SURABAYA MEDICAL JOURNAL
(SMJ IDI SURABAYA)

Volume 1, Issue 2, November 2023, p.79-84

eISSN: 2986-7584
pISSN: 2986-2469

OPINION

Effect of hyperbaric oxygen (HBO) therapy on kidney function in metabolic syndrome (MetS) patients

Hisnindarsyah [1*]

[1]Maritime Medicine Specialist, Faculty of Medicine, Hang Tuah University, Surabaya/Dr. Ramelan Naval Center Hospital Surabaya

Article Info

Article history:
Received: 05-08-2023
Revised: 16-09-2023
Accepted: 22-09-2023
Published: 10-11-2023

Keywords:
Hyperbaric oxygen therapy;
kidney disease;
metabolic syndrome;
renal hypoxia

ORCID ID
Hisnindarsyah
https://orcid.org/0000-0002-0295-3257

ABSTRACT

Background: Hyperbaric oxygen (HBO) therapy is a treatment that involves inhaling 100% pure oxygen in a hyperbaric chamber of more than one absolute atmosphere. Currently, the use of HBO therapy is increasingly widespread, not only for decompression sickness and diving problems but also for clinical therapy, cosmetics, and geriatric care. The American Food and Drug Administration (FDA) has also confirmed various clinical functions, especially those related to metabolic syndromes such as diabetes mellitus (DM) and diabetic foot ulcers (DFU). However, the use of HBO therapy for kidney disease has not been fully studied yet. **Purpose**: This article summarizes the scientific reasons to use this therapy as a complementary for patients with chronic kidney disease due to metabolic syndrome. **Opinion**: Several benefits of HBO have been reported. Reducing oxidative stress, alleviating vascular dysfunction and amyloid burden, treating ischemia and reperfusion injury, and increasing NO production. It has also been suggested to be useful as a complementary therapy in type 2 DM (T2DM) suspected with chronic kidney disease (CKD) as HBO therapy decreases proteinuria by 50%. Renal hypoxia is the underlying cause of CKD progression and is associated with hypertension. In hypoxic conditions, cells lack oxygen; thus, they carry out anaerobic metabolism or fermentation known as the Warburg effect. HBO therapy can assist in supplying oxygen more quickly at the cellular level (internal respiration) to allow metabolism to re-process aerobically. **Conclusion**: HBO therapy improves the patient's general condition in CKD cases with MetS, thereby preventing kidney disease complications. The effectiveness of HBO therapy for kidney disease still requires further research with more frequent and longer treatment.

Citation:
Hisnindarsyah. (2023) 'Effect of hyperbaric oxygen (HBO) therapy on kidney function in metabolic syndrome (MetS) patients', Surabaya Medical Journal, 1(2), p. 79-84. doi: 10.59747/smjidisurabaya.v1i2.32

Corresponding Author:
Hisnindarsyah, Maritime Medicine Specialist Faculty of Medicine, Hang Tuah University, Surabaya/Dr. Ramelan Naval Center Hospital Surabaya Tel.: +6281231571436
Email: hisnindarsyah@yahoo.com

Highlights

1. Hyperbaric oxygen therapy (HBOT) is one of the complementary treatments to increase oxygen flow in the blood and has proved to be an effective treatment for some diseases.

©2023 This is an open-access article distributed under the terms of the CreativeCommonsAttribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/)

2. The usefulness, advantages, and disadvantages belong to this treatment for renal disease.

BACKGROUND

Kidney disease is a non-communicable disease with a high incidence rate and serious impact on health, leading to mortality for its sufferers. Kidneys have an important role in the body's metabolism and homeostatic stability. There are many risk factors for kidney disease, one of which is metabolic syndrome. Metabolic syndrome (MetS) is a cluster or combination of various risk factors related to cardiovascular disease (Zhang dan Lerman, 2017). The mortality rate for patients with chronic kidney disease (CKD) who underwent hemodialysis ranged from 0.4 to 10.04 deaths per 100 people every year (Ramesh et al., 2016). The main type of mortality is sudden cardiac death, while it is stated 13 deaths occur to per 100 people every year (Mayer et al., 2020).

