Hyperbaric Oxygen Effects on Skeletal Muscle Metabolic Capacity in Type 2 Diabetic Rats with Obesity

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Abstract

In type 2 diabetic rats with obesity, we looked at whether hyperbaric oxygen improved the skeletal muscle's ability to burn calories through oxidative metabolism and reduced adipocyte hypertrophy. Otsuka, a five-week-old boy In the control and hyperbaric oxygen groups, Long-Evans Tokushima fatty (OLETF) and Long-Evans Tokushima Otsuka (LETO) rats were utilised as diabetic animals and nondiabetic controls, respectively. For three hours each day, animals in the hyperbaric oxygen group were subjected to an atmosphere with a pressure of 1.25 and an oxygen content of 36%. When compared to LETO rats, OLETF rats had significantly higher glucose levels at 27 weeks of age, but OLETF rats exposed to hyperbaric oxygen saw a reduction in this elevation. In the skeletal muscle, the slow-to-fast fibre transition was seen in OLETF rats, but it was suppressed in OLETF animals given hyperbaric oxygen. Hyperbaric oxygen also boosted the muscle fibres' oxidative enzyme activity. Although OLETF rats exposed to hyperbaric oxygen did not exhibit hypertrophied adipocytes, their adipocyte size was bigger than that of LETO rats. Hyperbaric oxygen improves skeletal muscle glucose and lipid metabolism, suggesting that it can prevent glucose rise and adipocyte hypertrophy in diabetic rats with obesity.

Keywords: Hyperbaric oxygen therapy; Aging intervention; Adipose tissue; Browning; Weight gain; Age-related disease; Oxidative stress; Cellular senescence.

Introduction

White adipocytes grow as a result of excessive eating and inactivity, which increases energy consumption. It is generally recognised that type 2 diabetes and obesity are brought on by hypertrophied adipocytes. It has been proposed that insulin resistance, which frequently follows obesity, is brought on by hypertrophied adipocytes that overexpress tumour necrosis factor. Additionally, in obesity, which is linked to the later development of type 2 diabetes, hypertrophied adipocytes decreased the expression of adiponectin. Chronically elevated blood glucose levels reduce skeletal muscle's sensitivity to insulin and lead to insulin resistance. Due to decreased insulin-stimulated glucose absorption in muscle fibres, skeletal muscles that are impacted by insulin resistance are unable to dispose of glucose in a sufficient manner [1].

Skeletal muscle, which is thought to be the primary site of glucose metabolism, is crucial to the regulation of glucose. Based on their contractile and metabolic characteristics, skeletal muscle fibres are divided into three types: slow-twitch oxidative (type I), fast-twitch oxidative-glycolytic (type IIA), and fast-twitch glycolytic (type IIB). The distribution of fibre types affects the skeletal muscle's metabolic capability. The rates of glucose uptake between different muscle fibre types show significant variations in glucose metabolism, and the rate of glucose uptake is higher in skeletal muscle made up likely of type I and IIA fibres than in those made up of type IIB fibers [2]. Additionally, skeletal muscles made up of type I and IIA fibres likely have more glucose transporters than muscles made of type IIB fibres. The metabolic capacity of skeletal muscle is disrupted by type 2 diabetes, and the distribution of different muscle fibre types is also affected. According to a number of studies, rats with type 2 diabetes have skeletal muscles that are more likely to include type IIB fibres than type I and IIA fibres. Additionally, type 2 diabetic rats' muscle fibres' mitochondrial oxidative enzyme activity was shown to be lowered. As a result, altered fibre type distribution and decreased mitochondrial oxidative enzyme activity of skeletal muscle fibres may both contribute to insulin resistance and poor glucose metabolism [3].

