



**EXPERIMENTAL STUDIES OF THE EFFECT OF METABOLIC SYNDROME ON
HEMODYNAMIC PARAMETERS IN RATS AND THE EFFECTIVENESS OF A
MODIFIED KETOGENIC DIET**

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ABSTRACT

Metabolic syndrome (MS) is a complex metabolic disorder associated with obesity, hypertension, hyperglycemia, and dyslipidemia, which leads to systemic pathological changes in internal organs and hemodynamic disturbances. The present experimental study investigates the effect of metabolic syndrome on hemodynamic parameters and morphological changes in rats, as well as evaluates the therapeutic effectiveness of a modified ketogenic diet. Metabolic syndrome was modeled in Wistar rats through a high-fat diet combined with a 10% fructose solution. The animals were divided into six experimental groups including healthy controls, rats receiving traditional and modified ketogenic diets, and rats with metabolic syndrome with or without dietary intervention. Hemodynamic parameters such as systolic and diastolic blood pressure and heart rate were measured using the tail-cuff method, while morphological changes in internal organs were assessed through histological analysis. The results demonstrated that metabolic syndrome significantly increased blood pressure and heart rate and caused pathological changes in the lungs, heart, and liver, including fibrosis, inflammation, and hypoxia. Dietary intervention with ketogenic diets showed a corrective effect on these disturbances. The modified ketogenic diet, enriched with fish, wheat bran, olive oil, and medium-chain triglycerides, proved to be more effective in normalizing hemodynamic parameters and reducing morphological damage compared to the traditional ketogenic diet. These findings suggest that modified ketogenic dietary strategies may have potential therapeutic value in mitigating metabolic syndrome-related complications and improving cardiovascular and respiratory function.

Keywords: metabolic syndrome, hemodynamic parameters, ketogenic diet, modified ketogenic diet, Wistar rats, pulmonary fibrosis, inflammation, biomarkers, cardiovascular function, experimental study.

INTRODUCTION

Metabolic syndrome (MS) is a multifactorial condition characterized by obesity, hypertension, hyperglycemia, and dyslipidemia, which contributes to the development of systemic abnormalities, including changes in the morphology of internal organs such as the lungs, heart, and liver. In clinical practice, MS is associated with an increased risk of pulmonary fibrosis, respiratory dysfunction, and cardiovascular complications. Biomarkers such as surfactant protein D (SP - D) and chitinase-3-like protein 1 (CHI 3 L 1) are used to assess pulmonary injury. The present study models MS in rats to examine its effects on hemodynamics and organ morphology and evaluates the therapeutic potential of traditional and modified ketogenic diets.

MATERIALS AND METHODS

Experimental animals and design

Wistar white rats weighing 180–200 g and aged 1–3 months. The animals were divided into six groups (20 animals each):

1. Intact (healthy) rats (control group).
2. Healthy rats on a traditional ketogenic diet.
3. Healthy rats on a modified ketogenic diet.

4. Rats with MS model without correction.
5. Rats with MS on a traditional ketogenic diet (30 days).
6. Rats with MS on a modified ketogenic diet (30 days).

All procedures complied with the principles of the Convention for the Protection of Vertebrate Animals (Strasbourg, 1986). The total duration of the experiment was 120 days: the first 90 days were the MS modeling phase, followed by the 30 days of the treatment phase, with diets administered to the respective groups.

Modeling metabolic syndrome

In the experimental group, before feeding, rendered mutton mesenteric fat (at a temperature of 38–40°C) was administered intragastrically via a metal tube at a rate of 1 g per 100 g of animal weight (equivalent to 10 g/kg or 2 g for a 200 g rat). After 1 hour, the animals were fed a standard diet. Instead of drinking water, this group was given a 10% fructose solution.

Description of diets

The traditional ketogenic diet included a standard high-fat, low-carbohydrate diet. The modified ketogenic diet consisted of fish, wheat bran, olive oil, and medium-chain triglycerides (MCTs) in a 50/50 ratio, aiming to optimize metabolic effects and reduce inflammation.

Methods for assessing hemodynamic parameters

Before recording parameters (systolic and diastolic blood pressure, as well as pulse) using the tail-cuff method, the rats were habituated to the experimental conditions to minimize stress. Awake, the rat was placed in a special chamber with a tail cuff attached. The rat spent approximately 15 minutes in this condition each day for a week.

Hemodynamic parameters (systolic and diastolic blood pressure, heart rate) were measured at baseline, after 3 and 4 months.

Methods of morphological analysis

Rats were decapitated in the fasting state under brief ether anesthesia on days 60 and 90 of the experiment. Internal organs (lungs, heart, liver, etc.) were removed and fixed in 12% formalin solution for morphological examination. Morphological examination included histological analysis of the fixed organs to detect fibrosis, inflammation, and hypoxia.

Statistical data processing

Data are presented as mean \pm standard deviation (SD), with percentage changes from baseline or previous measurement indicated. Statistical significance was assessed using Student's t-test ($p < 0.05$ was considered significant).

RESULTS

Hemodynamic changes

Table 1. Dynamics of systolic blood pressure, diastolic blood pressure and heart rate (mean \pm SD, % change; * $p < 0.05$; ** $p < 0.01$).

