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The Effects of Hyperbaric Oxygen Therapy on Blood Glucose Levels and Lipid Profile in Diabetes Mellitus Patients

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Abstract: Diabetes mellitus and its complications are still a major health problem in the world. Diabetes mellitus is closely related to the lipid profile, especially concerning the cardiovascular disease. A method that can be used to treat diabetes mellitus is hyperbaric oxygen therapy (HBO). This study aims to observe changes in blood glucose levels and lipid profiles in patients with diabetes mellitus with hyperbaric oxygen therapy. The determination of blood glucose levels and lipid profiles is done by photometry. A total of 30 patients with diabetes mellitus examined for their blood glucose level and lipid profile before and after hyperbaric oxygen therapy. In the Paired T-test, there were significant decrease in blood glucose levels ($p= 0,000$), total cholesterol ($p= 0,000$), and triglycerides ($p= 0,000$) after hyperbaric oxygen therapy. The conclusion of this study shows there is a significant decrease in blood glucose level and lipid profile (total cholesterol, and triglycerides) after hyperbaric oxygen therapy.

Keyword: hyperbaric oxygen therapy; glucose; lipid profile; diabetes mellitus

INTRODUCTION

Diabetes mellitus and its complications are still a significant public health problem, as well as a cause of increased morbidity, mortality, and disability. In patients with diabetes mellitus, chronic metabolic disorders occur with a variety of causes. Increased blood glucose levels characterize these, accompanied by impaired carbohydrate, lipid, and protein metabolism as a result of insulin function insufficiency (Poretsky, 2010; Ndisanget *al.*, 2017). The number of people with diabetes mellitus in East Java in 2018 ranks 5th in Indonesia. The prevalence of people with diabetes mellitus aged ≥ 15 years has increased from 6.9% in 2013 to 8.5% in 2018 (Kemenkes RI, 2018). Research shows that being overweight results in abdominal obesity, which causes cardiovascular disease and increases the risk of type 2 diabetes mellitus. Patients with obesity are at risk of developing hypertension, dyslipidemia, and hyperglycemia (Tangvarasittichai, 2017).

Along with technological advances in the health sector, some methods can be used in efforts to treat diabetes mellitus, namely hyperbaric oxygen therapy. Hyperbaric oxygen therapy is the use of 100% oxygen at pressures higher than atmospheric pressure. The patient will gradually inhale 100% oxygen, along with an increase in therapeutic chamber pressure to more than one absolute atmosphere (ATA). This therapy initially used to relieve the symptoms of decompression after diving, which occurs due to changes in pressure, such as when diving or boarding an airplane, which is the release and expansion of gas bubbles in the organs. If we

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return to the initial pressure, there will be changes in pressure that can interfere with the function of several organs/ decompression sickness. Hyperbaric oxygen therapy also developed to complement the effects of radiation on cancer care, supporting care during cardiac surgery, and carbon monoxide poisoning (Sourabh & Guruswamy, 2012; Shahriari *et al.*, 2014).

Hyperbaric oxygen therapy can improve and increase the amount of oxygen in the body, and have a significant impact on various clinical diseases, burns, post-stroke, fractures, and acute and chronic ischemia (Lakesla, 2009). Hyperbaric oxygen therapy can also increase tissue sensitivity to insulin so that it can reduce high blood glucose levels in people with diabetes mellitus (Zaetun *et al.*, 2015). Zakiyah & Anggraini's research (2019) shows a significant difference in blood glucose levels after HBOT. Putri & Setianingsih's research (2019) obtained significant differences in lipid profile levels in white rats (*Rattus norvegicus*) induced by high-fat diets and given hyperbaric oxygen therapy. Research results in Turkey have a significant effect on blood glucose levels and lipid profiles after HBOT (Karadurmuset *et al.*, 2010). However, it is different from Semadi & Irawan's (2017) study, which obtained an insignificant decrease in blood glucose levels after hyperbaric oxygen therapy and a significant increase in lipid profile levels. The study was conducted generally in diabetes mellitus patients with foot ulcers, which obtained a difference results were significant and not significant. From this background, it is necessary to observe the effect of HBOT on diabetes mellitus patients in general, to observe the effect of HBOT on blood glucose levels and their lipid profile.

