Review Article

The Balance between Pro-oxidants and Antioxidants in Cardiac Anesthesia: a Review

Seyed Mohammad Seyed-Alshohadaei[1*]

1. Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract

Due to the development of surgical techniques for controlling the conditions of patients, we are still faced with many conditions and risks in the management of patients' health during and after surgery. Hence, the creation of new methods, access to medicines and things that increase the quality of management and improve patient control conditions are on the agenda of many research teams around the world. Antioxidant substances and their effects on the control of free radicals (as one of the destructive factors on the health of patients undergoing surgery) is one of the research cases that has attracted many researchers in recent years. Cardiac surgery and cardiac anesthesia are among the most challenging types of surgeries. Control and management of patient conditions during this type of surgery is one of the most important challenges of anesthesiology team. This study tries to investigate the importance of antioxidants in controlling conditions and improving the status of patients undergoing cardiac surgery.

Keywords: Antioxidant; Pro-oxidant; Cardiac Anesthesia; Inflammation; Pain

Please cite this article as: Seyed-Alshohadaei SM. The Balance between Pro-oxidants and Antioxidants in Cardiac Anesthesia: a Review. J Cell Mol Anesth. 2018;3(3):122-5.

Corresponding Author:
Seyed Mohammad Seyed-Alshohadaei, MD, Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Tel: (+98) 21 22432572
E-mail: dr.seyed.seyed@gmail.com

Introduction

Oxidative stress is one of the risk factors for humans. These factors in various organs of the body cause numerous and various injuries, including: asthma in the lung, glomerulonephritis in the kidneys, atherosclerosis in the cardiovascular system, preeclampsia in the fetus, Alzheimer's disease in brain, cataract in the eyes, and even with the application of a multi organ mechanism can cause cancer, diabetes or inflammation. (1)

The source of oxidative stress should be in the balance between oxidative factors (free radicals) and antioxidants. (2)

In this situation, the body's redox system has changed and the consequences of this imbalance appear as stated. Antioxidants as the other pole of this balance are substances that act to protect cells against the harmful effects of free radicals and neutralize them. Antioxidants act their corrective effects in two ways, breaking the cycle or preventing it. In the form of breaking the cycle, when the radical freedom of a single electron is stealing, another free radical is produced, and the cycle continues until it is broken down by an antioxidant, including the antioxidants that act in this way like vitamin E or vitamin C. In the form of prevention, the production of oxidants is prevented by antioxidants, thus reducing the start of cycles. Glutathione peroxidase is an example of antioxidants that act as a preventive method (1)

Pain is considered as a consequence of all surgeries. The cardiovascular surgery as one of the most dangerous types of surgeries is no exception. Control of pain after cardiovascular surgery has a very important role in the success of these types of surgeries, and poor control of postoperative pain have serious complications for patients (3). On the other hand, pain itself causes the oxidative stress in the body (4), while the use of antioxidants in heart surgery has been accompanied by a reduction in oxidative reactions (5). The cardiovascular system is affected by the balance between oxidative stress and antioxidant substances. Therefore, it seems that the control of pain and oxidative damage separately or together can play a significant role in the success and control of the outcome of cardiac surgery.

Pain and oxidants effect:

Pain as an indicator can be a sign of various illnesses. The mechanism of production and the quality of pain vary in each disease; however, the effect of oxidants on pain has been studied and confirmed in several studies. This effect can be achieved by reducing inflammation, reducing the negative effect on nociceptors, cofactors of opioids production or protecting mitochondria (4, 6, 7, 8, and 9). Several studies have shown different results in antioxidant activity for pain relief; however, it is important to control the pain. For example, vitamin C and vitamin E antioxidants in women with pelvic pain and the history of endometriosis have decreased Pain and inflammatory factors in patient's abdominal fluids. Thus, the role of antioxidants in the treatment of these patients is significant (7). Another study has shown that the use of alpha-lipoic acid (as a natural antioxidant) has been effective in reducing peripheral neuropathic pain (10). Combination therapy of antioxidants has also been helpful in treating and relieving pain in patients. For example, the combination of selenium antioxidants, beta-carotene, vitamin C, vitamin E, and methionine shows these results in various studies (4). Melatonin and N-acetylcysteine have similar effects in protecting against oxidative damages and inflammatory markers in cardiac surgery (6).

