogenase, a member of the Aldo-ketoreductase family, oxidizing catechols (AKR pathway). Quinone redox cycling could result in the creation of ROS, which could lead to carcinogenesis through oxidative DNA damage.[32] Defects in the p53 protein, on the other side, maybe the cause of its high levels. Faulty mutations in the gene that encodes for the p53 protein, or point mutations in this site, can disrupt the construction of a tetramer, ultimately in the transformation of wild-type p53 into a mutant kind and decreased function. The formation of the p53 mutation elongates its half-life to many hours in humans.[33]

Various studies regarding antioxidant enzymatic and non-enzymatic have been done in clinical investigations of different Iraqi patients.[34,35] Our study chose two types of antioxidant enzymes (catalyze and glutathione peroxidase), to study their levels in the blood serum of the two study groups and their relationship with the levels of PAHs for both groups, found low levels in the levels of both catalase and glutathione peroxidase enzymes in the blood serum of traffic police personnel deployed in Baghdad city intersections compared to the levels of the two enzymes were in the control group represented by the office police, and the levels of these enzymes were inversely proportional to the levels of pollutants in the blood serum represented by polycyclic aromatic hydrocarbons. Also, some studies conducted to evaluate the effects of occupational exposure to pollutants on oxidative stress in the body have indicated a decrease in the levels of antioxidant enzymes. In a study of pollution-exposed taxi drivers,[36] reported a decrease in CAT and GSH-Px activities compared to the occupationally unexposed group. Cohort research done before, during, and after the Beijing Olympics has reported that when air pollution levels increased, indicators of total antioxidant status-declined.[37] The production of a sizable quantity of ROS by particulate matter in traffic exhausts is one theory for the reported negative health impacts. Aerosols in the environment contain smaller, more ROS-rich particles. Polycyclic aromatic hydrocarbons are also present in fine particles from vehicle exhaust (PAHs). Antioxidants have been shown to have a key part in the catalysis of the dismutation of (O_2) to H_2O_2 and the breakdown of H_2O_2 to H_2O, respectively. When the presence of reactive oxygen species overcomes the antioxidant buffering capability, oxidative stress happens. Once antioxidant enzymes are depleted, the cell is more vulnerable to the harmful effects of xenobiotics, which can lead to cell harm or death. As a result, frequent exposure to gasoline vapors has the potential to cause oxidative stress by lowering the body's antioxidant defenses' cellular functions.[38]

Poor nutritional status can also contribute to oxidative stress, for example, selenium deficiency, which is associated with increased oxidative stress; optimization of nutritional status of Se may result in higher G-Px activity. Small amounts of antioxidants have been associated with a greater risk of cancer in epidemiological research studies. G-Px loss resulted in endothelial dysfunction, decreased angiogenesis, and increased infarction severity and vascular permeability in experimental animals,[39] as seen the activity of catalase, superoxide dismutase, and glutathione peroxidase have a substantial negative relationship with the risk of coronary artery disease in patients.[40] In response to oxidative stress, prolonged antioxidant enzyme deficiency enhances tissue sensitivity and severity.[41]

Conclusion

Exposure to air pollutants like PAHs can result in lower levels of antioxidant enzymes and oxidative stress, which can damage DNA and cause a variety of cancers. However, natural biomolecules such as p53 protein can reverse these carcinogenic effects of PAHs. Its high levels are thus necessary to serve as an anticancer agent, reducing the effects of oxidative stress and preventing the formation of cancers in traffic cops. ■

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