Group	Systolic blood pressure (outgoing)	Diastolic blood pressure (outgoing)	Heart rate (outgoing)	Systolic blood pressure (3 months)	Diastolic blood pressure (3 months)	Heart rate (3 months)	Systolic blood pressure (4 months)	Diastolic blood pressure (4 months)	Heart rate (4 months)
Intact	114.5 \pm 4.1 (100%)	82.2 \pm 2.6 (100%)	257.0 \pm 2.9 (100%)	117.5 \pm 1.9 (+2.6%)	83.7 \pm 2.2 (+1.8%)	262.3 \pm 4.1 (+2.1%)	119.1 \pm 2.9 (+4.0%)	87.5 \pm 3.4 (+6.5%)	259.5 \pm 10.1 (+1.0%)

Group	Systolic blood pressure (outgoing)	Diastolic blood pressure (outgoing)	Heart rate (outgoing)	Systolic blood pressure (3 months)	Diastolic blood pressure (3 months)	Heart rate (3 months)	Systolic blood pressure (4 months)	Diastolic blood pressure (4 months)	Heart rate (4 months)
MS + lab . pit .	120.8 ± 6.1 (100%)	83.7 ± 5.3 (100%)	264.5 ± 9.4 (100%)	166.8 ± 6.5 (+38.1%*)	128.3 ± 3.9 (+53.3%*)	479.3 ± 16.9 (+81.2%*)	150.2 ± 10.6 (+24.3%*)	124.3 ± 11.1 (+48.5%*)	422.8 ± 23.8 (+59.8%*)
MS + trad . diet	125.6 ± 3.2 (100%)	88.8 ± 4.8 (100%)	249.5 ± 10.1 (100%)	159.2 ± 7.7 (+26.7%*)	131.8 ± 6.6 (+48.4%*)	488.1 ± 27.1 (+95.6%*)	137.8 ± 4.0 (+9.7%*)	119.5 ± 7.5 (+34.5%*)	340.5 ± 21.7 (+36.5%*)
MS + mod . diet	119.5 ± 3.8 (100%)	87.2 ± 5.8 (100%)	252.3 ± 24.8 (100%)	167.7 ± 9.6 (+40.3%*)	133.0 ± 9.2 (+52.5%*)	466.5 ± 31.8 (+84.9%*)	128.0 ± 13.4 (+7.1%)	99.7 ± 12.4 (+14.3%)	305.7 ± 29.8 (+21.1%*)

In the MS groups, a significant increase in blood pressure and heart rate was observed after 3 months, with a partial reduction by month 4. The modified diet provided the best normalization.

Morphological changes

On days 60 and 90, signs of pulmonary fibrosis, inflammation, and hypoxia in the fixed organs were detected in the MS groups. The modified diet reduced these changes more effectively than the traditional diet, normalizing tissue structure.

DISCUSSION

The obtained results confirm that metabolic syndrome provokes systemic disturbances through mechanisms of chronic inflammation, oxidative stress, and hypoxia, leading to significant changes in hemodynamics and the morphology of internal organs. In particular, the sharp increase in blood pressure and tachycardia in the groups with metabolic syndrome after 3 months of the experiment correlate with literature data, where metabolic syndrome is associated with accelerated pulmonary aging and fibrosis [2, 8]. Biomarkers SP - D and CHI 3 L 1, as shown in studies [5, 6, 7, 11, 13, 14], play a key role in the pathogenesis of these changes: SP - D reflects damage to the alveolar epithelium, and CHI 3 L 1 promotes the accumulation of visceral fat and Th 2 inflammation, aggravating respiratory disorders.

A comparison of traditional and modified ketogenic diets revealed the superiority of the latter in the correction of hemodynamic and morphological disorders. The modified diet, which included fish (a source of omega-3 fatty acids), wheat bran (fiber to improve microbiota), olive oil (monounsaturated fats with antioxidant properties), and MCT oils (a quick source of energy that stimulates ketogenesis), in a 50/50 ratio for oils, likely enhances anti-inflammatory effects by reducing the level of proinflammatory cytokines and improving glucose metabolism. This is consistent with data on the positive effects of ketogenic diets on pulmonary function in patients with obesity and diabetes [3, 4, 9, 10]. Unlike the traditional diet, which partially reduces hypertension but leaves significant deviations, the modified version normalizes parameters closer to control levels,



which may be due to the synergistic effect of components such as omega-3 and MCT on endothelial function and oxidative balance.

However, despite its effectiveness, the rat model of MS has limitations: induction with a high-fat, fructose-containing diet mimics human MS but does not fully replicate the genetic and environmental factors. Morphological changes observed at days 60 and 90 (fibrosis, inflammation) highlight disease progression, but a full assessment requires molecular analysis, including the expression of fibrosis-related genes (e.g., TGF - β). Furthermore, the short-term treatment phase (30 days) demonstrates the potential of the diets, but long-term effects, including possible rebound after withdrawal, require further study.

In the context of clinical practice, these data highlight the importance of biomarker integration . SP - D and CHI 3 L 1 in the diagnosis of pulmonary complications of MS, as recommended in [1, 15]. Dietary interventions, especially modified ketogenic diets, can serve as adjuvant therapy for the prevention of respiratory disorders, but require adaptation to the individual, taking into account individual factors such as age and comorbidities . Future research should focus on the mechanisms of action of modified diets, including the effects on the gut microbiome and epigenetic changes, to optimize therapeutic strategies.

CONCLUSION

MS leads to hemodynamic and morphological disturbances that are corrected by ketogenic diets. The use of biomarkers and spirometry for monitoring, as well as dietary interventions for prevention, are recommended.

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