

Assessing Renal and Systemic Manifestations in Rats with Food-Induced Allergic Reactions

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Abstract

This study aimed to investigate the renal damage and associated skin and intestinal manifestations in rats with food allergies. An animal model of food allergy was induced via oral administration of ovalbumin. Rats were randomly divided into three groups: control, lactose, and ovalbumin groups, with a 50-day experimental cycle. Serum levels of IgG4 and IgE were measured for all groups. Anti-Glomerular Basement Membrane (anti-GBM) antibodies were detected using immunofluorescence. Skin and intestinal manifestations, as well as renal tissue changes, were observed in histological sections. Statistically significant differences in skin and intestinal manifestations were observed between the ovalbumin group and both the control and lactose groups ($P < 0.01$, $P < 0.05$, respectively), with the lactose group also showing significant differences compared to the control ($P < 0.05$). The ovalbumin group exhibited a significantly higher serum IgE level compared to the control group ($P < 0.001$), and a significant difference in serum IgG4 level was noted between the ovalbumin and lactose groups ($P < 0.05$). No significant difference was found between the ovalbumin and control groups for IgG4 ($P > 0.05$). The ovalbumin group had a significantly higher positive rate of anti-GBM antibody expression in glomerular basement membrane sections than the control and lactose groups ($P < 0.01$). Food-allergic rats exhibited pronounced kidney damage and skin and intestinal manifestations, with acute cases being particularly severe. Timely detection, clear diagnosis, and avoidance of allergenic foods are crucial to prevent further adverse effects on the organism.

Keywords

Food Allergy, Renal Injury, Serum IgG4, Serum IgE

1. Introduction

Food Allergy (FA) is a complex immunological response to food antigens, acting

as allergens, which can trigger adverse reactions across various body systems, including the digestive tract, skin, vasculature, and kidneys, with a particular impact on the skin and gastrointestinal system. Food antigens are among the first allergens that infants encounter postnatally, leading to a spectrum of allergic conditions from chronic lactose intolerance due to lactase deficiency to acute allergic reactions to proteins found in eggs, peanuts, and milk [1]-[3]. These reactions are often characterized by IgE-mediated or non-IgE-mediated immune responses to food or food additives. FA is frequently regarded as the inaugural event in the allergic march. Comparative immunology has revealed that rodents share significant immune regulatory parallels with humans, including the differentiation of Th1 and Th2 cells and the mediation of IgE in allergic responses [4]-[6].

The levels of serum IgG4 and IgE in children with food allergies increase with age. IgG4 was found to be more indicative in children with chronic allergic dermatoses, while IgE was more relevant in those with an acute onset of the disease. IgG plays a crucial role in the formation of immune complexes associated with nephritis. Ovalbumin (OVA), a phosphorus-containing glycoprotein known for its ready crystallization, is a common choice for preparing allergy models. This study aimed to investigate the renal damage and associated skin and intestinal manifestations in rats with food allergies.

2. Material and Methods

2.1. Laboratory Animals

Thirty male Sprague-Dawley (SD) rats, weighing 230 ± 20 grams and aged 2 to 3 months (equivalent to human juveniles to young adults), were procured from the Laboratory Animal Center of Sun Yat-sen University. The animals were housed under strict dietary standards, with feed provided and drinking water consisting of pure water from the Laboratory Animal Center. Prior to the intervention, all animals underwent a 7-day acclimatization period and were fed accordingly. Hairy areas, such as the neck, were shaved in preparation for the study. The standard feed consisted of Ovalbumin Punch, sourced from Xiangtan Jiayeyuan Biotechnology Co., Ltd., which is food-grade, egg-yellow powder with 98% active substance content, adhering to Good Manufacturing Practice (GMP) standards (*E. coli* and *Salmonella* negative), and within the validity period. Lactose was purchased from Hebei Baiyi Biotechnology Co., Ltd., also food-grade with 99% active substance content, GMP compliant (*E. coli* and *Salmonella* negative), and within the validity period.