The combination of antioxidants and analgesics will normalize oxidative stresses. As a result, the use of antioxidants in the treatment of pain can be used to reduce the dose of analgesics and reduce the negative effect of activated oxygen on nociceptors (11). In this case, vitamin C can be mentioned as a cofactor for the production of amide opioids, which high dose administration can reduce the need for opioids in surgery and cancer patients. (8). In another study, an antioxidant effect by Mito Tempo was investigated in neuropathic pain, in which antioxidant activity was assessed with malondialdehyde and reduced glutathione content and overall activity of serum superoxide dismutase in serum and spinal cord. Finally, the results show that antioxidants with mitochondrial effects have reduced neuropathic pain by protecting mitochondria from oxidative damage (9).

Effect of oxidants on CABG surgery:

The inverse relationship between the magnitude of oxidative stress and cardiac performance can be indicative of the effect of oxidative stress. Although this effect has not been seen in patients undergoing cardiac valve surgery, the magnitude of these stresses can be predictive of cardiac function in CABG (12, 13).

Hemodialysis, ischemia and perfusion injuries activate neutrophils during heart surgery and cause stress and activate inflammatory, pre-inflammatory and pre-apoptotic factors. This stress affects various organs in the body. Free radicals are molecules lacking free electrons, which makes them very active. Redox signals are activated in response to changes in the level of ROS (reactive oxygen species), mitochondria and during the cardio pulmonary pump. Blood transfusion from the non-endothelialized cycle is the main source of ROS production during cardiac surgery. The activation of neutrophils in the pulmonary pump is shown by the decrease in L-selectin and the increase of CD11b and CD18. Low level of trisphosphate in damaged area is due to ischemic injury mediated by hypoxanthine. After a period of ischemic injury, reperfusion plays a major role in oxidative stress by initiating a series of events. The pulmonary pump causes mechanical damage to red blood cells, which causes blood cell sensitivity to the membrane complex and, by causing hemoglobin leakage, results in the production of peroxidase. On the other hand, during transfusion, we will encounter oxidative stress. Acute pulmonary and renal damage, two common complications during cardiac surgery, is caused by oxidative damage. The hydroxyl phenol present in propofol is similar to vitamin E. L-arginine plays a role in the immune function and vascular hemostasis, and is a precursor of nitric oxide. Therefore, the addition of L-arginine to the cardioplegia solution decreases myocardial damage and decreases the damage as a result of the activity of superoxide dismutase. The alpha necrosis factor decreases with N-acetylcysteine "administration. Adding N-acetylcysteine" to the cardioplegia solution decreases MDA (Malondialdehyde), glutathione catalase, SOD (Superoxide dismutase), glutathione peroxidase, and glutathione reductase. Mitoquinone mesylate (MitoQ) is an antioxidant by targeting ROS, which is immediately captured by mitochondria and detoxifies ROS (14, 15).

In children, due to the immature heart cells and heart congenital problems, there is more vulnerability to oxidative factors, which leads to poor functioning of heart. Interventions such as glucocorticoids, bypass circuit miniaturization, prime-pump strategies and cardioplegia can reduce the oxidative stress in children's heart surgery (16).

Alpha-lipoic causes the production of other antioxidants, such as glutathione, provided by the block of NRF2 and increase in translation of the enzyme glutathione synthase (17). Glutathione antioxidant systems can stimulate oxidative stress in mitochondria and cause cell toxicity (18). Moreover, intracellular antioxidant systems, such as glutathione and NADPH, can produce ROS (19).

