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Development of a murine model of metabolic syndrome for evaluation with hyperbaric oxygen therapy

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Non-standard abbreviations:
MetS: Metabolic syndrome
HBOT: Hyperbaric Oxygen therapy

Abstract

The metabolic syndrome is a worldwide distributed clinical entity that significantly affects the functional state of the individual. The development of murine models for experimentation in this area has generally been associated with the use of drugs that generate irreversible acute damage to various organs. The objective of this study is to develop a murine model based on the sucrose administration for 20 weeks. Through this process, rats with weight gain, fat accumulation and biochemical parameters characteristic of metabolic syndrome were obtained for a subsequent evaluation with hyperbaric oxygen therapy.

Introduction

The Metabolic Syndrome (MetS) is a clinical entity with an important impact worldwide that is characterized by overweight or obesity, insulin resistance and pro-inflammatory processes, whose consequences are not limited solely to the functional state of the individual who develops it, but also in the economic, social and family [1].The presence of MS represents a notable increase in overweight and risk factors to develop type 2 diabetes mellitus, hypertriglyceridemia, increase in low density lipoprotein (LDL), decrease in high density lipoprotein (HDL), and systemic arterial hypertension. Conventional treatment alternatives for this clinical entity use different types of strategies such as drugs (statins, benzafibrates, oral hypoglycemic agents, among others), or modifications of dietary and hygienic habits, which have been repeatedly considered a therapeutic failure, since no epidemiological decrease of this clinical condition has been seen, but it is increasing [2].

Hyperbaric Oxygen Therapy (HBOT) is a therapy mainly indicated for the treatment of Decompressive Disease, Gaseous Aeroembolism and Carbon Monoxide Poisoning. There are other indications where benefits are appreciated for the patient, for example, as an adjuvant for scarring processes, refractory osteomyelitis, gas gangrene, just to mention a few. Of the conditions described above, the aid for scarring processes is undoubtedly the main reason why this treatment is used, being the lesions complicated by metabolic processes the main causes [3,4].

The development of murine models has historically shown great efficiency in basic research protocols, with advantages such as easy handling, low cost, easy reproduction and homogeneity of the study subjects, which represents a statistical advantage by reducing error factors. Commonly, the development of animal models with MetS involves the application of a drug that causes irreversible acute damage to the pancreas, liver or kidney [5].

With the aim of being able to evaluate the efficacy of treatment with HBOT in cases of MetS, in this work a murine model was fed with water with sucrose as an obesity inducer, developing fatty liver, increased blood pressure, tachycardia, alterations of the glycemia and significant weight gain [6], being clinically a better study model resembling the natural history of MetS.

Results and Discussion

Figure 1 shows the evolution of the body weight of rats that consumed sucrose during 20 weeks; rats in the Metabolic syndrome groups that ingested sucrose (MetS group) showed significant changes in the body weight with respect to the control group ($P<0.05$).From week 1 to week 14 there was a steady increase in the body weight of the MetS group with respect to the control group.These results are consistent with those reported by other authors who have used sucrose or fructose as dietary inducers of metabolic disorders in rats, such as insulin resistance, obesity and MetS [7,8]. Experimental evidence shows that the consumption of sucrose increases the caloric intake and therefore the body weight; the mechanism implicated has been related with the consumption of sugars (sucrose or fructose) in liquid form, both short [9] and long term [10] that is associated with a lower satiety due to the inability to stimulate the production of leptin and others hormones tending to increase the caloric intake during subsequent meals. [11].

After 20 weeks of sucrose intake, rats in the MetS group showed a significant increase in body weight of 38% ($P<0.01$), total fat (84%, $P <0.05$), adiposity index (33%, $P<0.05$) and triglicerydes (95%, $P<0.05$), while HDL decreased 48% ($P<0.05$). Finally, no difference was observed in the levels of serum glucose and caloric intake. All the results above were compared with respect to the control group (Table 1). In relation to the above, the MetS group developed a large amount of abdominal and epididymal fat. Regarding this phenomenon of adipose tissue storage, some authors have reported that the accumulation of intramuscular and visceral fat is a primary factor in the pathogenesis of a variety of metabolic disorders, including insulin resistance, type 2 diabetes and hyperlipidemia [12,13], but mainly, abdominal obesity that develops MetS and non-alcoholic fatty liver [14,15]. In humans, adipose tissue produces and secretes a large number of pro-inflammatory adipocytokines that causes an imbalance in the secretion of interleukins and anti-inflammatory protein, which is associated with the development of both health problems.

