

## Role of Ozone in Surgical Complication of Diabetic Patients

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### **Abstract:**

**Background:** Diabetes Mellitus (DM) is a metabolic disorder, caused by impaired carbohydrate metabolism makes many changes in the blood vessels affecting the response of endothelium and the smooth muscles. Polyol pathway activation, protein non-enzymatic glycosylation and increased ROSs(reactive oxidative species) play an important role in the complications of diabetes.Ozone activates glucose metabolism that results in increasing content of 2,3diphosphoglycerate in erythrocytes which provides better oxygen supply into the tissues. Patients with diabetes mellitus have the so called glycosylated hemoglobin forming very strong bonds with oxygen, thus, inducing hypoxia and determining the severity of the disease. That is why hypoxia control with the help of ozone therapy is of the key importance in the course of treatment.

**Conclusion:** Ozone therapy appears to be an effective method for DM treatment. The reason is in ozone mechanisms when it can perform a number of processes, which provide its positive effect.

**Keywords:** Ozone, Diabetes Mellitus,Surgical Complications.

### **Introduction:**

Diabetes Mellitus (DM) is a metabolic disorder, caused by impaired carbohydrate metabolism, improper insulin production, or consumptions which lead to glycosuria and hyperglycemia. (Izadi et al., 2016).Long-term complications are characterized by microvascular diseases caused by the thickening of the capillary basement membrane, microvascular disease with an increased risk of arteriosclerosis, neuropathy, and neuromuscular dysfunction with muscular dystrophy and reduced immune system response to infections and chronic disorders of the kidneys, eyes, nerves, heart and blood vessels, Increase risk of atherosclerosis is one of the leading cause of the deaths from diabetes, 75% of these death associated with coronary artery diseases. Neuropathy is often accompanied by distal numbness and development of neurotrophic ulcers especially at the soles of the feet. (Bocci et al., 2005)These changes, along with capillary and microvascular complications are the characteristics that may lead to gangrene following a leg injury

(Heng et al., 2007).Ozone is normally present as a gas made of three atoms of

Oxygen with a cyclic structure. The medical generator of ozone produces it from pure oxygen passing through a high voltage gradient (5–13 mV) according to the reaction: $3\text{O}_2 \rightarrow 2\text{O}_3$ Ozone is 1.6-fold denser and 10-fold more soluble in water (49.0 mL in 100 mL water at 0°C) than oxygen. Although ozone is not a radical molecule, it is the third most potent oxidant after fluorine and persulfate. (Okada et al ., 2003).

### **Diabetes mellitus:**

Diabetes makes many changes in the blood vessels affecting the response of endothelium and the smooth muscles.(Martinez et al ., 2005)Vascular endothelium seems to be a sensitive target for hyperglycemia induced metabolic changes.(Al-Dalain et al ., 2001). Polyol pathway activation, protein non-enzymatic glycosylation and increased ROSs (reactive oxidative species) play an important role in the complications of diabetes (Kitabchi et al .,2009). Ozone was used as a therapeutic agent, and its beneficial effects were

observed. However, only a few biochemical and pharmacokinetic mechanisms are described so far.

Oxidative stress is suggested to have an important role in the development of complications in diabetes. Because ozone therapy can activate the antioxidant system, influencing the level of glycemia and some markers of endothelial cell damage, These results show that medical ozone treatment could be an alternative therapy. in the treatmentof diabetes and its complication. (**Chiang et al ., 2014**).

### **Ozone:**

Ozone therapy proved to be effective in the treatmentof complicated forms of diabetes mellitus.In patients with diabetic foot syndrome ozone therapy, combined with topical treatment of purulent necrotic focus and with total metabolic effect, allowed to half-shorten the period for wound detersion from pyo-necrotic mass and development of regenerative processes, to lessen the number of limb amputations and offatal outcomes, to decrease invalidism(**H Urban et al .,2009**).Ozone can be effective though oxidative preconditioning, stimulation of endogenous antioxidant systems and obstruction of xanthine oxidase pathways for ROS production, as shown in the examinations from the damage induced by Carbon Tetrachloride (CCl<sub>4</sub>) or renal and hepatic ischemia re-flow In addition, it has been shown that oxidativepreconditioning of ozone maintains the glycogen content and reduces the formation of lactate and uric acid through controlling the oxidative stress induced by CCl<sub>4</sub> consumption in rat. (**Martinez et al., 2005**) It has also been shown that intravenous ozone therapy in patients with myocardial infarction has a beneficial effect on blood lipid metabolism by reducing the blood cholesterol. Ozone therapy improved glycemic control, increased the aldose reductase, fructoselysine content, advanced oxidation protein products in the whole pancreas, and prevented the oxidative damage. In addition, the antioxidant properties of ozone inhibited the B cell function and reduced hyperglycemia. Overall, these results show

that this approach may represent a potential supplement for the treatment of diabetes and its complications.(**Al-Dalainet al., 2001**).

