Animal Model for Diabetes Co-existing with Metabolic Syndrome

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Citation: Rajesh Kumar Suman. Animal Model for Diabetes Co-existing with Metabolic Syndrome. ERWEJ. 2022; 2[4]:211-220. 10.54136/ERWEJ-0204-10041

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Abstract

Metabolic syndrome includes diverse disorders together with truncal obesity, dyslipidemia, high blood pressure, and hyperglycemia. The occurrence of metabolic syndrome is growing globally. The unfavorable results of metabolic syndrome have brought on research efforts to broaden new interventions to reduce the weight of the healthcare system. Because of its multifactorial nature, it may be hard to pick out the best experimental version that high-quality represents the pathophysiology of human metabolic syndrome. Many animal models have evolved and been studied to clarify the molecular mechanisms and useful modifications associated with metabolic sicknesses. Properly characterized and clinically applicable experimental models are taken into consideration as crucial tools for testing new pills and information on their molecular foundation, their pathogenesis, and mechanism of movement. In this review, we collate and discuss the various animal models of metabolic syndrome and the suitability of diabetes co-existing with metabolic syndrome animal models for research also be discussed to provide the readers with a comprehensive overview of the selection of the best animal models to meet their research purpose.

Introduction

Diabetes with metabolic syndrome

Metabolic syndrome (METS) forms a spectrum of disorders including truncal hypertension, obesity, and hyperglycemia [1]. The metabolic syndrome will increase the threat of developing type II diabetes (T2DM) by interfering with insulin's profound regulatory outcomes on glucose, lipid, and protein metabolism [2-3]. The wide variety of diabetics with metabolic syndrome is considerable and its prevalence is growing globally [4,5].
Many animal models, such as genetic models, chemically or nutritionally brought about models, and genetically engineered models had been advanced and studied to clarify the molecular mechanisms and purposeful changes associated with metabolic diseases. A properly characterized and clinically applicable experimental version is considered an important device for testing new active agents to understand their molecular basis, pathogenesis, and mechanism of movement. The combination of streptozotocin (STZ) and alloxan (ALX) in a high-fat diet model successfully mimicked the natural progression of human type II diabetes to the development of diabetic and metabolic function [6,7]. The metabolic syndrome will increase the risk of developing type II diabetes (T2DM) by interfering with insulin's profound regulatory outcomes. Similarly, a few researchers have used high carbohydrate (fructose, sucrose) and excessive-fats food plan components in rodents to study metabolic syndrome [8]. However, no chronic animal model exists in which diabetes and metabolic syndrome coexist, making it useful for screening therapeutic agents useful in such conditions. Therefore, to control these two pathologies, it is of utmost importance to establish a unique animal model that closely mimics post-onset changes in human diabetes and metabolic syndrome.

**Type II diabetes model**

Animal models of type II diabetes are currently at the forefront of research to investigate disease mechanisms and drug therapies. To apply to humans, animal models must reproduce as intently as feasible the phenotype located in patients, however, it's also perfect to imitate the developmental procedure of the sickness. models which are clean to generate, reasonably priced, and may be advanced in a well-timed way are desired over highly-priced models. DB/db mice, ob/ob mice, and Zucker fats rats, which have been extensively studied within the literature [9-14] and are generated using genetic abnormalities inside the leptin signaling pathway, are usually related to environmental Its outcomes from a couple of genetic polymorphisms mixed with factors. Similarly, Goto-Kakizaki GK rats are insulin resistant but stay lean [15, 16], complicating the evaluation of the human condition and affiliation with obesity. in addition, an excessive-fat food plan on my own is not effective in changing heart and systemic metabolism except fed on over a long period [17]. A tremendously new rat model was first proposed with the aid of Reed et al. [18] and modified by way of Srinivasan et al. We aimed to result in type II diabetes using a high-fat weight-reduction plan to induce peripheral insulin resistance, accompanied with the aid of low-dose pancreatic beta-mobile toxin streptozotocin [STZ] [19]. has been traditionally used at high doses to set off type I diabetes because it causes impaired insulin secretion from β cells [8,20]. This version has turned out to be increasingly popular in the latest years for both studying the mechanisms involved in type II diabetes and checking out potential therapeutics [19-21], but, the volume of diabetes precipitated, the quantity of STZ used, background exposure, and preliminary body weight differ extensively in this research.

