RESEARCH ARTICLE
High fructose diet-induced metabolic syndrome and the functional abnormalities in the liver and kidney of Wistar albino rats

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ABSTRACT

Background: Metabolic syndrome is the combination of several medical conditions that increase the risk of developing heart diseases, stroke, cancer, non-alcoholic fatty liver, and diabetes mellitus. Different varieties of animal models have been used for the therapeutic studies of diabetes, hyperlipidemia, and kidney diseases. The establishment of appropriate experimental animal models of metabolic syndrome is very important for evaluating the pathophysiology of the disease in humans. Aim and Objective: The aim of the study was to assess the functional abnormalities associated with high fructose diet (HFrD)-induced metabolic syndrome in Wistar albino rats. Materials and Methods: Metabolic syndrome is induced in adult male Wistar albino rats by feeding a combination of HFrD (55%) and fructose enriched water (15%) for 75 days and kept as Group 2 or HFrD group. Normal male Wistar albino rats were kept as normal control. During the entire course of study, weight gain was monitored once a week in both groups. Biochemical investigations such as lipid profile, liver function test, and renal function test were carried out using standard methods. The obtained data were statistically analyzed by students' "t-test" and the values were considered statistically significant at p < 0.05. Results: Chronic administration of HFrD resulted in obesity, abnormal hepatic, and renal functions in Wistar rats. Conclusion: Chronic consumption of HFrD produces functional abnormalities in liver and kidney of Wistar rats.

KEY WORDS: High Fructose Diet; Obesity; Metabolic Syndrome; Renal Function Test; Dyslipidemia; Liver Function Test

INTRODUCTION

Modern lifestyle today has a deleterious effect on our health as it often violates the principles of natural living. Unhealthy food habits and sedentary lifestyle are factors that invite disease rather confronting it. These are collectively known as lifestyle disorders, which are playing a pivotal role in the development of metabolic syndrome. Metabolic syndrome is the combination of several medical conditions that increase the risk of developing heart diseases, stroke, cancer, non-alcoholic fatty liver, and diabetes mellitus.¹ It is characterized by the concurrent existence of obesity, hypertension, hyperglycemia, and dyslipidemia.²⁻³ The risk of developing metabolic syndrome in human depends on synergy of both genetic and environmental factors.⁴ The worldwide prevalence of metabolic syndrome ranges from 10% to 84% depending on the age, gender, race, and ethnicity, and it is 5–7% in young adults.⁵ Different varieties of animal models have been used for the therapeutic studies of diabetes, hyperlipidemia, and kidney diseases.⁶⁻⁷ Although, studies are still on progress in developing better rodent models. The establishment of appropriate experimental animal models of metabolic syndrome is very important for evaluating the...
pathophysiology of the disease in humans. The present study is an attempt to explore the influence of high fructose diet (HFrD) on the metabolism of rats fed with a combination of HFrD and ‘fructose enriched’ water for 75 days.

MATERIALS AND METHODS

This research protocol was approved by the Institutional Animal Ethics Committee, S D M Centre for Research in Ayurveda and Allied sciences, Udupi (CPCSEA/IAEC/15-16-KT.20). Twelve healthy adult male Wistar albino rats, weighing between 180 and 240 g, were selected for the study. The animals housed under suitable temperature (22 ± 2°C), humidity, and at 12 h of day-night cycle and received standard pellet diet and purified water ad libitum. The duration of the study was 75 days. Animals were grouped into two, comprising six animals in each. Rats in Group I were fed with normal laboratory diet and kept as the normal control group. Rats in Group II were fed with fructose enriched water (15%) for the initial 30 days, followed by HFrD (55%) for further 45 days. The animals were acclimatized to the experimental conditions 7 days before the initiation of study.

Metabolic and Biochemical Assays

After 75 days of treatment, fasting blood sample was collected from retro-orbital puncture technique under light ether anesthesia. Biochemical investigations such as lipid profile, liver function test, and renal function test were carried out using commercial kits (Erba) with a fully automated clinical analyzer (ERBA-EM-200).

Statistical Analysis

Students “t-test” was used for testing statistical significance between groups. p < 0.05 considered significant. All the data were presented as Mean ± SD.

RESULTS

Body Weight

From the 1st week to the end of the study, a gradual increase in body weight was observed in normal control group, whereas the rate of increase in body weight was much higher in the fructose control towards the end of study, which is statistically significant p < 0.05. The rate of increase in the body weight is depicted in Table 1.

Biochemical Analysis

The lipid profile of high fructose group showed increased total cholesterol level, low-density lipoprotein (LDL), triglyceride whereas serum high-density lipoprotein (HDL) level was noticeably decreased, these values appeared statistically significant when compared to normal control group (P < 0.05) [Table 2].

Liver function markers such as serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), alkaline phosphatase, and total bilirubin level in the HFrD group were increased (P < 0.05), whereas total protein, serum albumin level, and serum globulin level showed a mild and statistically insignificant (P > 0.05) increase in HFrD group [Table 2].

The renal function markers such as serum creatinine and uric acid were elevated in HFrD rats when compared with the normal rats (P < 0.05) and serum urea levels showed minimal and statistically insignificant increase [Table 2].

DISCUSSION

The goal of the present work was to shed some light on the functional abnormalities in the liver and kidneys of rats with high fructose-induced metabolic syndrome to develop a more efficient animal model to mimic the metabolic syndrome in human. A progressive increase of weight in the high fructose fed rats indicated the direct relationship between high fructose consumption and obesity. Abnormal and statistically significant altered lipid profile values were noted in the fructose treated group. Liver function tests revealed statistically significant increase in SGPT, SGOT, alkaline phosphatase, and total bilirubin level in the HFrD group. Renal profile showed significantly high serum creatinine and uric acid levels.