### **Surgical complication of diabetes**

The complicationsofdiabetes mellitus are far less common and less severe in people who have well-controlled blood sugar levels. Acute complications include hypoglycemia and hyperglycemia, dia betic coma and nonketotic hyperosmolar coma (**Korhonenet al ., 2006**)

Chronic complications occur due to a mix of microangiopathy , macrovascular disease and immune dysfunction in the form of autoimmune disease or poor immune response, most of which are difficult to manage. (**Jia et al .,2006**)

Microangiopathy can affect all vital organs, kidneys, heart and brain, as well as eyes, nerves, lungs and locally gums and feet. Macrovascular problems can lead to cardiovascular disease including erectile dysfunction.

### **Conclusion:**

Ozone therapy appears tobe aneffective method forDM treatment. The reason is in ozone mechanisms when it can performanumber of processes, which provide its positive effect.

First, ozone improves the penetration of cellular membranes for glucose. It is achieved by stimulating pentose-phosphate pathway and aerobic glycolysis thatin caseofDM are inhibited. It

promoteshyperglycemiadecreasedueto bettertransportofglucoseintotissues.

Ozone activates glucose metabolism that results in increasing content of 2,3diphosphoglycerate in erythrocytes which provides better oxygensupply into the tissues. Patients with diabetes mellitus have the so called glycosylated hemoglobin forming very strong bonds with oxygen, thus, inducing hypoxia and determining the severity of the disease. That is why hypoxia

control with the help of ozone therapy is of the keyimportance in the course of treatment.

**Reference:**

**Al-Dalain M, Martinez G, Candelario-Jalil E. (2001).** Ozone treatment reduces markers of oxidative and endothelial damage in an experimental diabetes model in rats. *Pharmacol Res*, 396-391:(5) 44.

**Bocci V, Aldinucci C, Bianchi L.(2005).** The use of hydrogen peroxide asa medical drug. *Riv Ital Ossigeno Ozonoterapia*, 4:30–39.

**Causes of Diabetes (2014).** National Institute of Diabetes and Digestive and Kidney Diseases. Archived from the original on 2016. Retrieved 2016.

**Chiang JL, Kirkman MS, Laffel LMB. (2014).** Type 1 Diabetes Through the Life Span: A Position Statement of the American Diabetes Association. *Diabetes Care*, 37 (7): 2034– 54.

**H Urban RJ .(2009).** Management of blood glucose in type 2 diabetes mellitus. *American Family Physician*, 79 (1): 29–36.

**Heng S, Yeung KL, Djafer M. (2007).** A novel membrane reactor for ozone water treatment. *J Membr Sci*, 289:67–75.

**Huijberts MS, Schaper NC, Schalkwijk CG.(2008).** Advanced glycation end products and diabetic foot disease. *Diabetes Metabolism Research and Reviews*, 24(S1):S19–S24.

**Huijberts M, Wolffenduttel B, Boudier H. (2005).** Aminoguanidine treatment increases elasticity and decreases fluid filtration of large arteries from diabetic rats. *Journal of Clinical Investigation*, 92(3):1407.

**Izadi M, Jonaidi-Jafari N, Hänsler V.(2016).** Ozone, information for patients (1st ed). Baqiyatallah University of Medical Sciences, Tehran, Iran.

**Jia L, Bonaventura C, Bonaventura J.**

**(2006).** S- nitrosohaemoglobin : A dynamic activity of blood involved in vascular control. *Nature*, 380(6571): 221–226.

**Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. (2009).** Hyperglycemic crises in adult patients withdiabetes. *DiabetesCare*, 32(7).

**Korhonen T, Karppinen J, Paimela L. (2006).** The treatment of disc herniation-induced sciatica with infliximab: One-year follow-up results of FIRST II, a randomized controlled trial. *Spine*, 31(24): 2759–2766.

**Martinez G, Al-Dalain SM, Menendez S. (2005).** Therapeutic efficacy of ozone medical treatments in patients with diabetic foot. *Eur J Pharmacol*, 523:151-161.

**Okada S, Shikata K, Matsuda M. (2003).** Intercellular adhesion molecule-1-deficient mice are resistant against renal injury after induction of diabetes. *Diabetes*, 52:2586-2593.