We have established that hyperbaric oxygen increases the skeletal muscles' and their fibres' capacity for oxidative metabolism through the building of a hyperbaric chamber with an oxygen concentrator and an air compressor. The oxygen concentration and atmospheric pressure can both be maintained at high levels in the hyperbaric chamber; this boosts the partial pressure of oxygen, increases blood flow, and raises the concentration of dissolved oxygen in blood plasma. Elevated oxygen levels and air pressure both trigger a switch from fast to slow fibres in skeletal muscles by activating mitochondrial oxidative enzyme activity. Hyperbaric oxygen has been shown to be effective in treating type 2 diabetes; it inhibits the fraction of type I and IIA fibres in skeletal muscle from declining, which in turn stops the glucose level from rising [4]. Although hyperbaric oxygen increases the skeletal muscles' oxidative metabolic capacity and lowers blood glucose levels in obese and type 2 diabetes patients, it is not yet known how this affects adipocytes. Insulin resistance brought on by obesity is correlated with adipocyte size, and the presence of hypertrophied adipocytes promotes the development of insulin resistance. Adipocyte hypertrophy may encourage macrophage infiltration into adipose tissue, and the cytokines secreted by macrophages cause the emergence of insulin resistance. We postulated that hyperbaric oxygen increases the skeletal muscles' capacity for oxidative metabolism, avoiding the adipocyte hypertrophy linked to insulin resistance. The current study set out to determine whether type 2 diabetic rats with obesity exhibit attenuated adipocyte hypertrophy when exposed to hyperbaric oxygen [5].

Materials and Methods

The Kyoto University Animal Experimentation Regulation was followed in the conduct of this study, which received approval from the institution's Animal Care and Use Committee. The National Institutes of Health's Guidelines for the Care and Use of Laboratory Animals were followed in all of the experiments [6].

Age-matched male Long-Evans Tokushima Otsuka (LETO, n = 9) rats were utilised as nondiabetic control animals without obesity, while five-week-old male Otsuka Long-Evans Tokushima fatty (OLETF, n = 1 1) rats served as type 2 diabetic animals with obesity. Randomly chosen control hyperbaric oxygen groups were given to all of the animals. The groups are designated as LC for LETO control, LH for LETO exposed to hyperbaric oxygen, OC for OLETF control, and OH for OLETF subjected to hyperbaric oxygen, respectively. For animal testing, we created a hyperbaric chamber that included an oxygen tank, an oxygen concentrator, and an air compressor [7]. The chamber was 70 cm in diameter and 180 cm long, and a computer-assisted system automatically maintained the hyperbaric environment. From 5 to 27 weeks of age, the animals in the hyperbaric oxygen group were subjected to an atmospheric pressure of 1.25 and an oxygen concentration of 36% for three hours each day. Based on the outcomes of a prior study that obtained successful results with regard to oxidative metabolic capacity in the neuromuscular system, the

ideal air pressure and oxygen content were determined. Except for those that were exposed to hyperbaric oxygen, all animals were housed in controlled environments with fixed 12:12 h light: dark cycles and room temperatures regulated at 2 2 2°C. All groups received unlimited access to food and drink [8].

The extensor digitorum longus muscle was taken after blood was drawn, promptly frozen in acetone, cooled using dry ice, and kept at 80°C until analysis. From the middle of the muscular belly in the extensor digitorum longus muscle, serial transverse slices of 10 m thickness were cut using a cryostat (CM-1510S, Leica Microsystems, and Mannheim, Germany) and mounted on glass slides. According to a prior study, the sections were stained for myofibrillar adenosine triphosphatase (ATPase) to classify the muscle fibre types as type I, IIA, or IIB. The slices were preincubated in barbital acetate buffer (pH 4.45) for 5 min at room temperature before to ATPase staining [9].

The sections were washed with 0.1 M barbital buffer containing 0.18 M CaCl2 (pH 9.4) for 30 seconds, and then incubated for 45 min at room temperature in 0.1 M barbital buffer containing 0.18 M CaCl2 and 4 mM ATP (pH 9.4). The sections were then washed with 0.01 M sodium barbital, 1% CaCl2, and 2% CoCl2 every three minutes. The portions were cleaned with distilled water and then visualised with 1% ammonium sulphide. Succinate dehydrogenase (SDH) and cytochrome were additionally stained on the sections to quantify the level of mitochondrial oxidative capacity. The slices were incubated for 45 minutes at 37°C in 0.05 M phosphate buffer (pH 7.5) with 0.05% nitro blue tetrazolium and 0.05 M sodium succinate for SDH staining. The sections were treated with 0.1 M acetate buffer (pH 5.5), 0.002% 3, 3'-diaminobenzidine, 0.1% MnCl2, and 0.001% H2O2 for 60 min at 37°C to stain them with cytochrome. They were then washed in 1% CuSO4 for 5 min [10].

