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A Study Of The Effect Of Polycyclic Aromatic Hydrocarbon On Polymorphisms Gstp1 Gene On Thi-Qar Refinery Oil Workers

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Abstract

The influence of occupational exposure of chemical compounds on the detoxification gene GSTP1 in tar workers since these chemical compounds which have multiples effects. Therefore, the present study aimed to determining the influence of PAH and the role of GSTP1 gene according to some criteria (gender, age, smoking, location and family history). The current study included 50 workers with highest GSTP1 lacking of workers 48%compare with control 40%at the level of significant (P≤0.05). DNA was Extracted from the two sets and amplified GSTM1 gene with of technology of Polymerase Chain Reaction (PCR) so as Albumin gene (internal control). DNA was Extracted from the two sets and amplified GSTP1 gene with of technology of Polymerase Chain Reaction (PCR) so as Albumin gene (internal control). The higher percentage of GSTP1 lacking in workers (40%) compare with healthy controlled group (24%) at the level of significant (P≤0.05). Current study showed also not worthy that long work period in benzene and Tetra Ethyl Lead had an obvious lacking due to mutation, causing to delete that genes about ten times compare with others chemical compounds. When study samples are divided into old workers and new one, the results showed That old are subject to gene deletion more Than the new ones.

Keywords: PCR, GSTP1 gene, Detoxification, chemicals compounds

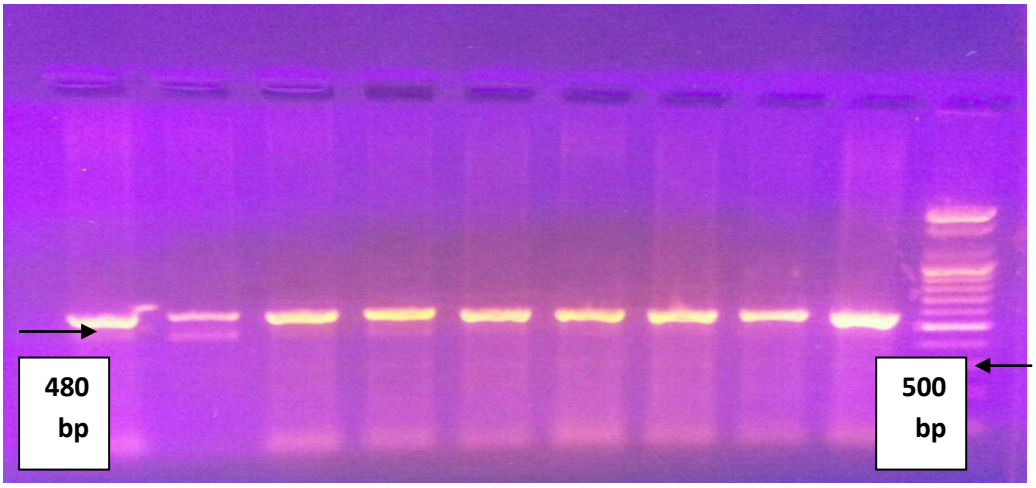
Introduction

Glutathione S-transferases (GSTs) are a family of enzymes that play an important role in detoxification of certain products of xenobiotics and carcinogens such as heavy metals, herbicides, solvents, pesticides, steroids and many other harmful pathogens by catalyzing the conjugation of many hydrophobic and electrophilic compounds with reduced glutathione [1]. Based on their biochemical, immunologic, and structural properties, the soluble GSTs are categorized into 4 main classes: alpha, mu, pi, and theta [2]. This GST family member is a polymorphic gene encoding active, functionally different GSTP1 variant proteins that are thought to function in xenobiotic metabolism and play a role in susceptibility to cancer, and other diseases [2,3]. GSTP1 is primarily located in your brain and lungs. GST detoxifies by linking toxic compounds with glutathione (GSH), thus forming a less reactive substance [4] GSTP1 genotypes are associated with increased risk of various cancers that is compounded by exposure to cigarette smoke. [3] GSTs are a family of isoenzymes that play an important role in protecting cells from cytotoxic and carcinogenic agents [1] Oxidative stress defines as imbalance between reactive oxygen species and anti-oxidant defense systems and it is associated with pathogenesis of

