J Renal Inj Prev. 2018; 7(3): 121-123.

http://journalrip.com

DOI: 10.15171/jrip.2018.29

Journal of Renal Injury Prevention

Antioxidant defense system versus 8-hydroxy-2’ -deoxyguanosine; a short look to recent findings

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ARTICLE INFO

Article Type:
Epidemiology and Prevention

Article History:
Received: 18 December 2017
Accepted: 10 April 2018
Published online: 21 May 2018

Implication for health policy/practice/research/medical education:
The impact of 8-hydroxy-2’ -deoxyguanosine as an oxidative stress biomarker has been detected in many diseases, including bladder and prostate cancer, rheumatoid arthritis and renal disease.

Please cite this paper as: Rahimpour S, Hasanpour Dehkordi A. Antioxidant defense system versus 8-hydroxy-2’ -deoxyguanosine; a short look to recent findings. J Renal Inj Prev. 2018;7(3):121-123. doi: 10.15171/jrip.2018.29.

Keywords: Free radicals, 8-hydroxy-2’-deoxyguanosine, Antioxidant defense system, 8-hydroxyguanine, Oxidative stress, Antioxidant system

Epidemiology and prevention

Free radicals are atoms or molecules that are constantly circulating in the body due to the presence of single electrons damaging the macromolecules of organisms such as lipids, proteins, carbohydrates and DNA. There is a system called “antioxidant defense system” in the body to prevent damages to free radicals. Normally, there is a balance between free radicals and this system in the body of a healthy person. However, when this balance is disturbed for any reason i.e. the number of free radicals is increased or the antioxidant system is weakened, a state called oxidative stress is created being involved in the development of hundreds of diseases (1,2). Free radicals, in the DNA structure of the body cells, can oxidase purine and pyrimidine bases, produce fractures in one or two strands, create cross-bridges between DNA and proteins, and change deoxyribose (3). Free radicals are capable of exposing vital biomolecules such as DNA to an oxidative attack creating changes in the DNA structure. The most common organic DNA base being exposed to oxidative attack by the free radicals is the position 8 of guanine base. During the attack of the free radicals to the organic C8 guanine is changed into 8-hydroxy guanine (Figure 1) (4).

The use of 8-hydroxy-2’ -deoxyguanosine (8-OHdG) as an oxidative stress biomarker has been studied in many diseases, including bladder and prostate cancer (6) rheumatoid arthritis (7) and renal disease. As a result of oxidative stress, cellular damage often arises due to changes in macromolecules, such as proteins, lipids, and DNA nucleic acids. Nuclear and mitochondrial DNA are usually the site of oxidative damage. Generally, radical hydroxyl has the ability to change the normal guanine and deoxyguanosine of the nucleus or mitochondria into an abnormal state of OH-dG-8 and 8-hydroxyguanine (8-OH-Gua) or 8-hydroxy-2’-deoxyguanosine 5’-triphosphate (8-OH-dGTP) (8). Causing damage to the DNA and oxidizing the organic base, the 8-hydroxyguanine (8-OH-Gua) is released from the DNA with the help of the human 8-oxoguanine DNA N-glycosylase 1 (hOGG1) enzyme

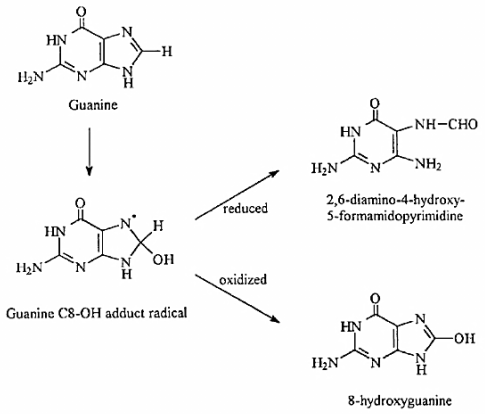

Figure 1. The products of damages of oxidative guanine through the attack of OH free radicals to C8 guanine (5).

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(8,9). However, enzymes that cause 8-OH-dG are still unknown. 8-hydroxyguanosine 5'-triphosphate (8-OH-GTP) is converted to the 8-hydroxy-2' -deoxyguanosine (8-OHdG) monophosphate via the MutT homolog 1 (MTH1) enzyme. Finally, its nucleotide form is created as 8-hydroxy-2' -deoxyguanosine (8-OHdG) (Figure 2). Additionally, 8-hydroxyguanine (8-OH-Gua) is obtained by free radical's attack on organic guanine base and DNA oxidation (Figure 3).

Form 8-hydroxy-2'-deoxyguanosine (8-OHdG) is associated with the physiological factors of individuals (age and gender), lifestyle (smoking, drinking and exercise), and diseases (cancer, diabetes and arthritis) (11). The results of the recent researches indicated the beneficial effects of regular exercise in reducing and preventing diseases associated with oxidative stress, which are due to strengthening the antioxidant system of the body in the course of regular, long-term and moderate exercise activity (12). Cigarette smoke is a powerful source of free radicals inducing oxidative stress in individuals (13).

In addition 8-hydroxy-2' -deoxyguanosine (8-OHdG) is created by apoptotic cells obtained through oxidative stress. As a result, to study the oxidative damage to DNA, we measure the quantity of 8-hydroxydeoxyguanosine (14). Various methods have developed for quantitative evaluation of urinary 8-OHdG concentrations, including gas chromatography-mass spectrometry [GC-MS], enzyme-linked immunosorbent assay (ELISA), liquid chromatography with mass spectrometry(LC-MS) (15-19). LC-MS and high performance liquid chromatography (HPLC) as the two methods are based on solid phase extraction (SPE) columns (19,20).

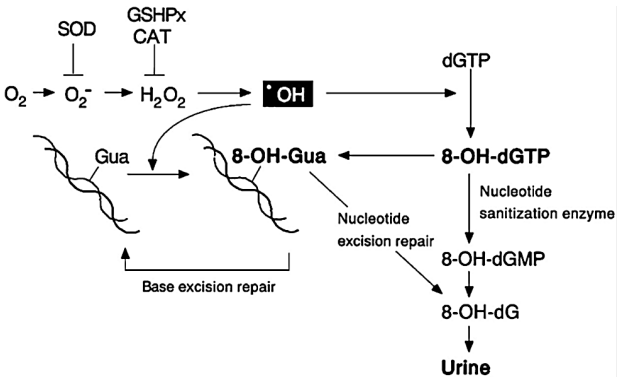

Figure 2. OhdG-8 urinary sources (10).

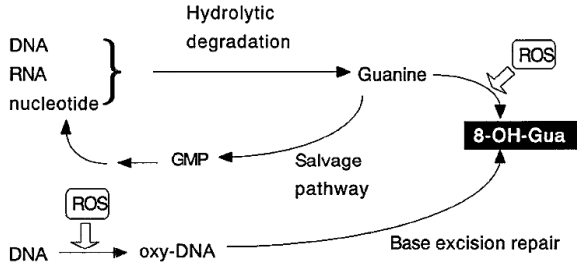

Figure 3. Urinary and serum OH-Gua-8 sources.

Authors' contribution

SR and AHD contributed equally to the study.

Conflicts of interest

The authors declare no conflict of interest.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

None.

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