The physical and metabolic characteristics developed in this model, allow us an important approach to the common conditions in a case of MetS.

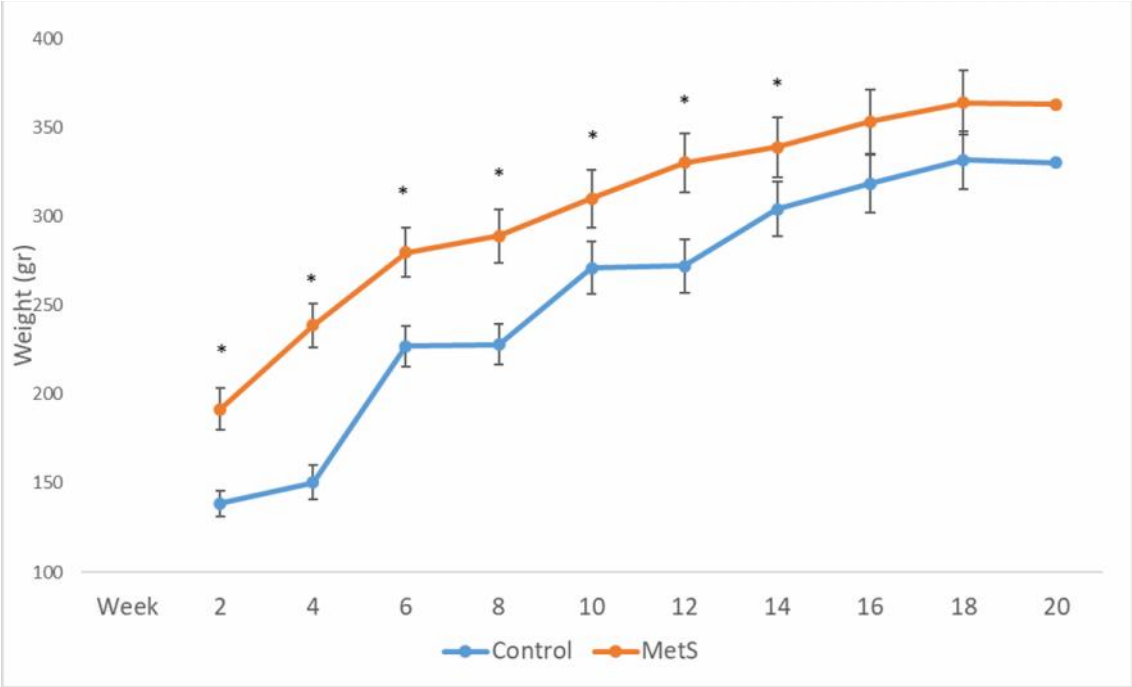

Figure 1. Body weight of rats during 20 weeks feeding. Male wistar rats were divided into the MetS group (n = 15) and the control group (n = 5). Both groups received a standard diet (2014 Teklad global). For the MetS group, a 30% sucrose solution was added to its feed and to the control group purified water *ad libitum* for 20 weeks. The weight is expressed in grams. * *P<0.05*

Table 1. Body weight, fat total and biochemical parameters after 20 weeks feeding. Serum glucose levels, HDL and triglycerides, were measured using enzymatic methods in an automated Selectra-E equipment.Values are mean ± SD (Control, n-5; MetS, n-15). * P<0.05, **P<0.01

	Control Group	MetS Group
Body weigth (g)	300±35	415±30**
Fat total (g)	20.40±1.17	37.53±1.76**
Adiposity Index	6.80±0.72	9.04±0.42*
Glucose (mg/dL)	151±11.72	158.00± 6.43
Triglycerides (mg/dL)	105.00±3	205.00±10*
HDL (mg/dL)	60.61±6.66	31.74±4.00*
Total Kcal/day/100 g bw	61.05±20.06	93.03±16.91

Fat Total= Abdominal fat + Epididymal fat
Adiposity index = (Abdominal fat weigth + Epididymal fat weigth/Body weigth) 100
Total Kcal/day/100 g bw = Kcal in drinking water + Kcal in food

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