2.2. Animal Grouping and Modeling

Rats were randomly assigned to three groups: experimental, lactose, and control, with 10 rats per group. The experimental group received 1 mg/mL ovalbumin via gavage (1 mL/day), the lactose group received 2 mg/mL lactose via gavage (1 mL/day), and the control group received saline via gavage (1 mL/day). Throughout the modeling period, rats had *ad libitum* access to food and water, and gavages were ad-

ministered daily at 8:30 a.m. to monitor trait variations. In the experimental group, ovalbumin was administered orally without adjuvant to induce the food allergy model. After 50 days of continuous gavage, a single dose of 100 mg ovalbumin was given on the 51st day to stimulate the model, and a single dose of 100 mg lactose was given to the lactose group. One hour post-gavage, 1 mL of blood was collected from the ocular venous plexus, and serum was separated and stored at -20°C for subsequent analysis.

2.3. Assessment of Skin and Intestinal Reactions

Allergic symptoms were observed and scored continuously for 60 minutes in both groups. Skin reaction scoring criteria were as follows: grade 0, no symptoms; grade 1, nose and head-scratching; grade 2, periocular and perioral edema; grade 3, trunk and limb edema; grade 4, skin petechiae and hair standing. Intestinal reaction scoring criteria were: grade 0, no symptoms; grade 1, reduced appetite; grade 2, diarrhea. Each grade corresponds to a specific score.

2.4. Measurement of Serum IgG4 and IgE Levels

Serum IgG4 and IgE antibody levels were determined using the ocular venous plexus blood collection method and Enzyme-Linked Immunoassay (ELISA), following the manufacturer's instructions precisely.

2.5. Analysis of Renal Lesions and Indicators in Rats

Glomerular basement membrane changes were observed microscopically. Thickening of the glomerular basement membrane and glomerular ischemia were considered positive lesions; normal conditions were negative. Kidney tissue served as antigen, and Anti-Glomerular Basement Membrane (AGBM) antibody was measured by indirect immunofluorescence, with normal conditions being negative.

3. Statistical Analysis

Data were statistically analyzed using SPSS 22.0 software. Independent samples t-tests were used for group comparisons, and data are presented as Mean \pm Standard Deviation (SD).

4. Results

4.1. Intestinal Manifestations in Rats

After 61 days of stimulation, among the 10 rats in the ovalbumin group, 3 exhibited poor appetite and 1 displayed diarrhea. In the lactose group, 2 out of 10 rats showed poor appetite, while all 10 rats in the control group presented mild symptoms. The difference in intestinal manifestations between the ovalbumin group and the control group was statistically significant ($P < 0.01$). Additionally, there was a significant difference in serum IgE levels between the ovalbumin and lactose groups ($P < 0.01$). A significant difference was also observed when comparing the lactose group with the control group ($P < 0.05$). For detailed data, refer to **Table 1**.

Table 1. Effects on skin and intestinal reactions in rats ($x \pm s$).

Group	Quantity	Dose (mg/mL)	Skin reaction	Intestinal reaction
Control group	10	/	0.26 \pm 0.10	0.71 \pm 0.18
Lactose group	10	2 mg/mL	1.19 \pm 0.11*	1.28 \pm 0.24*
Ovalbumin group	10	1 mg/mL	4.29 \pm 0.14** $\Delta\Delta$	1.86 \pm 0.25** Δ

Note: Compared with control group, *P < 0.05, **P < 0.01; compared with lactose group, Δ P < 0.05, $\Delta\Delta$ P < 0.01.

4.2. Skin Reactions in Rats

In the ovalbumin group, 3 out of 10 rats scored 3 on the scale for paleness around the mouth and tail; 5 scored 2 for swelling around the eyes or mouth, and 2 scored 1 for nose scratching and head scratching. In the lactose group, 1 rat scored 2 for swelling around the eyes or mouth, and 2 scored 1 for nose and head-scratching. The control group of 10 rats had mild symptoms. The differences in skin reactions between the ovalbumin group and the control group were statistically significant (P < 0.01). There was also a significant difference in serum IgE levels between the ovalbumin and lactose groups (P < 0.01), and between the lactose group and the control group (P < 0.05). See **Table 1** for specific values.

4.3. Serum IgE and IgG4 Levels in Rats

The serum IgE level difference between the ovalbumin group and the control group was highly significant (P < 0.001), and the same comparison with the lactose group also yielded a significant difference (P < 0.01). Serum IgG4 levels showed a significant difference between the ovalbumin and lactose groups (P < 0.05), but no significant difference was observed when compared with the control group (P > 0.05), as detailed in **Table 2**. The lactose group did not show a significant difference in serum IgE compared with the control group (P > 0.05), yet a significant difference in serum IgG4 was noted (P < 0.05), as shown in **Table 2**.

