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A STUDY ON BIOCHEMICAL AND HISTOPATHOLOGICAL CHANGES IN KIDNEY OF DIET INDUCED OBESE RATS

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Abstract:

Introduction: High level of caloric intake has been associated with many diet-induced complications, including metabolic syndrome, cardiovascular disease and non-alcoholic fatty liver disease, Kidney diseases. Obesity remains the number one risk factor for kidney disease because it mediates diabetes and hypertension;

Material method: Wistar rats were used in this study. Rats of either sex, 10-12 weeks old, weighing 170- 220g were assigned in the present study. Grouping: Rats divided into 2 groups Group 1: Control, Group 2: Obesity induced rats. The study group cafeteria diet was given for 50days duration and normal rat diet was given for control group for same duration. It consisted of condensed milk, bread, chocolate, peanuts, biscuits, dried coconut. Parameters studied: Body weight of the animal was measured at Day 0, 50 days, Kidney function tests i.e, Serum creatinine, Uric acid, Blood urea levels by Urease, histopathological changes in kidney tissue.

Results: Cafeteria diet fed rats showed significant increase in gain in body weight from day 20- day 50, altered renal function tests i.e, extreme significantly ($p<0.001$) increases serum creatinine, uric acid levels and decreased blood urea levels.

Conclusion: Dietary induced Obesity model is widely accepted for induction of obesity. Cafeteria diet fed rats showed significant increase in gain in body weight, altered renal function tests i.e, significantly increases serum creatinine, uric acid levels and decreased blood urea levels.

Keywords: Obesity, Cafeteria diet, Kidney function

Introduction

Altered eatinghabit togetherwith decreasedphysicalactivity distort the usual balance of nutrient intake and energy expenditure and leadanet accumulation of nutrients leads to obesity. World Health Organization (WHO) predicts that overweight and obesity may soon replace traditional public health concerns such as under nutrition and infectious diseases as the most significant cause of poor health. Because of its costs, prevalence and health effects obesity is a public health and policy problem.[1] Adverse clinical consequences of obesity are so harmful that a 20% increase above the ideal weight is associated with a 20% increase in the mortality rate.[2]

Obesity is associated with various diseases, including cardiovascular disorders, type 2 diabetes, stroke, certain types of cancer,[3] and osteoarthritis, but the strength of the link between obesity and specific conditions varies. High level of caloric intake has been associated with many diet-induced complications, including metabolic syndrome, cardiovascular disease and non-alcoholic fatty liver

disease (NAFLD), Kidney diseases.[4] Obesity remains the number one risk factor for kidney disease because it mediates diabetes and hypertension; these two factors are common etiologies for end-stage kidney disease. Multiple mechanisms have been postulated whereby obesity directly impacts kidney disease including hyperfiltration, increased glomerular capillary wall tension, and podocyte stress. People with metabolic syndrome (Obesity) are 20 to 30 percent more likely to develop kidney disease than people without it.[5]Weight loss reduces glomerular filtration rate and effective renal plasma flow along with proteinuria.[6]

The recent evidence has indicated that adipose tissue produces bioactive substances that contribute to obesity-related kidney disease, altering the renal function and structure. In parallel, proinflammatory processes within the adipose tissue can also lead to pathophysiological changes in the kidney during the obese state.[6-8]

Obesity can be induced in experimental animals by variety of methods, eg; neuroendocrine, dietary or genetic changes. These models have shown that it is the central nervous system that regulates food intake and energy expenditure, and it has also identified interrelationships among glucocorticoids, dietary behavior and the autonomic nervous system in the development of obesity.[9,10]

Various animal models for obesity have been established to help better understanding the pathophysiology in metabolic diseases and to develop new therapies. In this study, we investigated the biochemical and histopathological changes in the kidney tissues of fatty rat.

Materials and Methods

Study design: Experimental animal based study

Study locations: Department of Pharmacology and Pathology

Ethical aspect: Our study protocol was approved by the Institutional Animal Ethics Committee (IAEC) and experiment was carried out as per the norms laid by Committee for the Purpose of Control and Supervision of Experimentation on Animals (CPCSEA)[11]

Study duration: 6months

Sample

Inclusion criteria: Wistar rats were used in this study. Rats of either sex, 10-12 weeks old, weighing 170- 220g were assigned in the present study.[12]

Exclusion criteria: Rat showing abnormal activity and 10-12 weeks old but showed over weight.

Sample size: Six rats in each group

Grouping: Rats divided into 2 groups

Group 1: Control (Normal rats)

Group 2: Study group (Obesity induced rats)

Study protocol

Rats were housed at a temperature of 24 ± 2°C, with 14 with 1416 air changes per hour and relative humidity (60 ± 5%) and kept on a 12 h light dark cycle for acclimatization of laboratory environment before the experiment started. The animals had to food and water ad libitum.

Hypercalorie / Cafeteria diet:[1,13,14] The study group cafeteria diet was given for 50 days duration and normal rat diet was given for control group for same duration.

