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Brief Report

Association of 8-Oxo-2'-Deoxyguanosine, *hOGG1* Ser326Cys Gene Polymorphism with Reactive Oxygen Species in Depression Patients

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Abstract

The present work was suggested to study the relation 8-Oxo-2'-deoxyguanosine (8-oxo-dG) with ROS level and *hOGG1* gene polymorphism in depression disorder patients, blood samples were collected from study groups to estimate ROS and 8-oxo-dG in addition to DNA extraction to detection *hOGG1* Ser326Cys polymorphism using SSCP technique, The results show that there was non-significant in 8-oxo-dG level (P=0.174) and significant differences (P=0.174) in ROS level in study groups, The correlation coefficient between ROS and 8-oxo-dG in shows weak positive correlation in patients group (r-0.188, P 0.426) and non-significant weak invers corelation in control group (r-0.074, P 0.719), the target sequence of hOGG gene was amplified to produced 290 pb and genotyping shows three patterns include (3,2 and single haplotype). The pattern of 3 haplotypes didn't observed in patients while appeared in high percentage of control (61.535%) in significant differences (P=0.0046), the 2 haplotypes pattern was more frequent in patient (73.68%) than control group (7.69%) in significant differences (P 0.010), the single haplotypes was recorded in low percentage in patients (26.31%) than control group (30.76%),The impact of *hOGG1* gene polymorphisms in the 8-oxo-dG and ROS levels show non-significant differences among haplotypes, the 2 haplotypes causes elevation in the 8-oxo-dG in patients while causes decrement in control group, the single haplotypes causes decreasing in the 8-oxo-dG in patients than control group and finally slightly differences were observed in ROS level among haplotypes in study groups. From present study can be concluded the 8-oxo-dG and ROS were strong related with depression and strong associated with OGG1 Ser326Cys gene polymorphism.

Keywords: ROS level • DNA damage • Disorder

Introduction

The Depression is a multifactorial disorder causes by interaction different factors such as genetics, psychological, environmental, and biological factors, the unbalanced of neurotransmitters metabolism have role in depression etiology [1,2].

The depression disorder is one of the big health problem in the world that has a lifetime prevalence of 12% [3], and it's related to the suicides that are as much as 16 per 100,000 [4].

Oxidative stress produced by unbalanced between free radicals production and antioxidant molecules, the free radicals is a by-products of oxidative phosphorylation in mitochondria which included reactive oxygen species and reactive nitrogen species [5], the free electron in free radical can be contributed in tissue damage, lipids and proteins in addition to DNA damage [6,7]. The oxidative stress become one of the important factor contributed in different disease incidence such as neuropsychiatric diseases like Depression [8], the effect of ROS in etiology of DD have been found by various mechanisms included inflammation, autoimmune processes such as tissue damage by apoptosis and neurodegeneration [9-11].

The DNA damage is caused by exposure to different molecules that lead to structural alteration in DNA strands and different mutations types; 8-oxo-dG is an oxidized derivative of de-oxy guanine in DNA exposed to oxidation molecules and its concentration used as indicators of DNA oxidation [12-16]. The hOGG is gene encodes glycosylase that recognizes and removes oxidative modified DNA bases, it regulates the excision and removal of 8-OH-dG adducts through the base excision repair pathway, the *hOGG1* (rs1052133 C>G) SNP may influence the DNA repair capacity as the mutant genotype has a reduced protein activity [17]. Belong to main role in DNA repair its enrolled in present study in addition to detect DNA damage by measured 8-oxo-dG and its relation with ROS level in DD.

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Methodology

Study design

A 20 depression disorders cases were enrolled with 25 healthy individuals in present study, samples were collected to DNA extraction and serum isolated for ROS detected.

Biomarkers: ROS and 8- Human 8-Hydroxyguanine were detected using colorimetric for ROS and ELIZA kit (E3867Hu) provided from bioassay technology Lab.

DNA extraction: The DNA extracted from whole blood using favor gene extraction kit with high concentration and purity.