diseases. In human, genes involved in antioxidant defenses are highly polymorphic and show association with several multifactorial traits [14,23,24]. Cancer is a primary human health risk of exposure to PAHs. Exposure to PAHs has also been linked with cardiovascular disease and poor fetal development. PAHs have been linked to skin, lung, bladder, liver, and stomach cancers in well-established animal model studies[5] An adduct formed between a DNA strand and an epoxide derived from a benzo[a] pyrene molecule (center); such adducts may interfere with normal DNA replication [8]. Mutagenic PAHs, such as benzo[a] pyrene, usually have four or more aromatic rings as well as a "bay region", a structural pocket that increases reactivity of the molecule to the metabolizing enzymes []17,23).Chemical compounds that affect cancer initiation are typically first chemically modified by enzymes into metabolites that react with DNA, leading to mutations. When the DNA sequence is altered in genes that regulate cell replication, cancer can result.

Materials and Methods

Data and information on workers with chemical compounds exposure were obtained from Thiqar fuel stationary for year 2020.The number of workers is 50workes was collected information on samples collection, work duration, and occupation. Samples blood from healthy men and workers were extracted based on the leaflet attached to kit extraction in manufactured by Gene aid (Korean origin). PCR technique was used to amplify GSTP1 gene according to the method of [7]. DNA samples were detected by electrophoresis [19]. Statistical analysis using SPSS software



Picture (1): electrophoresis of PCR –products of GSTP1 gene on Agarose gel at concentration of 2%.

Results

The results of the current study showed The highly percentage of gene deletion in fuel stationary workers 80% compare with control groups 48% with significant different at (P≤0.05) Results statically analysis have been shown significant different at (P≤0.05). gene deletion increased about (4.33) four times for workers compare with control group OR=4.33,95%CI=1.7810.52)**.** as show in Table 1. The results of the current gene absent distributed to both chemical compounds (Benzene & Tetra Ethyl Lead) were the highest rate of gene absent in workers that deal with Benzene materials66%, (58.17%. Tetra Ethyl Lead 33%) the lowest percentage at workers deals with toluene about (33.33, as shown in (Table2).

Table 1: Comparison between fuel stationary workers and control gene deletion

Genotypes	control	Fuel stationary workers	OR	95%CI*
(+) GSTP1	26(52%)	10(20%)	1.0	_____
GSTP1(-)	24(48%)	40(80%)	4.33*	10.52-1.78

(+) present gene, (-) Absent gene, OR = Odds Ratio and 95%CI =Confidence Interval. *=significant

Table 2: Relationship between chemical compounds and gene deletion

Work material occupation	Net	GSTP1 Null	Present(+)	Normal
Benzene	40	24(66.6%)	10 (25%)	0
H2S	14	12 (41%)	12(35%)	2(28.5%)
Petrol	24	16(60%)	6(25%)	0
Toluene	14	6(33.33%)	4(22.22%)	2(33.33%)
Tetra Ethyl Lead	34	14(58.17%)	2(14.28%)	1(8.33%)

Null = gene deletion

The results of the current study show the risk present of a correlation between the genotypes of the GSTP1 gene and the periods of work for workers that have work more than 20 years ago compare with that which have worked less than 10 years ago, as the results show significant difference (OR=10,95% CI=2.501-0.02) between two different periods

Table 3: Genotypes Distribution of GSTP1 according to work periods.

Work period	GSTP1(-)	GSTP(+)	OR	95% CI
(1-10)	7(17.5%)	1(10%)	1.0	_____
(11-20)	15(37%)	2(20%)	1.07	11.99-0.07
(21-30)	17(42%)	8(80%)	10. 303	2.501-0.02

(+) present gene, (-) Absent gene, OR =Odds Ratio and 95% CI =Confidence Interval.