The values of the SDH and cytochrome staining intensities were expressed as optical density values, and the histochemical pictures stained by SDH and cytochrome were digitalized as gray-scale images. For the purpose of determining the distribution of different muscle fibre types, a measuring field was placed over the complete muscle cross-section. Each muscle fibre type's SDH and cytochrome activities were examined in at least 100 randomly chosen samples. The ImageJ software was used to measure the portions (NIH, MD, USA). After the extensor digitorum longus muscle was sampled, the epididymal white adipose tissue was also taken out and promptly frozen in acetone that had been chilled by dry ice without fixation. A little amount of the adipose tissue sample was chopped before being put on glass slides. Sudan Red was used to stain minced adipose tissues in order to determine the diameter and size distribution of the adipocytes. The ImageJ software was used to calculate the adipocyte diameter [11].

Discussion

The results of the current investigation showed that in type 2 diabetic mice with obesity, hyperbaric oxygen increases the oxidative metabolic capacity of skeletal muscles and reduces adipocyte hypertrophy. In type 2 diabetic rats with obesity, the distribution of fibre types in the skeletal muscle was changed, and elevated glucose and adipocyte hypertrophy were seen. Hyperbaric oxygen, on the other hand, stimulated mitochondrial metabolism and function in muscle fibres and stopped diabetic animals' slow fibres from becoming fast, preventing glucose elevation and adipocyte hypertrophy [12].

Numerous studies have demonstrated that type 2 diabetes patients' and animals' skeletal muscles exhibit abnormal fibre distribution. In addition, type 2 diabetic humans and animals' skeletal muscles showed a lower activity of mitochondrial oxidative enzymes. Additionally, we discovered that type 2 diabetes obese mice have lower percentages of type I and IIA fibres as well as lower activity levels of mitochondrial oxidative enzymes in type IIA fibres than age-matched nondiabetic animals. In the current work, hyperbaric oxygen improved the activity of all mitochondrial oxidative enzymes and stopped the conversion of slow to fast fibres in the skeletal muscle of type 2 diabetic rats. The increased ability of muscle fibres to oxidise substances may be a result of their adaptation to hyperbaric oxygen, which also increases the skeletal muscle's ability to oxidise substances metabolically. The oxygen in blood plasma becomes more available for diffusion into the tissues as both its pressure and concentration rise, increasing the oxidative capacity of the skeletal oxidative muscles. The oxidative metabolism of skeletal muscle may benefit from the increased oxygen availability. We come to the conclusion that hyperbaric oxygen suppresses glucose increase by preventing the changed distribution of fibre types and lower oxidative enzyme activity of fibres in the skeletal muscles of rats with type 2 diabetes [13].

Non-hyperbaric oxygen-exposed type 2 diabetic rats showed a larger proportion of hypertrophied adipocytes. Contrarily, in type 2 diabetic rats exposed to hyperbaric oxygen, the percentage fell. Through the beta-oxidation of lipids, fatty acids are transported into mitochondria where they are converted to acetyl-CoA. This acetyl-CoA is then used in the tricarboxylic acid (TCA) cycle during aerobic respiration to produce energy and electron carriers. An enzyme called SDH is found in mitochondria and is involved in the TCA cycle and electron transport system. The electron transport system's component cytochrome c, which is also found in mitochondria, plays a function in transporting electrons. SDH and cytochrome are both involved in the metabolism of lipids and glucose in muscle fibres. In the current study, type 2 diabetic rats receiving hyperbaric oxygen showed increased SDH and cytochrome activity in all skeletal muscle fibre types. In addition, compared to the rats not exposed to hyperbaric oxygen, the hyperbaric oxygen-exposed rats had a higher percentage of type I and IIA fibres, which have a higher capacity to oxidise fatty acids. These findings show that type 2 diabetic rats with obesity did not develop adipocyte hypertrophy because hyperbaric oxygen promotes the turnover of lipid and glucose metabolism in the skeletal system [14].

In type 2 diabetic mice with obesity, hyperbaric oxygen blocked the growth-related switch from slow to fast fibre types and the decline in fibre oxidative enzyme activity, avoiding glucose rise and adipocyte hypertrophy. These findings suggest that hyperbaric oxygen improves skeletal muscle's ability to metabolise glucose and lipids, delaying the onset of type 2 diabetes and obesity. After a prolonged endurance workout, improvements in the skeletal muscle's ability to process glucose and lipids were also seen. However, obese people find it challenging to sustain adequate exercise training since they frequently have comorbid physical dysfunctions including osteoarthritis and myopathy. As a result, we suggest that hyperbaric oxygen is used as an additional therapy for type 2 diabetic patients who are obese [15].

Conflict of Interest

None

Acknowledgement

None

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