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Oxidative Stress and Anesthesia in Diabetic Patients

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ABSTRACT

Free radical and peroxide production lead to intracellular damage. On the other hand, free radicals are used by the human immune system to defend against pathogens. The aging process could be limited by oxidative stress in the short term. Chronic diseases like Diabetes Mellitus (DM) are full-stress conditions in which remarkable metabolic functional destructions might happen. There is strong evidence regarding antioxidant impairment in diabetes. Performing a particular method for anesthesia in diabetic patients might prevent or modify excessive free radical formation and oxidative stress. It seems that prescribing antioxidant drugs could promote wound healing in diabetics.

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Introduction

When the body's biologic system cannot detoxify reactive oxygen species and remodel its subsequent harm, oxidative stress occurs (1). Free radical and peroxide production lead to intracellular damage. On the other hand free radicals are used by the human immune system to defend against pathogens. The aging process could be limited by oxidative stress in the short term (2). Free radical formation is a part of the cellular physiologic process. An increased rate of free radical production leads to lipid peroxidation. In a normal healthy situation, these formations are controlled by various antioxidant mechanisms including enzymatic and non-enzymatic defensive responses. Oxidative stress is the underlying cause or exacerbating factor of various diseases such as cancer, vitiligo, Alzheimer's, myocardial infarction, etc (3). Chronic diseases like Diabetes Mellitus (DM) are full-stress conditions in which remarkable metabolic functional destructions might happen. There is strong evidence about antioxidant impairment in diabetes. This oxidative stress might be the cause of developing microvascular and macrovascular complications in diabetic patients.

Several studies proved the role of free radical imbalance in insulin dependent diabetes. From different reports, it was resulted that in non-insulin dependent diabetes production of lipid peroxides increases and activation of preventive enzymes limits (4).

Hyperglycemia in DM is the main cause of Reactive Oxygen Species (ROS) production.

ROS transformation to hydroxyl radical, a high potent free radical, could cause damage in DNA, cellular membrane and proteins, and lipid peroxidation.

Various studies revealed that glutathione serum levels were reduced in diabetes (3): uncontrolled diabetes modulated cytokines or chemokines serum levels. For instance IL-1β and IL-8 levels might be reduced in diabetic patients instead of different infections. Agents could react and reduce ROS, decrease hyperglycemia severity and its damages, and inhibit P-53 activation.

A delayed wound healing process is common in diabetic patients and is a crucial issue in DM treatment as it leads to limb amputation in many cases. Impaired wound healing in DM is a result of oxidative stress, inflammatory response, and peripheral neuropathy. On the other hand, making an incision or limb amputation leads to free radical formation which has a great impact on neutrophil infiltration and endothelial dysfunction and accelerates membrane lipid and plasma lipoprotein peroxidation with inhibiting mitochondrial respiratory chain enzymes (5). Anesthetic drugs might have a considerable effect on the patient's oxidative stress during surgical management of diabetic wounds.

Discussion

2-5% of human daily oxygen consumption is transformed to ROS (2). Theses radicals are more

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highly activated than molecular oxygen. Inhalation anesthetic drugs increases free radical formation, particularly in cardiac cells. From different studies it was concluded that General Anesthesia (GA) might lead to neuroapoptosis by acute up regulating ROS and impaired mitochondrial morphogenesis (6). On the other hand, EPO production in brain depends on oxygen pressure, and EPO is an important neuroprotective factor in traumatic, hypoxic, or ischemic events. GA might suppress EPO production (7). Superoxide Dismutase (SOD), Glutathione Peroxidase (GPx) and Catalase (CAT) are the main biologic enzymes that counterbalance ROS effects.

Oxidative stress has a multifactorial base; GA induced hemodynamic changes and increased levels of cytokine in macrophages located in alveolus in inhaled volatile anesthetic agents' usage might be the two main mechanisms of free radical production and oxidative stress. Hyperglycemia could increase intracellular glucose levels and act as a trigger for ROS formation.

ROS activates insulin linked pathways which are stress sensitive. Nuclear factor-B activation leads to inflammatory and immune response and has an initial role in the induction of insulin resistant phenomenon.

These active pathways link to β -cell dysfunction and vascular complications in diabetic patients.

Mitochondria are the main intracellular organelle that could be affected by anesthesia and lead to oxidative metabolism impairment (6). Table-1 shows the effect of different anesthetic agents on oxidative stress.

Table1: different anesthetic agents and oxidative stress

Author	Title	Publication year	Anesthesia method	Outcome
Lee (8)	Effect of propofol on oxidative stress status in erythrocytes from dogs under general anesthesia	2012	Propofol and general anesthesia	Antioxidant effects in dogs
Kalimeris (9)	Cognitive function and oxidative stress after carotid endarterectomy: comparison of propofol to sevoflurane anesthesia	2013	Propofol vs sevoflurane	Antioxidant effects of propofol
Kulacoglu (5)	Prospective comparison of local, spinal, and general types of anesthesia regarding oxidative stress following Lichtenstein hernia repair.	2007	Local, spinal, and general types of anaesthesia	Local and spinal anaesthesia methods can be accepted
Özkan (3)	Propofol sedation in total knee replacement: effects on oxidative stress and ischemia-reperfusion damage.	2013	Propofol infusion	Propofol infusion may reduce oxidative damage

It was revealed from different studies that propofol has a protective effect in oxidative damage. Budic demonstrated that regional or local anesthetic drugs and propofol infusion reduced lipid peroxidation in children's lower limb surgeries (10).

In Bravo-Cuéllar's study, the CRP level was significantly lower in patients who underwent GA compared to regional anesthesia, and free radicals and oxidative agents had a higher serum concentration.

Inflammatory factor levels and oxidative product concentration could predict the chance of complications after anesthesia. For example, increased interleukin-6 level after surgery might enhance the postoperative delirium (11).

The risk of these kinds of complications should be evaluated in patients with chronic diseases like diabetes mellitus who need surgery and anesthesia, and they must be closely observed after procedures. It has been shown that propofol-induced anesthesia had no antioxidant ability, and its bolus infusion might have an antioxidant effect. Poor recovery after anesthesia might deteriorate oxidative stress and predict postoperative mortality. Different studies illustrated the role of oxygen toxicity, adults' respiratory distress syndrome, and halothane in free radical injuries in patients who underwent surgery with GA. Ketamine or propofol sedation could reduce lipid peroxidation in surgeries (12, 13).

Conclusion

Performing a particular method for anesthesia in diabetic patients might prevent or modify excessive free radical formation and oxidative stress. It seems that prescribing antioxidant drugs could promote wound healing in diabetics.

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