The body weight assessment study was aimed to draw a parallel between obesity and fructose consumption. In concordance to our results, Gomaa and Mohammed reported about the development of obesity in HFrD fed rats. Similar to our studies, Bocarsly et al. stated that over consumption of high fructose corn sugar could be a major factor in the development of obesity. The obesity associated with HFrD may be attributed to the post-prandial hypertriglycerideremia that enhances visceral adipose deposition.

Equilibrium among synthesis and degradation of biological tissues is maintained by lipid metabolism and abnormalities in this metabolism causes dyslipidemia, due to excessive and regular consumption of HFrD that augments lipid peroxidation, leads to delayed gastric emptying, and affects the digestion process. The present study exhibited altered lipid levels in HFrD fed rats. Similar to our studies, Prabhakar et al. also reported increased serum LDL, triglycerides, and total cholesterol levels and reduced HDL Levels in HFrD fed rats. This may be attributed to the fact that high dietary fructose induces a hepatic stress response resulting in cholesterol and lipid dysregulation.

A characteristic feature of the metabolic syndrome is the irregularities in hepatic and renal enzyme production. HFrD can induce dyslipidemia and lipid accumulation both in kidney and liver which is related to insulin resistance and lipotoxicity-induced cellular damage. Fructose has been
Table 1: The weekly changes in body weight expressed in grams

<table>
<thead>
<tr>
<th>Group</th>
<th>1st week</th>
<th>2nd week</th>
<th>3rd week</th>
<th>4th week</th>
<th>5th week</th>
<th>6th week</th>
<th>7th week</th>
<th>8th week</th>
<th>9th week</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC</td>
<td>1.66±0.54</td>
<td>3.28±0.73</td>
<td>5.87±0.97</td>
<td>6.96±1.06</td>
<td>9.09±1.13</td>
<td>7.06±1.43</td>
<td>9.89±1.26</td>
<td>8.6±1.71</td>
<td>13.83±2.16</td>
</tr>
<tr>
<td>HFrD</td>
<td>3.94±0.9*</td>
<td>4.73±1.09*</td>
<td>8.55±2.41*</td>
<td>8.94±4.33*</td>
<td>9.84±4.32*</td>
<td>10.77±4.45*</td>
<td>11.43±3.53*</td>
<td>13.84±3.64*</td>
<td>22.18±4.48*</td>
</tr>
<tr>
<td>% diff</td>
<td>137.34↑</td>
<td>59.45↑</td>
<td>45.65↑</td>
<td>28.44↑</td>
<td>8.25↑</td>
<td>52.54↑</td>
<td>15.57↑</td>
<td>60.93↑</td>
<td>60.37↑</td>
</tr>
</tbody>
</table>

All the values were expressed in Mean±SD. *Represents P<0.05. HFrD: High fructose diet

Table 2: Biochemical analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal control (mg/dl)</th>
<th>High fructose diet (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid profile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>43.16±2.18</td>
<td>64±4.54*</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>100.5±3.59</td>
<td>186.83±13.27*</td>
</tr>
<tr>
<td>HDL</td>
<td>39.66±1.35</td>
<td>21.66±1.08*</td>
</tr>
<tr>
<td>LDL</td>
<td>13.83±1.37</td>
<td>27.88±3.59*</td>
</tr>
<tr>
<td>Liver function markers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SGOT (U/L)</td>
<td>126±3.81</td>
<td>156±26.95*</td>
</tr>
<tr>
<td>SGPT (U/L)</td>
<td>66.33±1.83</td>
<td>108.83±30.14*</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>244.83±17.92</td>
<td>320.5±39.94*</td>
</tr>
<tr>
<td>Renal function markers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum uric acid (mg/dl)</td>
<td>24.6±1.5</td>
<td>25.16±2.08*</td>
</tr>
<tr>
<td>Serum uric acid (mg/dl)</td>
<td>1.06±0.04</td>
<td>1.86±0.55*</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>0.38±0.01</td>
<td>0.63±0.03*</td>
</tr>
</tbody>
</table>

All the values were expressed in Mean±SD. *Denotes statistical significance (P<0.05). LDL: Low-density lipoprotein, HDL: High-density lipoprotein, SGPT: Serum glutamic pyruvic transaminase, SGOT: Serum glutamic oxaloacetic transaminase

demonstrated to increase circulating uric acid concentrations in both animals and humans, and elevated concentrations of uric acid are correlated with increased fructose intake.[17] The present findings from our study supports these concepts and in accordance with studies of Varghese et al. and Khanal et al.[18,19]

Many of the available literatures in high fructose-induced metabolic syndrome are either diet induced or by providing fructose enriched water for <60 days. Instead we have experimented a combination of fructose enriched water and fructose diet to induce metabolic syndrome for 75 days’ period. We consider this as the strength of our study. Although biochemical parameters are well explained in this study, molecular level studies are not incorporated.

CONCLUSION

On the basis of the present investigation, overconsumption of high fructose for prolonged period may imbalance the metabolism, by accentuating obesity and inducing functional changes in liver and kidneys. This fructose-fed rat model may be useful to define potential treatments for Type 2 Diabetes or the metabolic syndrome.

ACKNOWLEDGMENTS

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