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Basic nutritional investigation

Immunologic and metabolic effects of high-refined carbohydrate-containing diet in food allergic mice

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ABSTRACT

Objective: Allergic mice show a reduction in body weight and adiposity with a higher inflammatory response in the adipose tissue similar to obese fat tissue. This study aimed to evaluate whether the low-grade inflammatory milieu of mice with diet-induced mild obesity interferes with the allergic response induced by ovalbumin (OVA).
Methods: BALB/c mice were divided into four groups: 1) non-allergic (OVA−) mice fed chow diet, 2) allergic (OVA+) mice fed chow diet, 3) OVA− mice fed high-refined carbohydrate-containing (HC) diet, and 4) OVA+ mice fed HC diet. After 5 wk, allergic groups were sensitized with OVA and received a booster 14 d later. All groups received an oral OVA challenge 7 d after the booster.
Results: Allergic groups showed increased serum levels of total IgE, anti-OVA IgE, and IgG1; a high disease activity index score; aversion to OVA; and increased intestinal eosinophil infiltration. Non-allergic mild-obese mice also showed aversion to OVA and an increased number of eosinophils in the proximal jejunum. After the allergic challenge, OVA+ mice fed chow diet showed weight loss and lower adiposity in several adipose tissue depots. OVA+ mice fed HC diet showed a loss of fat mass only in the mesenteric adipose tissue. Furthermore, increased levels of TNF, IL-6, and IL-10 were observed in this tissue.
Conclusions: Our data show that mild-obese allergic mice do not present severe pathologic features of food allergy similar to those exhibited by lean allergic mice. Mild obesity promoted by HC diet ingestion causes important intestinal disorders that appear to modulate the inflammatory response during the antigen challenge.

Introduction

Food allergy can affect the intestinal mucosa and cause local inflammation [1]. The main food allergy treatment is to avoid the food with the allergen that has a negative impact on the quality of life [2]. Despite great advances in our understanding of mucosal immunology, the causes underlying the increased rates of allergy remain unknown. Complex factors, such as environmental factors and modern lifestyle, mainly associated with the incidence of obesity, can initiate an allergic process [2,3].

Obesity is a risk factor for the development of allergic reactions [3]. Such an association may be related to the chronic low-grade inflammatory feature of obesity [4,5]. It has been demonstrated that the frequency of specific positive IgE levels in obese individuals is threefold higher than that found in non-obese [6]. According to Hancox et al. [7], 28% of patients with allergic asthma exhibit a positive correlation with overweight and obesity. Obesity may contribute to the increased

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prevalence of allergic diseases, particularly food allergy, because of systemic inflammation [8].

A study on patients with asthma found that weight loss lessened the symptoms of asthma, independent of the IgE levels, by modulating the action of T cells and thus the profile of proinflammatory cytokines [9]. Leptin, an adipocytokine that increases during obesity, increased twofold in overweight children with asthma compared with overweight children without asthma [10]. Other important cytokines in the inflammation process, such as TNF, IL-6, and eotaxin, are also modified in allergic individuals with obesity [9,11]. Despite strong evidence supporting obesity as a risk factor for allergy, this relationship remains to be clarified because of controversial results [12,13]. Researchers found no strong correlation between atopy or asthma and obesity in children [14]. Sidoroff et al. [15] concluded that a previous or current overweight state does not increase the risk of asthma or allergy in school-aged children but obesity may decrease allergic risk after bronchiolitis in infancy.

Our group has reported that allergic mice, despite having a reduction in body weight and adiposity, show a higher inflammatory response in the adipose tissue and a metabolic dysfunction [16,17]. This phenotype is quite similar to the adipose tissue inflammation observed in obese mice [4,18,19]. In fact, our group has previously found that a high-refined carbohydrate-containing (HC) diet increases adiposity without significant differences in overall body weight, causing mild obesity. In this model, the fat mass expansion is accompanied by an early induction of adipose tissue inflammation and metabolic dysfunction. On the basis of these results, the aim of the present study was to evaluate whether the low inflammatory milieu of mild-obese mice interferes with the allergy response induced by ovalbumin (OVA). In the present study, mild obesity promoted by the HC diet does not exacerbate the immunologic and metabolic response in allergic mice.

Materials and methods

Male BALB/c mice at 4 to 5 wk of age were obtained from our animal care center (Centro de Bioterismo [CEBIO]/Universidade Federal de Minas Gerais [UFMG]) and maintained in an environmental-controlled room under a 14-h light/10-h dark cycle. The animals had free access to food and tap water, and were maintained in accordance with the guidelines of the Ethics Committee on Animal Use of our institution (Comissão de Ética no Uso de Animais [CEUA]/UFMG Protocols 060/2010 and 299/2007). The mice were fed standard chow (Labina) or HC diet for 8 wk as described previously [4]. The HC diet contained at least 30% refined sugars, mostly sucrose. The animals were divided into four groups: 1) non-allergic (OVA−) mice fed chow diet, 2) allergic (OVA+) mice fed chow diet, 3) OVA− mice fed HC diet, and 4) OVA+ mice fed HC diet.