In the cardiovascular system, the antioxidant has a paradoxical ability to simulate oxidative stress (20). The imbalance and increase in the overall serum oxidative state in open-heart surgery can be related to the time of aortic clamp (21). In oxidative stresses in coronary heart disease, antioxidants such as superoxide dismutase 1 and 2, can be measured as biochemical markers for these stresses (22), a new, automated, cheap and easy method is available now to measure the total level of antioxidants versus free radicals (23). The metabolic syndrome is linked to activated protein C, the serum levels of uric acid and the balance of pro oxidants and antioxidants (24).

Conclusion

Control of pain and oxidation factors play an important role in the success of cardiovascular surgery. Pain can cause oxidative damage and also exacerbate the damaging effects of the oxidation of the agent caused by the use of heart pumps, transfusion and other destructive factors. In children, due to their vulnerability, these risks are more severe and the control of these factors seems more necessary. The use of antioxidant agents during cardiac surgery has reduced oxidative damage and decreased pain in patients. However, the use of these agents sometimes paradoxically provokes oxidative stimulation in mitochondria and cellular toxicity, which can be due to the imbalance of the cell oxidant and cell antioxidant factors, which made it vital to measure the balance of oxidant and antioxidant agents.

Future Prospective:

Assessment of the oxidative stress level and antioxidants during coronary heart disease surgeries by measuring stress biomarkers or free radical staining can be useful tool for assessing how antioxidant agents are used preoperatively, during operation and in the post-operative period. Assessing the balance and imbalance of oxidants and antioxidant factors on the course of the diseases by point of care diagnostic systems can determine how to use these vital substances properly.

Acknowledgment

The kind help and assistance received from Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran for this study is highly appreciated.

Conflicts of Interest

The author declares that there is no conflict of interest.

References

1. Pham-Huy LA, He H, Pham-Huy C. Free radicals, antioxidants in disease and health. Int J Biomed Sci. 2008; 4(2): 89–96.
2. Sies H. Oxidative stress: oxidants and antioxidants. Exp Physiol. 1997;82(2):291-5.

3. Zubrzycki M, Liebold A, Skrabal C, Reinelt H, Ziegler M, Perdas E, Zubrzycka M. Assessment and pathophysiology of pain in cardiac surgery. J Pain Res. 2018; 11: 1599–611.

4. Cai GH, Huang J, Zhao Y, Chen J, Wu HH, Dong YL, Smith HS, Li YQ, Wang W, Wu SX. Antioxidant therapy for pain relief in patients with chronic pancreatitis: systematic review and meta-analysis. Pain Physician. 2013;16(6):521-32.

5. Stanger O, Aigner I, Schimetta W, Wonisch W. Antioxidant supplementation attenuates oxidative stress in patients undergoing coronary artery bypass graft surgery. Tohoku J Exp Med. 2014;232(2):145-54.

6. Zakkar M, Guida G, Suleiman M, Angelini GD. Cardiopulmonary bypass and oxidative stress. Oxid Med Cell Longev. 2015;2015:189863.

7. Santanam N, Kavtaradze N, Murphy A, Dominguez C, Parthasarathy S. Antioxidant supplementation reduces endometriosis-related pelvic pain in humans. Transl Res. 2013;161(3):189-95.

8. Carr AC, McCall C. The role of vitamin C in the treatment of pain: new insights. J Transl Med. 2017;15(1):77.

9. Zhan L, Li R, Sun Y, Dou M, Yang W, He S, Zhang Y. Effect of mito-TEMPO, a mitochondria-targeted antioxidant, in rats with neuropathic pain. Neuroreport. 2018;29(15):1275-81.

10. Maglione E, Marrese C, Migliaro E, et al. Increasing bioavailability of (R)-alpha-lipoic acid to boost antioxidant activity in the treatment of neuropathic pain. Acta Biomed. 2015;86(3):226-33.