Hyperbaric oxygen therapy (HBOT) is one of the oldest adjuvant treatments in medical management, initiated by Dr. Henshaw in England in 1669. However, this therapy did not see significant progress. Despite hundreds of years passing, HBOT has had its ups and downs in terms of support and scientific evidence (Rosyanti et al., 2019). Along with the development of science and research, now HBOT can be used for clinical therapy according to indications that have been approved by the Food and Drugs Administration (FDA) and the Undersea and Hyperbaric Medical Society (UMHS) (Boykin dan Baylis, 2007; Food and Drug Administration, 2006; Rosyanti et al., 2019). However, the usefulness, effects, and side effects of HBOT as an adjuvant treatment for kidney disease have never been investigated before, especially in those with MetS.

OBJECTIVE

This paper was written to provide scientific evidence of usefulness, effects, and side effects of HBOT's as an adjuvant treatment for kidney disease with MetS since the role of HBOT for this disease has never been investigated before.

METABOLIC SYNDROME AND KIDNEY DISEASE

Before discussing HBOT, it is imperative to understand MetS and kidney disease. There are several definitions of metabolic syndrome. In this literature review, three definitions used were those from the World Health Organization (WHO), NCEP ATP-III, and the International Diabetes Federation (IDF) [7]. These three definitions can be seen in **Table 1**.

Table 1. Definition of metabolic syndrome (MetS) based on the WHO, NCEP, and IDF.

	WHO (1999)	**NCEP ATP-III (2001)**	**IDF (2005)**
Required	Insulin resistance (IR)		Waist circumference ≥ 94 cm for men or ≥ 84 cm for women
Number of abnormalities	≥ 2 of:	≥ 3 of:	≥ 2 of:
Obesity	WHR > 0.9 in men, or ≥ 0.85 in women; BMI ≥ 30 kg/m^2	WC ≥ 102 cm in men or ≥ 88 cm in women	
Triglycerides	≥ 150 mg/dL	≥ 150 mg/dL	≥ 150 mg/dL
HDL cholesterol	< 40 mg/dL in men or < 50 mg/dl in women	< 40 mg/dL in men or < 50 mg/dl in women	< 40 mg/dL in men or < 50 mg/dl in women
Hypertension	≥ 140/90 mmHg	≥ 130/85 mmHg	≥ 130/85 mmHg
Glucose		≥ 110 mg/dL	≥ 100 mg/dL
Microalbuminuria	Albumin/creatinine ratio > 130 mg/g Albumin excretion rate > 20 mcg/min		

Adapted from: (Al-Hamad dan Raman, 2017).

Surabaya Medical Journal (SMJ IDI Surabaya)
e-ISSN: 2986-7584; p-ISSN: 2986-2469

Many studies have found that MetS is associated with CKD, and each MetS component is associated with CKD incidence and progression, meaning MetS and CKD share a complex relationship (Steward, 1959). MetS increases the risk of stage III CKD (estimated GFR <60 mL/min) by 1.55-fold (Thomas et al., 2011). Other studies have found that MetS increases CKD incidence by 2.6-fold after 21 years, which also relates to the number of MetS components (Zhang dan Lerman, 2017b). It has been stated that the etiology of CKD is MetS as MetS's muliple risk factors (insulin resistance, inflammation, lipid metabolism alteration, and hypertension) lead to upregulation of the profibrotic factors (Xiao et al., 2022). Moreover, all MetS components have been found to increase the reactive oxygen species (ROS) in adipose tissue and endothelial cells, leading to oxidative stress. Oxidative stress is considered one of the causes of diabetic endothelial-angiopathy dysfunction. Hyperglycemia conditions induce oxidative stress via three pathways: the polyol pathway (Yuan et al., 2019), increased auto-oxidation (the Wolff pathway) (Yuan et al., 2019), and through protein glycosylates (Laguardia et al., 2012; Stirban et al., 2014).

