



High lipid and low carbohydrate content diet, immediately after weaning, causes hepatic injury, systemic oxidative stress and diminishment of lipids in white adipose tissue

Lidieli Pazin Tardelli, Leonardo Breda, Lucas Flores Marques, Natália Cristina Gomes Carvalho Lima, Thais Furtado de Camargo, Bruna Rafaela Scherer, Natália Fernandes Moreira, Janaína Francieli Dias, Rodrigo Augusto Dalia, Bruna Fontana Thomazini, Maria Esmeria Corezolla do Amaral, Armindo Antonio Alves*

Graduate Program in Biomedical Sciences, Centro Universitário Herminio Ometto, UNIARARAS, Araras, SP, Brazil

HIGHLIGHTS

- After weaning high lipid/low carbohydrate diet impaired the development of the animals.
- The diet offered to the treated animals induced a systemic oxidative stress status.
- The oxidative stress induced glucose intolerance and lipid accumulation in liver.
- The epididymal adipose tissue increased its mass but decreased its lipid content.

ARTICLE INFO

Keywords:

Hyperlipidic and low carbohydrate diet
Hepatic damage
Adipose tissue
Dyslipidemia
Oxidative stress
Reduced thiols

ABSTRACT

As obesity is now a global pandemic, greater research efforts are needed in order to fully understand the physiological effects of diets with high lipid and low carbohydrate contents, giving special attention to the factors that can lead to a condition of systemic oxidative stress. This condition is related to the onset and development of important diseases including diabetes, dyslipidemia, hypertension, stroke, and heart attack. In this work, immediately after weaning, Wistar rats ($n = 8$) were submitted to a hyperlipidic diet (34.5% lipids, 23.3% carbohydrates, 24.9% proteins) during 155 days. A control group ($n = 8$) consumed a standard diet for rodents (4.5% lipids, 48.0% carbohydrates, 25.3% proteins). The hyperlipidic diet did not cause obesity during the period of the experiment, but was detrimental to the development of mass and length of the animals during the first 57 days. A condition of oxidative stress was established, as demonstrated by decreases of plasma proteins and reduced thiols, as well as alterations of hemoglobin. Additional systemic damage was exhibited, including increased glucose intolerance and dyslipidemia, as well as hepatic damage evidenced by the plasma activities of the enzymes alanine transaminase, aspartate transaminase, and alkaline phosphatase. Decrease in lipid concentration in white adipose tissue, which would allow increased triacylglycerol synthesis and storage if dietary carbohydrates were increased. It could be concluded that the hyperlipidic diet induced severe hepatic damage and might contribute to the future development of obesity and diabetes if the content of carbohydrates in the diet was increased.

1. Introduction

High blood lipid levels have been associated with the occurrence of serious cardiovascular and hepatic diseases [1–3]. Dyslipidemia mainly occurs when the caloric content of the food ingested exceeds the energy expended, leading to the development of obesity [4]. The World Health

Organization now considers obesity to be a global pandemic [5,6]. Although obesity is closely related to carbohydrate-rich diets, it is also of interest to investigate the effects of a lipid-rich diet initiated immediately after weaning. This approach could contribute to understanding the early deleterious effects on systemic metabolism induced by increased lipids circulating in the blood. The literature reports

* Corresponding author. Centro Universitário Herminio Ometto, UNIARARAS, Av. Maximiliano Baruto 500, J. Universitario, Araras, SP, Brazil.
E-mail address: alvesaa@uol.com.br (A.A. Alves).

<https://doi.org/10.1016/j.jnim.2018.08.003>

Received 14 March 2018; Received in revised form 14 August 2018; Accepted 15 August 2018

Available online 22 August 2018

2352-3859/ © 2018 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

alterations in the intestinal absorption of Ca^{2+} and other minerals in animals submitted to lipid-rich diets [7,8].

Furthermore, higher levels of lipoproteins in the blood increase the likelihood of their oxidation and/or glycosylation, consequently enhancing the capture of these molecules by the intima of blood vessels. This causes atheroma, with diminished internal circumference of the blood vessels leading to increased blood pressure and a greater cardiac workload. It can also lead to thrombosis. All these conditions can result in myocardial infarction and stroke [2,9–11]. Furthermore, high levels of blood lipids can increase their accumulation in tissues such as the liver, where they can cause degenerative hepatic diseases [12].

Diets high in lipids are often low in carbohydrates. The associated drastic decrease in carbohydrate absorption induces ketoacidosis in the blood, due to the high input of lipids into hepatic cells, leading to increased acetyl-CoA in the mitochondrial matrix and inducing the production of ketone bodies, which are exported to the blood [13,14]. Under these conditions, in order to maintain blood glucose levels, activation of the gluconeogenesis pathway produces glucose using amino acids from the diet and from the degradation of endogenous proteins, glycerol, and lactate [15]. In addition, increased lipids in the blood can lead to peripheral insulin resistance, which worsens condition [16,17]. The expansion of adipose tissue is correlated with increases in the blood of adipokines (many of which are proinflammatory) and lactate, derived from anaerobic metabolism. Under adiposity conditions, the adipocytes use anaerobic glycolysis to obtain energy for metabolic processes [4,18–22].