The weight of the mice was measured once a week and the food consumption was assessed twice a week. During the week of the oral challenge (eighth to ninth week), the weight was measured on the first day and 7 d after the antigen challenge (see experimental design in Fig. 1). At the end of the treatment, the animals were anesthetized with ketamine (130 mg/kg) and xylazine (0.3 mg/kg), and euthanized.

Mice sensitization

After 5 wk of continuous intake of different diets, the animals were subjected to the allergy protocol (Fig. 1). For sensitization, the OVA− mice fed with chow or HC diet received a subcutaneous injection of 0.2 mL of saline (0.9%) and adjuvant [1 mg of $Al(OH)_3$]. OVA+ groups received 0.2 mL of saline (0.9%), adjuvant [1 mg of $Al(OH)_3$], and 10 μg of OVA (five-times-crystallized Hen's egg albumin; Sigma, St. Louis, MO, USA). Fourteen days after the sensitization, the OVA− groups received a subcutaneous injection with only 0.2 mL of saline (0.9%), and allergic mice received a booster of 0.2 mL of saline (0.9%) and 10 μg of soluble OVA. One week after the administration of the booster, the oral challenge was conducted. For all groups, drink water was replaced with a 20% OVA solution for 1 wk and quantified each day to verify aversion. This solution was prepared using a lyophilized egg white (Salto's, Belo Horizonte, Brazil) [2,20].

Disease activity index score

For the assessment of the disease activity index (DAI) score [16], body weight and stool were scored every day after antigen challenge as follows: body weight score (0 = no weight loss; 1 = 1–5% weight loss; 2 = 6–10% weight loss; 3 = 11–15% weight loss; 4 = >15% weight loss); stool viscosity (0 = normal; 2 = fluffy; 3 = pasty and liquid consistency; 4 = diarrhea); and stool occult blood (0 = normal; 1 = positive fecal blood; 2 = hemorrhage) by Hexagon OBScreen kit (Human GmbH, Wiesbaden, Germany).

Evaluation of serum total IgE, anti-OVA IgE, and IgG1

Total IgE, anti-OVA IgE, and IgG1 levels were measured by capture-ELISA using plates coated with rat antimouse IgE or IgG1, 50 μL of serum, and

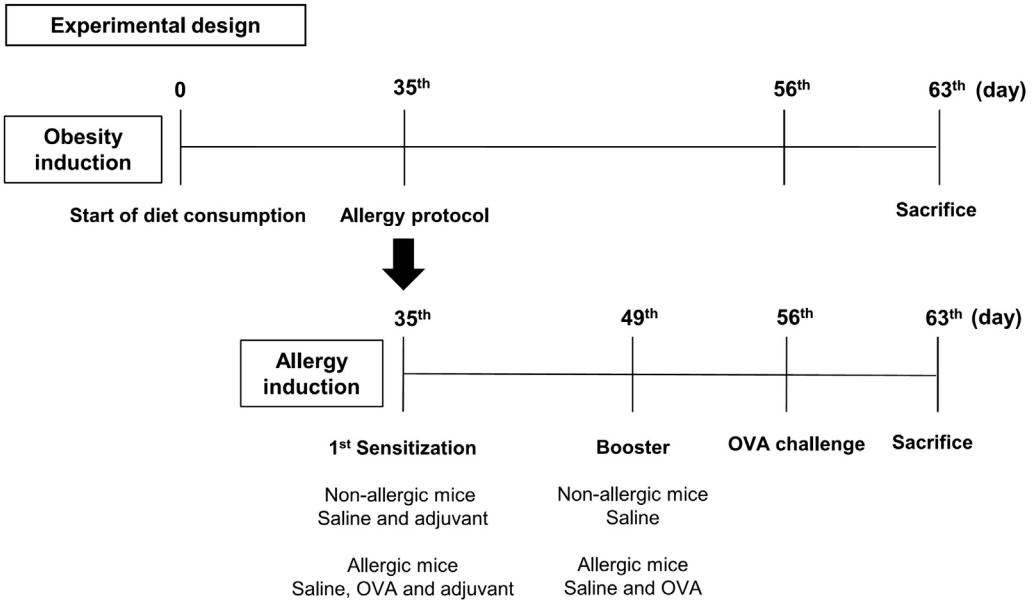

Fig. 1. Experimental design of obesity and food allergy induced by antigen in mice. According to the obesity protocol, the mice were fed chow or HC diet for 63 d. After 35 d, allergy induction was initiated through two immunizations. The challenge was performed through OVA ingestion. HC, high-refined carbohydrate-containing; OVA, ovalbumin.