In the vascular system, oxidative stress causes a decrease in nitric oxide (NO) production by endothelial cells. Decreased NO production causes endothelial dysfunction, thereby affecting the endothelium's diameter by narrowing of blood vessels. This leads to hypertension, which will exacerbate endothelial mechanical damage, causing endothelial inflammation to occur continuously (chronic inflammation) and leading to endothelial injury. These conditions lead to the formation of atherosclerotic plaques and interfere with the work of the cardiovascular system (Medina-Leyte et al., 2021; Pober et al., 2009). In an addition, the kidneys have an important role in controlling blood pressure, which is also known as the renin-angiotensin aldosterone system (RAAS). The RAAS involves not only the kidneys but also the lungs, systemic vasculature, adrenal cortex, and brain. When the kidneys and/or their glomerular capillary endothelial are injured, there will be atherosclerotic plaque to band the injured area. This plaque can prevent the blood from flowing easily and cause the cardiovascular system to overwork. This overworked cardiovascular system is recorded as hypertension. Increased glomerular capillary pressure for a long time will cause glomerulosclerosis. Glomerulosclerosis stimulates hypoxia and CKD (Statistician dan Applications, 2022).

The human body has two kidneys which are located on the right and left. The kidneys are macroscopically pea-shaped and have only about 7-12 cm long and 1.5-2.5 cm thick. Normal kidneys weigh around 120-170 grams (Kidney Research UK, 2010). Kidneys are vital organs that play an important role in maintaining homeostasis (environmental stability in the body), filtering (filtration), and removing waste products from the blood into urine (excretion). In addition to regulatory and excretory functions, the kidneys also secrete renin. Renin has an important role in regulating blood pressure, plays a role in forming vitamin D, regulates calcium, and contributes to erythropoietin synthesis to stimulate red blood cell production (Bajaj et al., 2018).

HYPERBARIC OXYGEN (HBO) THERAPY

HBOT is a therapy that provides oxygen at a concentration of up to 100% and a pressure of more than one atmosphere absolute (ATA). It is carried out in a high-pressure air chamber. This therapy can be used as the main form of therapy or as complementary therapy (Kirby et al., 2019; Rosyanti et al., 2019; Sen dan Sen, 2021). HBOT allows the patients to inhale 100% pure oxygen in a high-pressure closed chamber (Boykin dan Baylis, 2007).

HBOT was originated by Dr. Henshaw of England who built a hyperbaric chamber in 1662 to treat several types of ailments. Then, in 1921, Dr. J. Cunningham began to advance the basic theory of using hyperbaric oxygen to treat hypoxic states. However, his efforts failed because he did not have strong scientific evidence. In the 1930s, studies on the use of hyperbaric oxygen began to be carried out in a more focused and in-depth manner. Following that, around the 1950s, Dr. Borrema succeeded in presenting the results of his research on the use of hyperbaric oxygen. His research showed that hyperbaric oxygen dissolved physically in blood fluids, meaning it could give life to a state without hemoglobin, which is called life without blood. The results of his research on gas gangrene treatment with hyperbaric oxygen made him known as the father of HBOT. Since then, HBOT has developed rapidly and continues to be developed to this day (Ustad et al., 2012).

The working principle of HBOT utilizes the four laws of diving physics, namely (1) Boyle's law which states the greater the pressure, the smaller and denser the air volume; (2) Dalton's law which theorizes

if the pressure increases, the partial pressure also increases; (3) Henry's law which asserts the higher the partial pressure, the easier it is for the gas to dissolve in the liquid; and (4) Charles' law which concludes at constant pressure, if the volume of gas increases, the temperature will also increase (Mohamed et al., 2018).

The HBOT's mechanism includes several actions, namely (1) reducing gas bubbles' volume and accelerating its resolution; (2) ischemic and hypoxic areas receiving maximum O2 (hyperoxia); (3) increasing the formation of new capillaries (angiogenesis/neovascularization); (4) suppressing the growth of germs (antimicrobial); (5) increasing the formation of fibroblasts; (6) increasing leukocyte phagocytosis; and (7) improving fitness, beauty, and geriatric purposes (Mohamed et al., 2018). As a clinical therapy, HBOT also has appropriate doses that are adjusted to the indications, contraindications, and patient needs. The therapeutic dose of HBOT is generally given at 2.4 ATA with 100% pure oxygen, according to the dive chart guidelines. Especially in Indonesia, the Kindwall table composed by Prof. Guritno is used (Rosyanti et al., 2019).