11. Rokyta R, Holecek V, Pekárková I, et al. Free radicals after painful stimulation are influenced by antioxidants and analgesics. Neuro Endocrinol Lett. 2003;24(5):304-9.

12. Rahsepar AA, Mirzaee A, Moodi F, Moohebati M, Tavallaie S, Khorashadizadeh F, Mottahedi B, Esfehanizadeh J, Azari A, Sajjadian M, Khojasteh R, Paydar R, Mousavi S, Amini M, Ghayour-Mobarhan M, Ferns GA. Prooxidant-antioxidant balance and cardiac function in patients with cardiovascular disease following cardiac surgery. J Heart Valve Dis. 2013;22(3):408-17.

13. Baikoussis NG, Papakonstantinou NA, Verra C, Kakouris G, Chounti M, Hountis P, Dedeilias P, Argiriou M. Mechanisms of oxidative stress and myocardial protection during open-heart surgery. Ann Card Anaesth. 2015;18(4):555-64.

14. Fudulu DP, Gibbison B, Upton T, Stoica SC, Caputo M, Lightman S, Angelini GD. Corticosteroids in Pediatric Heart Surgery: Myth or Reality. Front Pediatr. 2018;6:112.

15. Moris D, Spartalis M, Tzatzaki E, Spartalis E, Karachaliou GS, Triantafyllis AS, Karaolanis GI, Tsilimigras DI, Theocharis S. The role of reactive oxygen species in myocardial redox signaling and regulation. Ann Transl Med. 2017;5(16):324.

16. Fudulu D, Angelini G. Oxidative stress after surgery on the immature heart. Oxid Med Cell Longev. 2016;2016:1971452.

17. Zhang J, Zhou X, Wu W, Wang J, Xie H, Wu Z. Regeneration of glutathione by α-lipoic acid via Nrf2/ARE signaling pathway alleviates cadmium-induced HepG2 cell toxicity. Environ Toxicol Pharmacol. 2017;51:30-7.

18. Zhang H, Limphong P, Pieper J, Liu Q, Rodesch CK, Christians E, Benjamin IJ. Glutathione-dependent reductive stress triggers mitochondrial oxidation and cytotoxicity. The FASEB J. 2012;26(4):1442-51.

19. Korge P, Calmettes G, Weiss JN. Increased reactive oxygen species production during reductive stress: the roles of mitochondrial glutathione and thioredoxin reductases. Biochim Biophys Acta. 2015;1847(6-7):514-25.

20. Handy DE, Loscalzo J. Responses to reductive stress in the cardiovascular system. Free Radic Biol Med. 2017 Aug;109:114-24.

21. Mentese U, Dogan OV, Turan I, Usta S, Dogan E, Mentese SO, Demir S, Ozer T, Aykan AC, Alver A. Oxidant-antioxidant balance during on-pump coronary artery bypass grafting. ScientificWorldJournal. 2014;2014:263058.

22. Peng JR, Lu TT, Chang HT, Ge X, Huang B, Li WM. Elevated levels of plasma superoxide dismutases 1 and 2 in patients with coronary artery disease. Biomed Res Int. 2016;2016:3708905.

23. Erel O. A novel automated method to measure total antioxidant response against potent free radical reactions. Cl Clin Biochem. 2004;37(2):112-9.

24. Ahmadnezhad M, Arefhosseini SR, Parizadeh MR, Tavallaie S, Tayefi M, Darroudi S, Ghazizadeh H, Moohebati M, Ebrahimi M, Heidari-Bakavoli A, Azarpajouh MR, Ferns GA, Mogharebzadeh V, Ghayour-Mobarhan M. Association between serum uric acid, highly sensitive C-reactive protein and pro-oxidant-antioxidant balance in patients with metabolic syndrome. Biofactors. 2018;44(3):263-71.