**Metabolic syndrome rat model**
A preceding look showed that the administration of a high-fat diet (HFD) to rats for two months may be swift and without problems set off metabolic syndrome associated with metabolic and oxidative issues without regulating blood sugar. [22, 23]. Table 1 shows the criteria proposed for the clinical diagnosis of metabolic syndrome. The study demonstrated a model that could promote peak hypercholesterolemia without compromising development in rats. The rats were fed a hypercholesterolemic diet containing cholesterol and varying levels of soybean oil, starch, casein, micronutrients, and dietary fiber, and thus differed in caloric value. Fecal volume, liver weight, and fat, cholesterol and percentages, serum biochemical parameters, and systolic blood pressure were assessed [24]. The high-fat diet in rats produced hypercholesterolemia, which led to an increase in the body weight total cholesterol, triglycerides, and attenuation in the levels of HDL as well as changes in the body temperature of animals. Temperature as compared to HFD-induced obesity [25].

Diet plays an important role as a food source in growth and development, but diet composition determines nutritional status. Increased caloric intake is associated with many diet-related complications, including metabolic syndrome, cardiovascular disease, and non-alcoholic fatty liver disease. Some of the effects of diet on signs and symptoms of metabolic syndrome in animal models have been described in Table 2.

**Prevalence of diabetes with metabolic syndrome**

Diabetes coexisting with metabolic syndrome has grown to be a not unusual social quandary due to modifications in way of life and dietary conduct. Diabetics with metabolic syndrome are growing internationally [27,28] via locating better remedies and new prevention strategies for type II diabetes metabolic syndrome, efforts must be directed in the direction of treating each sickness instead of in my view. To this end, properly differentiated and clinically significant experimental models for checking out new tablets and knowledge of the molecular basis, pathogenesis, and mechanism of motion of those therapeutics are accomplished. Animal models will deal with all factors of this human disorder, and all the main manifestations of diabetes and metabolic syndrome, especially obesity, dyslipidemia, high blood pressure, and probable fatty liver sickness and renal disorder.

It was recently reported that rats fed a combination of a high-fat diet and streptozotocin developed type II diabetes similarly to humans, low-dose streptozotocin induces mild impairment of insulin secretion [29]. Thus, a combination of a high-fat diet and a low-dose streptozotocin model successfully mimicked the natural progression of diabetes development and the metabolic function of human type II diabetes [30-32].

Achieving the goal of testing new and better therapies requires a characterized and clinically relevant animal model of type II diabetes. Each genetic spontaneous diabetes model experimentally caused non-spontaneous diabetes models to existing. An instance of an animal model of experimentally induced
diabetes is the high-fat food plan/streptozotocin-handled (HFD/STZ) rat model. In this model, a high-fat diet that induces hyperinsulinemia, insulin resistance, and/or impaired glucose tolerance is combined with a high-fat diet and possibly a high-sugar diet, followed by treatment with the B-cell toxin STZ. Functional b-cell mass [32,33]. According to Samira et al. For example, diabetes was induced by an 8-week high-fat/fructose diet followed by a sub-diabetic dose of streptozotocin, resulting in obesity, hyperglycemia, insulin resistance, and associated hepatic glycogen depletion and dyslipidemia [34]. This study documented a high-carbohydrate, high-fat diet, and low-dose administration of streptozotocin-induced MetS in rats [35].

**Standardization and development of a unique rodent model**

There are various animal models for diabetes as well as metabolic syndrome. However, there's no experimental version wherein each diabetes and metabolic syndrome co-exist. Consequently, it's far critical to set up models to goal this kind of risk elements for the treatment and discount of clustering factors of diabetes with metabolic syndrome as such unique pathogenesis cannot be adequately studied in both the animal models of diabetes and metabolic syndrome on my own. A few documented remedy strategies on such distinctive models suggest that it's far feasible to prevent the development of the metabolic syndrome and related problems. [35]. (Fig 1)

The observation by using Rajesh Suman et al [36] standardized unique doses of STZ (30, 35, 40 mg/kg) for use for induction of diabetes after HFD was fed to the experimental rats. Diabetes co-existing with metabolic syndrome turned efficiently mounted with a 40 mg/kg dose observed. The animals had been allowed to drink 5% glucose solutions in a single day to conquer drug-brought about hypoglycemia. The body weight and biochemical parameters have been estimated to be 7 days after the STZ injection showed the presence of metabolic syndrome with diabetes.
Figure 1: Metabolic syndrome and associated complications