THE ROLE OF HYPERBARIC OXYGEN THERAPY (HBOT) ON KIDNEY FUNCTION

Several benefits of HBOT that have been reported include reducing oxidative stress in diabetic patients [24], alleviating vascular dysfunction and amyloid burden [25], treating ischemia and reperfusion injury [26], and increasing NO production for wound healing [6]. It has also been suggested as an adjuvant therapy for type 2 diabetes mellitus (T2DM) as HBOT decreases proteinuria by 50% [27]. A preliminary study conducted in diabetic kidney disease (DKD) hypothesized that HBOT would work as an adjuvant as it alleviates the microvascular endothelial cells due to the reduction in renal injury's biomarkers, oxidant stress, and mitochondrial dysfunction [28]. An animal model study also supported this hypothesis that HBOT is able to reduce TNFα, pentraxin-3, malondialdehyde, total oxidant status, and oxidative stress index levels. However, it causes an increase in total antioxidant capacity values [29].

The rational reason why HBOT is beneficial to kidney function is increased oxygen plasma diffusion. Under normal air pressure conditions, about 97% of oxygen binds to hemoglobin, and about 3% dissolves in blood plasma. Whereas, in hyperbaric conditions, oxygen dissolved in blood plasma can increase many times with the amount of hyperbaric pressure applied. Oxygen dissolved in plasma can pass through various atherosclerosis blockage, allowing ischemic conditions to be resolved (Rosyanti et al., 2019). Renal hypoxia is the underlying cause of CK progression and is associated with hypertension (Bel et al., 2017). In hypoxic conditions, cells that lack oxygen will carry out anaerobic metabolism or fermentation. In anaerobic metabolism, very little ATP is produced, and every glucose molecule only produces two ATP. This means that if the renal tissue is hypoxic for a long time, there will be mitochondrial damage, an energy crisis, and cell death. This physiological condition is known as the Warburg effect (Heiden et al., 2009). HBOT can assist in supplying oxygen more quickly at the cellular level (internal respiration) to allow metabolism to re-process aerobically. Every glucose molecule is processed aerobically to produce 38 ATP (Choudhury, 2018).

A study on CKD patients who underwent HBOT found that there was a reduction in their sympathetic nerve activity (SNA) and lowered blood pressure (BP) (Kara et al., n.d.). A further study stated that the increment of blood pressure during HBOT was dose-dependent. Hemodynamic features such as SVR, heart rate, and cardiac output (CO) also increased (Bel et al., 2017). However, the underlying mechanism of this effect is still unknown. It has been suggested that oxygen corrects the hypoxic condition by increasing oxygen delivery and tension and attenuates effects mediated by hypoxia-inducible factors (HIF). Other effects include reducing ROS production, increasing vasoconstriction and angiogenesis, and reducing proinflammation responses (Choudhury, 2018).

Oxygen also plays an important role in wound healing by upregulating collagen synthesis and maturation. Collagen serves as the basic matrix of proliferation. Lack of oxygen will interfere with collagen synthesis (Sen, 2009). In addition, HBOT also stimulates angiogenesis by increasing various growth factor components, especially the vascular endothelial growth factor (VEGF) (Sen, 2009). HBOT has been proven to be able to maintain mitochondrial integrity, which is important in the production process of energy for the body's activities, including recovery. Moreover, with repetitive HBOT, there will be an adaptation against stimulus that will diminish the inflammatory responses, thus accelerating the damaged tissue's recovery.

Limitations

Surabaya Medical Journal (SMJ IDI Surabaya)
e-ISSN: 2986-7584; p-ISSN: 2986-2469

Due to a lack of evidence in the cellular stage, the role of HBO therapy could only be explained hypothetically. In Indonesia, this therapy could be useful as an adjuvant for MetS and renal diseases although this needs to be proved by a clinical study.

CONCLUSION

HBO therapy improves the patient's general condition in CKD with MetS, thereby preventing kidney disease complications. The effectiveness of HBOT in treating kidney disease still requires further research with more frequent and longer treatment.

Acknowledgment

None.

Conflict of Interest

The author declares no conflict of interest.