Amplification conditions and target sequences; the *hOGG1* Ser326Cys was targeted in present study using the following primers F- GGTGGCCCTAAAGGACTCTC, R- AAGGTGCTTGGGGAATTTCT to amplified 295 bp [18]. Then amplification product analyzed using single strand conformation polymorphism to detection the haplotypes [19].

SSCP technique

40% of acrylamide-bis-acrylamide was used with glycerol, TBE (5X) dH2O, TEMD and ammonium-per sulfate were used to preparation gel, the samples were denatured with loading dye (formamid, xylene cyanol, bromo-phenol blue and EDTA) 1:1 V/V under 95 for 7 min the chilled in ice for 2 min before applied in gel, after samples applied in gel 100 V with 0.5X of TBE used to electrophoresis gel for 40 min, finally gel was staining by ethidum bromide and visualized under UV documentation.

Results

The results show that there was non-significant in Patients group in 8-oxo-dG level (P=0.174) and significant differences (P=0.000) in ROS (Figure 1).

The correlation coefficient between ROS and 8-oxo-dG in patients and control shows weak positive correlation in patients group (r-0.188, P 0.426) and non-significant weak invers corelation in control group (r-0.074, P 0.719) (Figure 2).

The DNA extracted from whole blood shoes in Figure 3A and the target sequence of hOGG gene was amplified to produced 290 pb (Figure 3B), the *hOGG1* genotyping was studied using haplotype by SSCP technique , the output shows three patterns include (3,2 and single haplotype (Figure 3C).

The pattern of 3 haplotypes didn't observed in patients while appeared in high percentage of control (61.535) in significant differences (P 0.0046), the 2 haplotypes pattern was more frequent in patient (73.68%) than control group (7.69%) in significant differences (P 0.010), the single haplotypes was recorded in low percentage in patients (26.31%) than control group (30.76%) (Table 1).

The impact of *hOGG1* gene polymorphisms in the 8-oxo-dG and ROS levels were investigated, there was non-significant differences among haplotypes, the 2 haplotypes causes elevation in the 8-oxo-dG in patients (31.05 ± 5.48) while causes decrement in control group (12.98 ± 0.65), the single haplotypes causes decreasing in the 8-oxo-dG in patients (15.73 ± 4.01) and control group (19.77 ± 3.59). Slightly differences were observed in ROS level among haplotypes in study groups (Table 2).

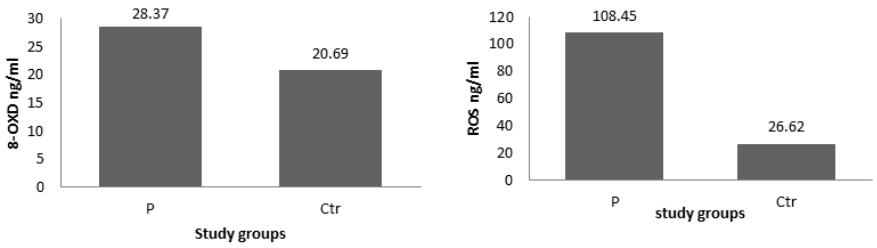

Figure 1. The 8-oxo-dG level and ROS levels in patients and control group.

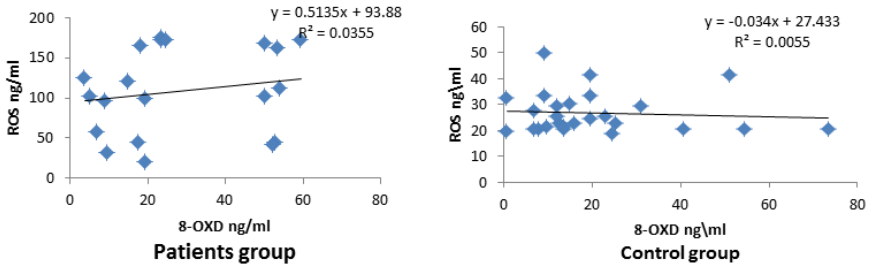

Figure 2. The correlation coefficient of 8-oxo-dG and ROS levels in patients and control group.