Discussion

[3]. Reported that chemicals materials is one of the most common factor which has been influence on human health since low molecular weight. Chemicals materials are prevalent in the environment, thus posing a significant risk to human health at the promotional phases of cancer and these result agree with our results. The statistically analyses of results show that there is significant difference between the mutant and chemicals materials influence. These results indicated that there is correlation between polymorphisms of GSTP1 and chemicals materials number of people with is increasing due to population growth chemicals materials, especially Benzo (a) pyrene, urbanization, aging, obesity and mobile phone radiation exposure [21]. has been shown to play a major role. The results of the present study have showed a table (3) the

percentage of workers which have work more than 20 years ago compare with that which have worked less than 20 years ago, as the results show significant difference (OR=10,95% CI=2.501-0.02) between two different periods was 42%, while those working in new work reached 37%. This is may be because old workers are more exposed chemical compounds than new workers, and old workers are less move to specialized centers and less to eat healthy food ,also old workers has been exposed to many risk factors such as mobile phone radiation, smoking and have infection with many chronic diseases than new workers [6,10] .This result agree with[15,16].the highest percentage Carbone exhausts in urban due to truck and car exhaust and this car exhausts avoid the linking between GST and toxic compounds such as heavy toxic metal, solvents and cheered food and this lead to reactive substances forming. This study differed from a study conducted by [15] which showed that there was significant difference between the frequency of GSTP1 genotype and incidence of chemical materials when compared fuel stationary workers and control groups was also different from the study conducted by [11,12,18] Which showed that there was no effect of benzene difference among workers and **H2S** Benzene is highly prone to electrophilic substitution reactions compared to addition reactions as it loses it's a aromaticity during addition reaction. As benzene contains delocalized electrons spanning over carbon atoms in the ring, it is highly attractive to electrophiles and is also highly stable to electrophilic substitutions. Generally, the electrophilic substitution reaction of benzene is a three-step process involving Generation of the electrophile, Intermediate carbocation formation and removal of proton from carbocation intermediate and these results disagree with our result which has been shown correlation between old workers and new workers (OR=10.303). The main factors that make older workers higher than younger are related with several another factors such as long period exposure to chemical materials molecule which increased influence with ages progressive and this result agree with that [11]. The results of the current study showed that there were significant differences in occupation, with the highest percentage of benzene workers (24%) and petrol workers (16%) that's agreed with results of [17] it's showed (19%) benzene workers (18%) petrol workers, As well as the study by[14] where the percentage of benzene workers with infertility was 20.4%, while petrol workers were 37.6%.study of[12] , recorded the percentage of benzene workers is (21.5%) and petrol workers (17.5%).

This study differed from a study conducted by [20] which showed that there was significant difference between the frequency of GSTP1 genotype and incidence of PAH when compared refinery oil workers and control groups It also differed from the study conducted by[10,16] which showed that there was no significant difference between the family history ,while this study showed significant between workers who has family history and GSTP1 lacking(GSTP1-) as the OR=1.625 was also different from the study conducted by[18] Which showed that there was no effect of smoking difference among smoking workers and nonsmoking (OR=0.3239) and these results disagree with our result which has been shown correlation between smokers and nonsmokers workers (OR=7.0) so as between heavy and light smokers were (OR=1.875). The main factors that make older workers higher than younger are related with several another factors such as long period exposure to PAH molecule which increased influence with ages progressive (OR=10.0) and this result agree with that [11] (Chalmers et al., 2018). Benzene is toxic environmental pollutant and an established animal and human carcinogen. The mechanism of benzene toxicity, particularly its leukemogenic effect, is not fully understood. The modified base 8-hydroxy-deoxyguanosine (8-OHdG) is a sensitive marker of the DNA damage due to hydroxyl

radical attack at the C8 of guanine. This damage, if left unrepaired, has been proposed to contribute to mutagenicity and cancer promotion. We conducted this biomonitoring study with the aim of evaluating the association between excretion of 8-OHdG and level of exposure to benzene and other aromatic compounds among occupationally exposed people...benzene lead to an adduct formed between DNA and an epoxide droved from Benzo (a) pyrene molecules an interfered with DNA replication.

Conclusion

According to these results, we can conclude that occupation chemical compounds were played important influence on the gene detoxification deletion. Risk factors such as work periods, occupation, and kind of work have been appeared differentiation relationship with the GSTP1 gene deletion, where the highest percentage was found in workers work period more than 20 years.

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