Funding

None.

Author Contribution

Hisnidarsyah plays a role in conceptualizing, drafting, and editing the manuscript.

REFERENCES

Al-Hamad, D., Raman, V., 2017. Metabolic syndrome in children and adolescents. Transl. Pediatr. 6, 397–407.

Bajaj, P., Chowdhury, S.K., Yucha, R., Kelly, E.J., Xiao, G., 2018. Emerging kidney models to investigate metabolism, transport, and toxicity of drugs and xenobiotics. Drug Metab. Dispos. 46, 1692–1702.

Bel, R. van der, Çaliskan, M., van Hulst, R.A., van Lieshout, J.J., Erik, E.S., Krediet, C.T.P., 2017. Blood pressure increase during oxygen supplementation in chronic kidney disease patients is mediated by vasoconstriction independent of baroreflex function. Front. Physiol. 8, 1–8.

Boykin, J. V., Baylis, C., 2007. Hyperbaric Oxygen Therapy Mediates Increased Nitric Oxide Production Associated With Wound Healing: A Preliminary Study. Adv Ski. Wound Care 20, 382–388.

Capó, X., Monserrat-Mesquida, M., Quetglas-Llabrés, M., Batle, J.M., Tur, J.A., Pons, A., Sureda, A., Tejada, S., 2023. Hyperbaric Oxygen Therapy Reduces Oxidative Stress and Inflammation, and Increases Growth Factors Favouring the Healing Process of Diabetic Wounds. Int. J. Mol. Sci. 24.

Choudhury, R., 2018. Hypoxia and hyperbaric oxygen therapy: A review. Int. J. Gen. Med. 11, 431–442.

Food and Drug Administration, 2006. Hyperbaric Oxygen Therapy.

Harrison, L.E., Giardina, C., Hightower, L.E., Anderson, C., Perdrizet, G.A., 2018. Might hyperbaric oxygen therapy (HBOT) reduce renal injury in diabetic people with diabetes mellitus? From preclinical models to human metabolomics. Cell Stress Chaperones 23, 1143–1152.

Heiden, M.G. Vander, Cantley, L.C., Thompson, C.B., 2009. Understanding the Warburg Effect: The Metabolic Requirements of Cell Proliferation. Science (80-.). 324, 1029–1033.

Kara, T., Hering, D., Zdrojewski, Z., Kro, E., Kucharska, W., Somers, V.K., Rutkowski, B., n.d. tonic chemoreflex activation in CRF pts.pdf 157–161.

Kidney Research UK, 2010. The Kidneys – a Basic Guide. Kidney Heal. Inf. 1, 13–25.

Kirby, J.P., Snyder, J., Schuerer, D.J.E., Peters, J.S., Bochicchio, G. V., 2019. Essentials of Hyperbaric Oxygen Therapy: 2019 Review. Mo. Med. 116, 176–179.

Laguardia, H.A., Hamm, L.L., Chen, J., 2012. The metabolic syndrome and risk of chronic kidney disease: Pathophysiology and intervention strategies. J. Nutr. Metab. 2012.

Mayer, B., Lameira da Costa, P.T., Echevarría-Guanilo, M.E., Silveira Kempfer, S., Da Silva Pieri, K.M., 2020. Kidney disease and hemodialysis: identification of blood biomarkers to detect heart failure and kidney failure. Rev. Colomb. Nefrol. 7, 44–54.

Medina-Leyte, D.J., Zepeda-García, O., Domínguez-Pérez, M., González-Garrido, A., Villarreal-Molina, T., Jacobo-

Albavera, L., 2021. Endothelial dysfunction, inflammation and coronary artery disease: Potential biomarkers and promising therapeutical approaches. Int. J. Mol. Sci. 22.

Mohamed, A.S.E., Abdelrahman, A.A., Aly, U.F., Khaled, K.A., 2018. Hyperbaric oxygen therapy: A review. Eur. J. Clin. Pharm. 20, 263–269.

Pober, J.S., Min, W., Bradley, J.R., 2009. Mechanisms of endothelial dysfunction, injury, and death. Annu. Rev. Pathol. Mech. Dis. 4, 71–95.