The condition described above is likely to lead to the emergence of a systemic inflammatory process that can alter animal development. This alteration is reflected in the body composition, in both the development phase and in adulthood, increasing the risk of diseases [8,23–25]. Therefore, the aim of this work was to analyze metabolic alterations induced in rats by a diet containing 34.5% lipids and 23.3% carbohydrates. Monitoring was performed of food consumption and alterations in the growth of the animals. Blood analyses investigated changes observed in the intraperitoneal glucose tolerance test, the concentration of lactate, and markers of liver function and oxidative stress.

2. Materials and methods

2.1. Animals

Sixteen male Wistar male rats were provided by the UNIARARAS institutional vivarium, after weaning (aged 21 days). During the experimental period (155 days), the animals were housed in collective cages (4 animals in each), in a controlled environment with a 12-h light/dark cycle. The procedures adopted in this work complied with the norms of the Brazilian College for Animal Experimentation (COBEA) and received prior approval of the UNIARARAS Ethics Committee for Animal Experimentation (CEA/UNIARARAS, protocol 063/2014).

2.2. Groups and diets

The animals were divided into two groups ($n = 8$). The control group (C) was fed with standard rodent feed (Nuvilab, Colombo, Paraná, Brazil), while the treatment group (T) was fed with a hyperlipidic feed (Prag Solutions, Jaú, São Paulo, Brazil). The feeds and potable water were offered *ad libitum*. The percentages of the main components of the feeds were provided by the suppliers. The group C feed contained 48.0% carbohydrates, 4.5% lipids, 25.3.0% proteins and 10.3% moisture. The group T feed contained 23.3% carbohydrates, 34.5% lipids, 24.9% proteins and 5% moisture. Details of the two diets are described in Table 1. Concentration of protein and moisture were confirmed according to AACCI (American Association of Cereal Chemists) (2010): moisture (method 44–15.02) and protein (method 46–13.01, 6,25 as conversion factor).

Table 1

Composition of the diets according suppliers information. *The concentration of protein and moisture were confirmed according to AACCI (2010): moisture (method 44–15.02) and protein (method 46–13.01, 6,25 as conversion factor).

Ingredients	C		T	
	g/Kg	%	g/Kg	%
Protein:				
Soybean bran*	271.5	27.2	249.5	25.0
Digestible carbohydrates:				
Maize starch	344.7	34.5	80.5	8.0
Sucrose	72.0	7.2	76.0	7.6
Maltodextrin	63.0	6.3	66.5	6.7
Digestible Fats:				
Lard	0.0	0	296.9	29.7
soybean fatty acids	45.0	4.5	47.5	4.8
Fibers:				
microcrystalline cellulose	57.3	5.7	80.0	8
Other components:				
L-cystine	1.6	0.2	1.7	0.2
Choline chloride	1.4	0.1	1.4	0.1
Butylhydroxytoluene	$1.3e^{-2}$	$1.3e^{-3}$	$2.7e^{-2}$	$2.7e^{-3}$
Mineral mix	31.5	3.2	40.5	4
Vitamin mix	9.0	0.9	9.5	1
Moisture*	103.0	10.3	50.0	5
Total	1000.0	100.0	1000.0	100.0

C- carbohydrates = 48,0%; protein = 25.3%; lipids = 4,5%, moisture = 10.3%.

T - carbohydrates = 23.3%; protein = 24.9%; lipids = 34,5%, moisture = 5%.

2.3. Feed consumption and measurements of mass and length of the animals

The daily feed consumption was noted using simple averages. On a weekly basis, always at the same time of day, the animals were weighed and measurements were made of their naso-anal lengths. The data reported by suppliers were used to calculate the daily caloric intake (Fig. 1B): diet C - 3938 KCal/kg and T - 5494 KCal/kg.

2.4. Intraperitoneal glucose tolerance test (IGTT) and blood lactate concentration

The IGTT test was performed on four occasions during the experiment (on days 35, 80, 135, and 145), always starting at 08:00 a.m. The animals were previously submitted to 12-h fasting and received a glucose overload (2 mg/g), delivered intraperitoneally. Blood samples were collected by tail puncture, before and 30, 60, 90, and 120 min after delivery of the glucose overload [26,27]. Blood glucose was determined using an Optium glucometer (Abbott, Oxford, UK). Simultaneously, blood samples for lactate analysis were collected using heparinized capillary tubes. The blood was deproteinized by addition of 4% trichloroacetic acid solution and the lactate concentration was assayed as described in the literature [28,29]. Both results were presented as area under the curve (AUC) values, as described by Le Floch et al. [26].

2.5. Euthanasia of animals and collection of samples

After the experimental period (155 days), the animals (previously fasted for 24 h) were anesthetized with a 3:1 ketamine (Syntec)/xylazine (Bayer) solution. Blood was collected by cardiac puncture, using EDTA as an anticoagulant. Shortly thereafter, the plasma was separated and the erythrocyte fraction was washed twice with pH 7.4 PBS buffer (5 mmol/L phosphate plus 0.9% NaCl). The plasma and erythrocyte preparations were maintained under refrigeration until the assays. At the same time, collection was made of samples of liver and epididymal white adipose tissues. The sample was immediately frozen at -80°C until homogenate preparation.

Download English Version:

<https://daneshyari.com/en/article/9955194>

Download Persian Version:

<https://daneshyari.com/article/9955194>

[Daneshyari.com](https://daneshyari.com)