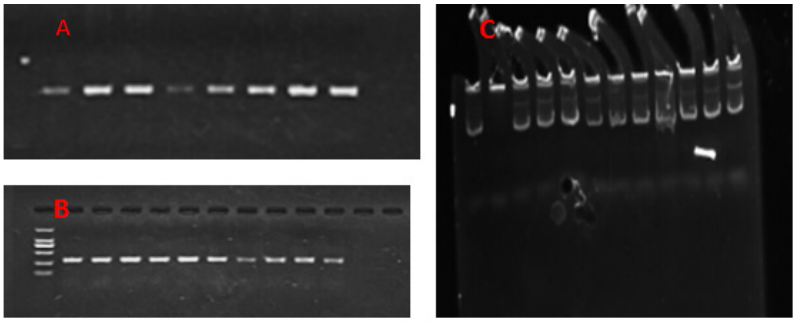

Figure 3. (A) DNA extraction from whole blood from patients and control; (B) the PCR product of *hOGG1* gene (295 bp) for patients and control groups; (C) The SSCP electrophoresis pattern of *hOGG1* gene (70 V, 0.5 TBE for 40 min).

Table 1. The haplotypes of *hOGG1* gene in patients and control group.

Haplotypes patterns	Patients (%)	Control (%)	Odd ratio	P value
3 haplotypes	0 (0%)	16(61.53%)	67.7368	Memory
3.65 - 1253.99	0.0046	Memory	Memory	Memory
2 haplotypes	14(73.68%)	2 (7.69%)	11.2000	Memory
1.75 - 71.63	0.0107	Memory	Memory	Memory
Single haplotypes	5(26.31%)	8(30.76%)		

Table 2. Impact of OGG1 gene haplotypes in the 8-oxo-dG and ROS in study groups.

Haplotypes patterns	Patients 8-oxo-dG	Patient ROS	Control 8-oxo-dG	Control ROS
3 haplotypes	0	0	21.58 ± 5.25	27.26 ± 2.23
2 haplotypes	31.05 ± 5.48	107.93 ± 14.15	12.98 ± 0.65	24.97 ± 4.57
Single haplotypes	15.73 ± 4.01	109.55 ± 30.12	19.77 ± 3.59	26.14 ± 2.37
sig	0.130	0.957	0.132	0.998

Discussion

Present study focusing on the DNA damage represented by 8-oxo-dG and it's related with ROS and *hOGG1* gene polymorphism, the results show non-significant elevation in 8-oxo-dG and significant elevation in ROS in patients group, the 8-oxo-dG is generated by DNA exposure to free radicals and this proved by ROS high level in patients, other study pointed that there was high level of 8-oxo-dG in urine of Patients with depression and proved by some studies in different samples like leukocyte serum, plasma whole and urine the increased 8-oxo-dG in DNA led to accumulation mutations that led to development other disease in depression disorders patients [14,20-22]. Furthermore other investigation suggested using 8-oxo-dG as biological markers of diagnosis, state and treatment response in bipolar disorder. The correlation in patients was weak positive relation between 8-oxo-dG and ROS while weak invers relation observed in control group; this changes in correlations clarified the association ROS and 8-oxo-dG with depression disorders patients in Iraqi population.

The *hOGG1* Ser326Cys haplotypes were studied in present study using SSCP technique, strong association between haplotypes and depression patients, the hOGG gene encodes to glycosylase that recognizes and removes oxidative modified DNA bases [23]. A study conducted by Czarny et al, found that there were association between the c.977C4G in hOGG and mental diseases with limited impact on the risk of depression disorder recurrent type occurrence, the genotype C/C at the .977C4G–*hOGG1* (rs1052133) site together with others genetics factors may significantly decrease this risk. The study concluded that there was association between depression with ROS, 8-oxo-Dg and haplotypes of hOGG gene at SNP rs1052133.

Conclusion

The current results concluded that there was a strong association between DD and ROS, but didn't lead to increment DNA damage represented by the level of 8-oxo-dg. The impact of *hOGG1* gene polymorphisms in the 8-oxo-dG and ROS levels show non-significant differences among haplotypes, the 2 haplotypes causes elevation in the 8-oxo-dG in patients while causes decrement in control group, the haplotypes of hOGG gene at SNP rs1052133 was strong association with DD and didn't affect in the level of ROS and 8-oxo-dg.

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