Ramesh, S., Zalucky, A., Hemmelgarn, B.R., Roberts, D.J., Ahmed, S.B., Wilton, S.B., Jun, M., 2016. Incidence of sudden cardiac death in adults with end-stage renal disease: A systematic review and meta-analysis. BMC Nephrol. 17, 1–9.

Rosyanti, L., Hadi, I., Rahayu, D.Y.S., Wida, A.B.B., 2019. Theoritical Review Hyperbaric Oxygen Therapy/HBOT. HIJP Heal. Inf. Junal Penelit. 11, 182–205.

Sancak, E.B., Tan, Y.Z., Turkon, H., Silan, C., 2017. Attenuation of partial unilateral ureteral obstruction - induced renal damage with hyperbaric oxygen therapy in a rat model. Int. Braz J Urol 43, 946–956.

Sedlacek, M., Harlan, N.P., Buckey, J.C., 2021. Renal Effects of Hyperbaric Oxygen Therapy in Patients with Diabetes Mellitus: A Retrospective Study. Int. J. Nephrol. 2021.

Sen, C.K., 2009. Wound healing essentials: Let there be oxygen. Wound Repair Regen. 17, 1–18.

Sen, Suman, Sen, Sheuli, 2021. Therapeutic effects of hyperbaric oxygen: Integrated review. Med. Gas Res. 11, 30–33.

Shapira, R., Gdalyahu, A., Gottfried, I., Sasson, E., Hadanny, A., Efrati, S., Blinder, P., Ashery, U., 2021. Hyperbaric oxygen therapy alleviates vascular dysfunction and amyloid burden in an Alzheimer's disease mouse model and in elderly patients. Aging (Albany. NY). 13, 20935–20961.

Statistician, M., Applications, E., 2022. Article History Article. Scholar.Archive.Org 71, 143–148.

Steward, P., 1959. Physiology of the kidney. Updat. Anaesth. 13, 24–406.

Stirban, A., Gawlowski, T., Roden, M., 2014. Vascular effects of advanced glycation endproducts: Clinical effects and molecular mechanisms. Mol. Metab. 3, 94–108.

Sureda, A., Batle, J.M., Martorell, M., Capó, X., Tejada, S., Tur, J.A., Pons, A., 2016. Antioxidant response of chronic wounds to hyperbaric oxygen therapy. PLoS One 11, 1–14.

Thomas, G., Sehgal, A.R., Kashyap, S.R., Srinivas, T.R., Kirwan, J.P., Navaneethan, S.D., 2011. Metabolic syndrome and kidney disease: A systematic review and meta-analysis. Clin. J. Am. Soc. Nephrol. 6, 2364–2373.

Ustad, F., Ali, F.M., Ustad, T., Aher, V., Prasant, M.C., Suryavanshi, H., 2012. Uses of Hyperbaric Oxygen Therapy: A review. Evol. Med. Dent. Sci. 1, 892–906.

Wu, H.H., Huang, C.C., Chang, C.P., Lin, M.T., Niu, K.C., Tian, Y.F., 2018. Heat shock protein 70 (HSP70) reduces hepatic inflammatory and oxidative damage in a rat model of liver ischemia/reperfusion injury with hyperbaric oxygen preconditioning. Med. Sci. Monit. 24, 8096–8104.

Xiao, H., Shao, X., Gao, P., Zou, H., Zhang, X., 2022. Metabolic Syndrome Components and Chronic Kidney Disease in a Community Population Aged 40 Years and Older in Southern China: A Cross-Sectional Study. Diabetes, Metab. Syndr. Obes. 15, 839–848.

Xu, L., 2018. Analysis on Indoor Plant Landscapes in Interior Design Styles 232, 530–533.

Yuan, T., Yang, T., Chen, H., Fu, D., Hu, Y., Wang, J., Yuan, Q., Yu, H., Xu, W., Xie, X., 2019. New insights into oxidative stress and inflammation during diabetes mellitus-accelerated atherosclerosis. Redox Biol. 20, 247–260.

Zhang, X., Lerman, L.O., 2017a. The metabolic syndrome and chronic kidney disease. Transl. Res. 183, 14–25.