http://www.cjmb.org

Open Access Short Communication

Crescent Journal of Medical and Biological Sciences
Vol. 1, No. 4, Autumn 2014, 151-153

eISSN: 2148-9696

The Importance of Oxidative Stress in Early Week Pregnancy Losses

Mustafa Bilici[1*]

Abstract

Objective: Although the etiopathogenesis of pregnancy losses has not been clearly explained yet, uterine anomalies, infections, chromosomal anomalies, thrombophilia and free radicals are among the main reasons. Pregnancy losses may also repeated in the following pregnancies. Oxidative stress occurs due to an imbalance between oxidants and free radicals and antioxidants.

Conclusion: Oxidative stress may also result in damage in trophoblastic cells where the metabolism is high, such as placenta, and play a role in the etiopathogenesis of pregnancy losses. In this review, we aim to present the role of oxidative losses in pregnancy losses with literature.

Keywords: Antioxidant, Free Radical, Oxidative Stress, Pregnancy Loss

Introduction

Oxidative stress

It is considered that oxidative stress plays a significant role in the etiopathogenesis of many diseases, such as diabetes, cancer, and cardiovascular diseases. Oxidative stress result in various diseases, including neurodegenerative diseases, Alzheimer, Parkinson, amyotrophic lateral sclerosis, inflammatory diseases, rheumatoid arthritis, cardiovascular diseases, and muscular dystrophy. Moreover, it is known that oxidative stress causes allergies, immune system disorders, dysfunctions, aging and various types of cancer. For example, inflammatory cells, inflammation, and chemical mediators generate reactive oxygen species (ROS) in the tissue and when this occurs, extremely high ROS levels cause cell damage and inflammation, especially ROS, affects relevant cell defense mechanisms negatively. It blocks the antioxidants and prevents them from performing their functions. This way it stops the detoxification (1,2).

Antioxidants stop the activities of free radicals and play significant roles as blocking agents in the process of many diseases. Many synthetic and natural antioxidants have a useful importance in human health, and it is also revealed that they play a preventive role in diseases (3). The function of antioxidants is important to prevent the formation of free radicals or break the chain. Therefore, it is suggested that the antioxidants neutralize free radicals and prevent cell damage (2,4).

Superoxide dismutase (SOD)

It is an enzyme that is generated endogenously and makes up the organism. Cellular SOD is a group of metalloenzyme with various prosthetic groups. The SOD has five different forms, 1- The most common zinc copper Cu-Zn-SOD is in the cytoplasm, 2- Mn-SOD is found in mitochondria, 3- Fe-SOD manifests itself as a special condition where SOD enzyme is used, containing Fe in anaerobic environment in Escherichia coli, Bacteroides fragilis and Propionibacterium shermanii bacteria and Mn in aerobic environment. 4- Ni-SOD is an isoenzyme that contains homotetrameric nickel defined in the *Streptomyces* griseus bacteria (5,6).

Glutathione (GSH)

It is created in the body directly from cysteine, glutamate, and glycine. As a reactant of the redox reaction, GSH is useful in the elimination of hydroxyl radicals and singlet oxygen. In addition to destroying free radicals directly, it shows enzymatic reaction with glutathione peroxidase (GPx). GSH plays a very important role in ensuring that the enzyme and

Received: 25 May 2014, **Revised:** 13 Jun 2014, **Accepted:** 18 Jul 2014, **Available online:** 15 Sep 2014

[1] Department of Chemistry, School of Science, University of Yuzuncu Yil, Van, Turkey
*Corresponding Author: Mustafa Bilici, Department of Chemistry, School of Science, University of Yuzuncu Yil, Van, Turkey
Tel: +90 432 2150470, Email: mbilici65@hotmail.com

other cellular organelles remain reduced in the cell. GSH is mostly generated in the liver. Almost 40% of the GSH is disposed through the bile. According to the studies, it is believed that this GSH in the bile helps the body defend itself against xenobiotics in the diet, prevents lipid peroxidation in the bowel lumen and protects bowel epithelium against oxygen radicals (6,7).

Catalase

Catalase is a protein that is found in peroxisomes and cytosols, and it functions in the conversion of H_2O_2 into molecular oxygen and water and catalyze this reaction. Furthermore, the catalase ensures reduction of small molecules such as methyl hydro peroxide and ethyl hydro peroxide, and does not make an impact on high molecular weight lipid hydro peroxides. It forms catalase-H_2O_2 compound as an intermediate product first in the plans to neutralize hydrogen peroxide and the enzyme decomposes creating water (H_2O) and oxygen (O_2) as a result of this reaction (6,8).