MATERIALS AND METHOD

This research is experimental laboratories using blood samples of patients with diabetes mellitus before and after hyperbaric oxygen therapy. The certificate of ethics obtained from the Ethics Commission of the Faculty of Dentistry, Airlangga University, Surabaya, Indonesia, with a number of ethical clearance certificate: 070/HRECC.FODM/II/2020. Hyperbaric oxygen therapy (HBOT) using 2.4 ATA high-pressure oxygen in a special room with hyperbaric chamber oxygen for ten patients per session for 2 hours. The study conducted at the Tiandte Gedangan Sidoarjo clinic in March 2020. This study used 30 blood samples of diabetes mellitus patients in the Tiandte Gedangan Sidoarjo clinic, with glucose levels > 200 mg/dl. Determination of glucose, total cholesterol, and triglyceride levels in the blood using a photometer Wap Lab WP-9200 at a wavelength of 546 nm. Blood glucose levels using the GOD-PAP method, total cholesterol by the CHOD-PAP method, and triglycerides by the GPO-PAP method. Data were analyzed statistically by Paired T-Test using SPSS 22.

RESULTS AND DISCUSSION

The characteristics of the research subjects according to gender and age are shown in Table 1. 30 research subjects were consisting of 30% men and 70% women. Based on age, there were 33.3% of patients with diabetes mellitus aged 40-49 years, 30% of patients aged 50-59 years, 20% aged 60-69 years, and 16.7% aged 70-79 years. There are 33.3% of patients with diabetes mellitus range in age from 40-49 years. Women of reproductive age (over 40 years) have a higher risk of developing diabetes mellitus than men. This is because physically, women have a higher chance of experiencing an increase in body mass index. Monthly and postmenopausal cycle syndromes result in the distribution of body fat that quickly

accumulated due to hormonal processes that are at risk of suffering from type 2 diabetes (Wahyuni&Alkaff, 2013).

The results of the average glucose, total cholesterol, and triglyceride levels before and after the patient's hyperbaric oxygen therapy decreased (Table 2). The average blood glucose level before and after HBOT has decreased from 307 mg/dl to 269 mg/dl. The mean total cholesterol level also decreased from 270 mg/dl before HBOT to 241 mg/dl after HBOT. Similarly, the average triglyceride levels before and after HBOT decreased from 286 mg/dl to 258 mg/dl. The diagram of the data can be seen in Figure 1.

Table 1. Characteristics of Research Subjects

No.	Variable	Category	Frequency	Percentage (%)	Total (%)
1.	Gender	Man	9	30	100
		Woman	21	70	
2.	Age	40-49 years	10	33,3	100
		50-59 years	9	30	
		60-69 years	6	20	
		70- years	5	16,7	

Table 2. Average \pm SD Glucose, Total Cholesterol, and Blood Triglyceride Levels

	Before HBOT			After HBOT		
Glucose (mg/dl)	Total Cholesterol (mg/dl)	Triglycerides (mg/dl)	Glucose (mg/dl)	Total Cholesterol (mg/dl)	Triglycerides (mg/dl)	
307 \pm 73.122	270 \pm 49.040	286 \pm 75.663	269 \pm 68.086	241 \pm 44.736	258 \pm 75.972	

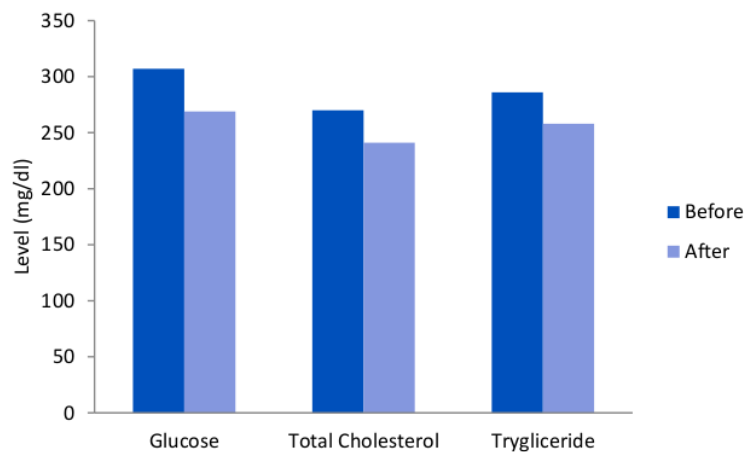


Figure 1. Average Comparison of Glucose, Cholesterol, and Triglyceride Levels Before and After HBOT

Diabetes mellitus is closely related to the lipid profile, especially concerning the cardiovascular disease. This study's data indicate that patients with diabetes

mellitus have hyperglycemia accompanied by high levels of lipid profiles in their blood. This is in accordance with Priyadi&Saraswati's (2012) research, showing an association between hyperglycemia and lipid profiles. This is because high blood glucose levels affect the condition of blood vessels. Under normal circumstances, insulin can increase the uptake of free fatty acids into fat tissue cells and inhibit lipolysis occurrence. However, in patients with diabetes mellitus, the amount of free fatty acids in the blood increases so that the level of lipid profile also increases and can aggravate comorbidities and complications (Sherwood, 2018).