It consisted of 3 variants; i) condensed milk + bread + peanuts + pellet chow (4:1:4:1), ii) chocolate + biscuits + dried coconut + pellet chow (3:2:4:1), and iii) cheese + boiled potatoes + pellet chow (4:2:1). The different variants were fed on alternate days throughout the treatment period.

Parameters studied: Body weight of the animal was measured at Day 0, Day 10, 20,30,40 and 50 days in order to assess the obesity in study group and normal rats weight also taken to assess statistical significance. Kidney function tests i.e, Serum creatinine was estimated by Modified Jaffe's method, Uric acid levels by Uricase TOPS method, Blood urea levels by Urease/Glutamate dehydrogenase (GLDH) methodology were done to assess the kidney function and animals in both the groups were sacrificed at the end of the study,kidney tissues wereremoved and studied for histopathological changes.

Statistical Analysis

All the values will be expressed as the mean ±SEM and analyzed by paired student-t test and one-way analysis of variance (ANOVA) in order to test differences between groups. The level of statistical significance will be set at $p<0.05$.

Results

Table-1: comparison of body weight between control and test group

Body weight in grams	Control	Test group
Oday	204.17±5.34	197.2±6.64
10 days	214.33±5.71	219.8±3.81
20days	223.16±5.15	237±6.39**
30 days	227.33±5.96	255.17±5.49***
40 days	236.17±5.91	277.5±7.06***
50 days	239.83±6.77	296.83±9.28***

Data presented as Mean±SD, **p<0.01 and ***p<0.001.

Table 2: Kidney function test

Parameter	Control	Test group
Sr creatinine	0.71±0.05	1.05±0.05***
Blood urea	51.22±1.87	31.5±1.82***
Uric acid	2.98±0.21	4.03±0.18***

Data presented as Mean ± SD, **p<0.01 and ***p<0.001.

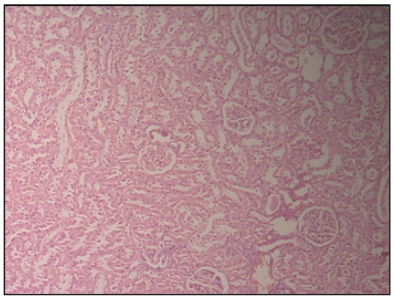

Figure 1. Shows normal histology of cortex of kidney tissue of normal control rat (10x)

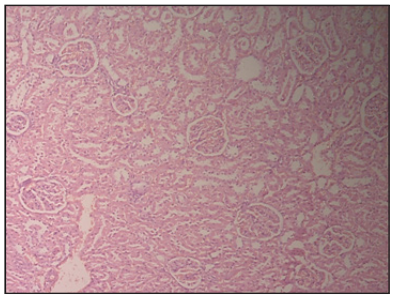

Figure 2. Shows histology of cortex of kidney tissue of obese rat (10x)

Discussion

In this study we used Cafeteria diet induced obesity (DIO) model. It is widely accepted model for induction of obesity. High fat diet inevitably causes hyperphagia resulting in increased body weight (table 1). This gain in body weight is largely due to increased fat mass, to some extent.[15-17]

Some reports have attributed obesity induced by high-fat diets to their high food efficiency (g body-weight gain per kJ food consumed). Energy from fat has a larger effect on body-weight than has energy from non-fat sources.[18-20] Diet-induced thermogenesis is the energy for digesting, absorbing and storing nutrients. It leads to loss of energy from the body which is 2–3% for fats, 25–30% for proteins and 6–8% for carbohydrates. Therefore, the efficiency of nutrient utilisation differs among macronutrients and fats have an efficiency of 97–98%, whereas efficiency is 70–75% for proteins and 92–94% for carbohydrates.[19-22] In addition, it costs energy to build long chain fatty acids from glucose or amino acids, whereas dietary fat contains long-chain fatty acid pre-formed. Some studies have shown that a fat-rich diet induces obesity by increasing energy intake. Some studies have reported that not all fats are obesogenic and the dietary fatty acid profile rather than the amount of energy from fat is an important variable in developing dietary obesity,[19-23] but there is some controversy on this matter since there are reports showing non-significant differences in final body weight and/or body-weight gain of the animals consuming various fatty acids.[24-26]

Consumption of cafeteria diet led to decrease in blood urea levels significantly (p<0.001).T. Barber et al, also found decreased urea levels and reduced activity of several enzymes involved in urea cycle on cafeteria diet feeding. In our results,Cafeteria diet fed rats showed significant increase in gain in body weight from day 20- day 50, altered renal function tests i.e, extreme significantly (p<0.001) increases serum creatinine, uric acid levels and decreased blood urea levels. However, H&E stains of kidney tissue of both the groups showed no significant changes (Figure 1 & 2).

Conclusion

Dietary induced Obesity model is widely accepted for induction of obesity. Cafeteria diet fed rats showed significant increase in gain in body weight, altered renal

function tests i.e, significantly increases serum creatinine, uric acid levels and decreased blood urea levels.

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