Table 2. Effect on serum IgE and IgG4 levels in rats ($x \pm s$).

Groups	Quantity	Dose (mg/mL)	IgE (μ g/mL)	IgG4 (mg/mL)
Control group	10	/	10.86 \pm 0.21	0.58 \pm 0.12
Lactose group	10	2 mg/mL	1.46 \pm 0.20	1.56 \pm 0.15*
Ovalbumin group	10	1 mg/mL	5.56 \pm 0.11** $\Delta\Delta$	0.92 \pm 0.18 Δ

Note: Compared with control group, *P < 0.05, **P < 0.01; compared with lactose group, Δ P < 0.05, $\Delta\Delta$ P < 0.01.

4.4. Analysis of Glomerular Filtration Membranes in Rat Kidneys

The positive rate of anti-glomerular basement membrane antibody expression in the glomerular basement membrane sections of rats in the ovalbumin group was significantly higher than that in both the control and lactose groups (P < 0.01) (see

Table 3). This finding may be associated with the formation of large molecule immune complexes *in vivo*, potentially leading to the deposition in the kidneys, thickening of the glomerular basement membrane, and the development of various forms of nephritis, ultimately causing further renal damage.

Table 3. Effect on glomerular basement membrane in rats ($x \pm s$).

Group	Number	Expression of anti-glomerular basement membrane antibodies			Observation of glomerular basement membrane sections		
		Positive	Positive rate (%)	P	Positive	Positive rate (%)	P
Control group	10	0	0	<0.01	0	0	<0.01
Lactose group	10	2	20	<0.01	0	0	<0.01
Ovalbumin group	10	5	50		5	50	

5. Discussion

The pathogenesis of food allergy is intricate, encompassing both acute allergic reactions and chronic allergies, often referred to as food intolerance. Acute allergies are typically associated with elevated serum IgE levels, while chronic allergies are linked to increased levels of IgG, IgM, and IgA, with IgE also being elevated in response to raw food [7] [8]. Lactose intolerance serves as a quintessential example of food intolerance, rendering the development of animal models for such conditions highly significant [9] [10]. However, the screening and modeling of animal species for chronic allergies present considerable challenges, not least because they require monitoring serum IgG levels and are sensitive to very few animals. Breakthroughs in this area, such as the one achieved in this study, hold guiding significance for understanding the pathogenesis of chronic allergies (food intolerance) and for developing treatments. Consequently, the lactose group was distinctly separated in this study to discern potential conclusions from the variances in manifestations compared to the acute allergy group. The results revealed significant differences in skin and intestinal manifestations between the lactose group and the control group ($P < 0.05$), as well as between the ovalbumin group and the control group ($P < 0.01$). Additionally, a statistically significant difference in serum IgE levels was observed between the ovalbumin group and the lactose group ($P < 0.01$), indicating that acute allergic reactions in skin and intestinal manifestations are more rapid and pronounced.

The significantly higher positive rate of anti-glomerular basement membrane antibody expression in the glomerular basement membrane sections of rats in the acute allergic ovalbumin group compared to the control and lactose groups ($P < 0.01$) may be attributed to the formation of immune complexes by ovalbumin *in vivo*, leading to their deposition in the kidneys. This results in thickening of the glomerular basement membrane and increased permeability. The short experimental cycle of 50 days may not have been sufficient to capture the more subtle

chronic inflammatory responses. Therefore, it is imperative to enhance kidney-related examinations, such as urinalysis, which could provide additional insights. The higher skin and intestinal manifestations observed in the lactose group compared to the control group may be due to the fermentation process of lactose, which can increase intestinal peristalsis and osmotic pressure, leading to lactose intolerance manifestations. In terms of renal manifestations, the lactose group's higher values compared to the control group might be due to the formation of certain macromolecular immune complexes in the body that cannot pass through the glomerular filtration membrane, thereby blocking it and resulting in elevated glomerular filtration pressure. Such renal effects could further lead to hypertension, edema, and other clinical manifestations. Therefore, in clinical practice, it is essential to conduct a comprehensive analysis of test indices and all clinical manifestations.

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Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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