At the time of hyperbaric oxygen therapy, hemoglobin in venous blood saturation increases the pressure of O₂ in blood vessels. Oxygen diffusion is influenced by differences in pressure so that O₂ from the blood vessels will be distributed to the tissues. Blood oxygen dissolves in plasma fluid bound to hemoglobin, and only a small portion found in dissolved form. Tissues more efficiently use the form of dissolved oxygen in hyperbaric oxygen therapy through direct diffusion than oxygen is bound through the hemoglobin's oxygen system (Guritno, 2005; Collins, 2015).

In this study, a significant difference obtained in blood glucose levels before and after HBOT shown by the results of significance ($p = 0,000 < 0.05$). This is because HBOT can increase tissue sensitivity to insulin and cause a decrease in blood sugar levels. This is consistent with the study of Zakiyah&Anggraini (2019), which showed a significant difference ($p = 0,000$) in blood glucose levels before and after HBOT. The use of high-dose oxygen pressure of 2.4 ATA oxygen 3x30 minutes for 2x5 days interspersed with a one-week break can cause an increase in blood insulin levels in people with diabetes mellitus, due to increased pancreatic beta-cell function resulting in increased levels of insulin in the blood (Ishihara, 2007; Jain, 2017).

The data of this study indicate a significant decrease in blood glucose levels and lipid profiles, namely, total cholesterol ($p = 0,000$) and triglycerides ($p = 0,000$). This is consistent with studies in Turkey where there was a significant effect ($p < 0.001$) on blood glucose levels and lipid profiles after HBOT and showed that glycemic control, atherosclerosis, and inflammatory markers significantly improved in patients undergoing HBOT in patients with diabetes mellitus with diabetic foot ulcers (Karadurmuş *et al.*, 2010). Another study showed that HBOT could reduce total cholesterol levels ($p < 0.05$) and triglycerides levels ($p < 0.05$) in diabetes mellitus patients. In patients with diabetes mellitus, metabolic changes can damage vasodilation and causes tissue hypoxia and microvascular pathology. HBOT can significantly improve the outcome of ischemic conditions and reduce vascular complications (Resanovic, 2019).

HBOT has no adverse effect on the function of High-Density Lipoprotein and carries the potential to cause changes in lipid metabolism that can reduce atherosclerosis in patients (Erenet *et al.*, 2019). 100% oxygen therapy can increase five times the volume of dissolved oxygen to 15 ml per liter of blood, and during HBOT at 2.5 ATA, almost 60 ml of dissolved oxygen in each liter of blood (Londahl, 2012). Increased oxygen in the blood can increase cells and body tissues and metabolism in cells to increase tissue sensitivity to insulin and reduce blood glucose levels (Ishihara, 2007). HBOT has the same effect as exercise so it can activate AMPK (AMP-activated protein kinase), so glucose can be used as an energy resource (ATP), which affects vasodilation by stimulating Synthase Oxid nitrate (NOS) and increasing insulin sensitivity through AMPK activation (Isbandiati, 2011). Nitric oxide synthase (NOS) activity needed for mobilization of SPC (stem/progenitor cells) from

the bone marrow. SPC mobilization disrupted in patients with diabetes due to reduced activity of nitric oxide synthase caused by hyperglycemia and insulin resistance. HBOT can mobilize SPC by stimulating NOS in the bone marrow (Londahl, 2012).

HBOT can provide the effect of restoring vascular reactivity through modulation of vasoconstrictor and vasodilator production and increasing vessel sensitivity to these factors (Karadurmuset *et al.*, 2010). Lipid peroxidation has a relationship with elevated blood glucose levels and high oxidative stress in patients with diabetes mellitus. Improved lipid profile in diabetes mellitus, especially with foot ulcers induces overexpression of lipid peroxidase, superoxide dismutase (SOD) activity, and catalase, which suggest compensatory mechanisms by the body to prevent further tissue damage (Bhattacharyya *et al.*, 2019). The potential effects of HBOT on endothelial function cause a significant reduction in atherosclerotic, glycemetic, and inflammatory markers. Endothelial dysfunction is closely related to the development of diabetic retinopathy, nephropathy, and atherosclerosis in diabetic patients. Also, endothelial dysfunction is closely related to insulin resistance so that increased tissue sensitivity to insulin increases vascular endothelial function and vice versa.

This study has several limitations. Patients used as research subjects have a small amount with various comorbidities and drugs used for their disease management. The study also did not consider the number of times hyperbaric oxygen therapy had been undertaken by diabetes mellitus patients. In future studies, a higher number of patients and more complete examination parameters needed to find the effect of hyperbaric oxygen therapy on patients with diabetes mellitus.

CONCLUSION

There is a significant decrease in blood glucose level and lipid profile (total cholesterol, and triglycerides) after hyperbaric oxygen therapy (HBOT).

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CONFLICT OF INTEREST

The authors have no potential conflicts of interest with regard to this study.

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