Spontaneous abortion is the abortion without any intervention before the 20th gestational week or before the fetal weight is < 500 g and fetus reaches the viability. The incidence of spontaneous abortion is 12-24% of all pregnancies (9).

According to the majority of definitions, recurrent pregnancy loss means having more than two or three pregnancy losses before the 24th gestational week. It is a multi-factorial condition and can be seed in 1-5% of patients. The reason is not known in the majority of cases. Uterine anomalies, chromosomal anomalies of the embryo, defective immunological response between fetus and mother, infections, autoimmune diseases, thrombophilia and imbalanced free radicals can be listed among the reasons for recurrent pregnancy loss (10).

Oxidative stress occurs as a result of the imbalance between pro-oxidant and antioxidant levels. This rate may happen with the reduction of antioxidant defense mechanisms or change of increased levels of ROS and/or reactive nitrogen species (11). It may cause disorders in normal redox levels of tissues, peroxides in all cellular compartments, including DNA, RNA, lipids and proteins, and toxic effects because of a generation of free radicals. Combination of oxidative damage and mitochondrial dysfunction may lead to energy depletion, accumulation of cytotoxic mediators and cell death (12). During the pregnancy, the mother experiences metabolic changes for the development of fetus and oxidative stress increases compared with the pre-pregnancy period. As a result, mitochondrial activity increase and high metabolic rate are observed. The source of this oxidative stress is placenta. The oxidative stress during the pregnancy occurs in response to the fetoplacental energy demand. Placental tissues contain antioxidant in low level and activity during the first trimester of pregnancy, and trophoblastic cells are especially sensitive to oxygen-mediated damage. In the first trimester, oxygen pressure in the intervillous space is about 20 mmHg and placental tissues contain catalase, SOD, GPx, Cu/Zn and Mn as main antioxidants in low activity. The tissue becomes vulnerable to oxidative stress due to low concentrations in syncytiotrophoblasts. Placental function and fetal growth depend on the use of oxygen and restriction of generation of ROS. Abnormal fetal growth and modified placental remodeling occur because of over-generation of ROS (13).

Placenta is the immunoprotective tissue that ensures the exchange of nutrient, oxygen and hormone between mother and fetus. Oxidative stress can be found in many organs with high oxygen metabolism, such as placenta. It is believed that oxidative stress may exist in the main mechanism in the pathogenesis of diseases such as spontaneous abortion and eclampsia. The damage induced by oxidative stress and the ROS could be important as missing pieces of the puzzle in recurrent pregnancy loss with unknown damage etiology and abortions with a known reason (14).

In a study where Yigenoglu et al. research the level of oxidative stress in pregnant women in first trimester with a history of recurrent pregnancy loss and healthy pregnant women in the same trimester, they established that the values of total oxidant level and oxidative stress index are higher, while total antioxidant capacity is lower in the patient group (15). Some studies suggest that low antioxidant level increases the risk of spontaneous abortion (16,17). In their study, Zhu et al. compare ROS, SOD and hypoxia-inducible factor-1 alpha (HIF-1α) levels in trophoblastic tissues between the cases with patients having missed abortion in the first trimester and cases with control group having abortion in the same trimester. It is established that the ROS level is higher in the patient group compared to the control group while SOD enzyme activity and HIF-1α level are lower in the patient group compared to the control group. As a result of this study, they suggest three factors in the pathogenesis of missed abortion. First, the ROS can cause the lipid peroxidation injury in the embryo. Second, increasing ROS levels can change oxygen partial pressure in embryonic cells. Third, increased generation of ROS can lead to a vicious circle of ischemia-reperfusion injury in the embryo and thus to incomplete growth. In conclusion, they argue that ROS, SOD and HIF-1α levels could be important in missed abortion (18). It is suggested that the use of N-acetylcysteine, an antioxidant, can prevent pregnancy loss in cases with recurrent pregnancy loss (19).

Conclusion

Oxidants and free radicals that emerge during metabolic reactions in the cell physiology are brought under control by antioxidants and no cell injury occurs. During the pregnancy, placenta, which plays a key role in the growth and development of

the fetus, must have a high metabolism. When there is an imbalance between oxidants and free radicals and antioxidant level, oxidative stress occurs, and this causes injury in trophoblastic tissues. In cases where it is impossible to control such injury, pregnancy losses can occur.