Table 1: Criteria Proposed for Clinical Diagnosis of Metabolic Syndrome

<table>
<thead>
<tr>
<th>Clinical measure</th>
<th>World Health Organization</th>
<th>International Diabetes federation</th>
<th>American Heart association</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Criteria</strong></td>
<td>Insulin resistance + any other 2</td>
<td>Increased waist circumference + any other 2</td>
<td>Any 3 of 5</td>
</tr>
<tr>
<td><strong>Insulin resistance</strong></td>
<td>Impaired glucose tolerance/Impaired fasting glucose + Insulin resistance</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Blood glucose</strong></td>
<td>Impaired glucose tolerance/Impaired fasting glucose</td>
<td>≥100 mg/dL</td>
<td>≥100 mg/dL, Type 2 diabetes</td>
</tr>
<tr>
<td><strong>Dyslipidemia</strong></td>
<td>Triglyceride ≥1.69 mmol/L and high-density lipoprotein Men ≤ 0.90 mmol/L, women ≤ 1.01 mmol/L</td>
<td>Triglyceride ≥1.69 mmol/L and high-density lipoprotein Men ≤ 1.02 mmol/L, women ≤ 1.29 mmol/L or high density lipoprotein treatment</td>
<td>Triglyceride ≥1.69 mmol/L and high-density lipoprotein Men ≤ 1.29 mmol/L or high density lipoprotein treatment</td>
</tr>
<tr>
<td><strong>Blood pressure</strong></td>
<td>≥140/90 mmHg</td>
<td>≥130/85 mmHg or on antihypertensive medication</td>
<td>≥130/85 mmHg or on antihypertensive medication</td>
</tr>
<tr>
<td><strong>Obesity</strong></td>
<td>waist : hip ratio</td>
<td>waist circumference ≥ 0.85</td>
<td>waist circumference ≥ 0.85</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Microalbuminuria</td>
<td>Men ≥102 cm, Women ≥88 cm</td>
<td>-</td>
</tr>
</tbody>
</table>
Table 2: Effects of diet model on the development of Metabolic Syndrome

<table>
<thead>
<tr>
<th>Types of diet</th>
<th>Component of metabolic syndrome</th>
<th>Study duration</th>
<th>Strains of animal</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saturated fat</td>
<td>Obesity</td>
<td>21 weeks</td>
<td>Male Wistar rats</td>
<td>Apgar et al (37)</td>
</tr>
<tr>
<td></td>
<td>Hyperglycemia</td>
<td>8 weeks</td>
<td>Male Sprague-Dawley rats</td>
<td>Mahmoud and Estrella et al (38)</td>
</tr>
<tr>
<td></td>
<td>Hypertension</td>
<td>10 weeks</td>
<td>Male Sprague-Dawley rats</td>
<td>Sanchez-Lemus et al (39)</td>
</tr>
<tr>
<td></td>
<td>Dyslipidemia</td>
<td>10 weeks</td>
<td>Male Sprague-Dawley rats</td>
<td>Messina et al (40)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7 weeks</td>
<td>Male Sprague-Dawley rats</td>
<td>Overholtzman et al (41)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 weeks</td>
<td>Male Sprague-Dawley rats</td>
<td>Hombach et al (42)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24 weeks</td>
<td>Female Sprague-Dawley rats</td>
<td>Dorendt et al (43)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14 weeks</td>
<td>Male Sprague-Dawley rats</td>
<td>Padin et al (44)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24 weeks</td>
<td>Male Sprague-Dawley rats</td>
<td>Collinson-Jones et al (45)</td>
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<tr>
<td></td>
<td></td>
<td>40 weeks</td>
<td>Male Sprague-Dawley rats</td>
<td>Zhou et al (46)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14 weeks</td>
<td>Male Sprague-Dawley rats</td>
<td>You et al (47)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14 weeks</td>
<td>Male Sprague-Dawley rats</td>
<td>Perel et al (48)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 weeks</td>
<td>Hypercholesterolemia diet and fructose drinking water</td>
<td>Barroso-Ramos et al (49)</td>
</tr>
</tbody>
</table>

The table represents the effects of diet on each component of metabolic syndrome. The (+) and (-) indicate the presence and absence of significant effects of the sign of metabolic syndrome, while (X) indicate the effects on the component not being evaluated in the study.
Conclusion

We can conclude that the benefit of using animal models to look at metabolic syndrome with diabetes is the potential to monitor histological, functional, and biochemical modifications, that are hard to behavior in people. Subsequent research is recommended for the use of a combination or modification of present mounted techniques. Such specific experimental models lead them to be beneficial for analyzing the efficacy and mechanisms of recent pills in the setting of diabetes and metabolic syndrome.

Patient consent: N/A
Conflict of Interest: Nil
Financial Disclosure: None

Acknowledgment

The authors would like to acknowledge Dr. Nilesh Paul for his support and assistance during the development of the manuscript.

References