Ethical issues

We have no ethical issues to declare.

Conflict of interests

We declare that we have no conflict of interests.

Acknowledgments

The author would like to thank the School of Science, University of Yuzuncu Yil, Turkey, for their support of this study.

References

1. Hybertson BM, Gao B, Bose SK, McCord JM. Oxidative stress in health and disease: the therapeutic potential of Nrf2 activation. Mol Aspects Med 2011; 32: 234-46.
2. Bilici WM, Cim N, Width HD. Pre and post-operative oxidative stress level in cases with ovarian neoplasia Width1Width1Mustafa Bilici1, Numan Cim2, Halit Demir Width1. Medical Science and Discovery 2014; 1: 215-117.
3. Bagchi D, Bagchi M, Stohs SJ, Das DK, Ray SD, Kuszynski CA, et al. Free radicals and grape seed proanthocyanidin extract: importance in human health and disease prevention. Toxicology 2000; 148: 187-97.
4. Gokpynar S, Koray T, Akcicek E, Goksan T, Durmaz Y. Algal Antioksidanlar . Aqua Culture Journal 2006; 1: 85-9.
5. Baskin S, Salem H. Oxidants, Antioxidants and Free Radicals. New York, NY: CRC Press, 1997.
6. Çaylak E. Hayvan ve bitkilerde oksidatif stres ile antioksidanlar. Týp Aratýrmalarý Dergisi: 2011; 9: 73-83.
7. Maher P, Lewerenz J, Lozano C, Torres JL. A novel approach to enhancing cellular glutathione levels. J Neurochem 2008; 107: 690-700.
8. Gechev T, Willekens H, Van MM, Inze D, Van CW, Toneva V, et al. Different responses of tobacco antioxidant enzymes to light and chilling stress. J Plant Physiol 2003; 160: 509-15.
9. Jurkovic D, Overton C, Bender-Atik R. Diagnosis and management of first trimester miscarriage. BMJ 2013; 346: f3676.
10. Vaiman D. Genetic regulation of recurrent spontaneous abortion in humans. Biomed J 2014.
11. Agarwal A, Aponte-Mellado A, Premkumar BJ, Shaman A, Gupta S. The effects of oxidative stress on female reproduction: a review. Reprod Biol Endocrinol 2012; 10: 49.
12. Rudov A, Balduini W, Carloni S, Perrone S, Buonocore G, Albertini MC. Involvement of miRNAs in placental alterations mediated by oxidative stress. Oxid Med Cell Longev 2014; 2014: 103068.
13. Marseglia L, D'Angelo G, Manti S, Arrigo T, Barberi I, Reiter RJ, et al. Oxidative stress-mediated aging during the fetal and perinatal periods. Oxid Med Cell Longev 2014; 2014: 358375.
14. Ishii T, Miyazawa M, Takanashi Y, Tanigawa M, Yasuda K, Onouchi H, et al. Genetically induced oxidative stress in mice causes thrombocytosis, splenomegaly and placental angiodysplasia that leads to recurrent abortion. Redox Biol 2014; 2: 679-85.
15. Yigenoglu Ö, Ugur MG, Balat Ö, Erel Ö. The Role of Oxidative Stress in Recurrent Pregnancy Loss. Inönü Üniversitesi Tip Fakültesi Dergisi 2011; 18: 236-9.
16. Barrington JW, Lindsay P, James D, Smith S, Roberts A. Selenium deficiency and miscarriage: a possible link? Br J Obstet Gynaecol 1996; 103: 130-2.
17. Vural P, Akgul C, Yildirim A, Canbaz M. Antioxidant defence in recurrent abortion. Clin Chim Acta 2000; 295: 169-77.
18. Zhu LJ, Chen YP, Chen BJ, Mei XH. Changes in reactive oxygen species, superoxide dismutase, and hypoxia-inducible factor-1alpha levels in missed abortion. Int J Clin Exp Med 2014; 7: 2179-84.
19. Amin AF, Shaaban OM, Bediawy MA. N-acetyl cysteine for treatment of recurrent unexplained pregnancy loss. Reprod Biomed Online 2008; 17: 722-6.

Citation: Bilici M. **The Importance of Oxidative Stress in Early Week Pregnancy Losses**. Crescent J Med & Biol Sci 2014; 1(4): 151-3.