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Induction and evaluation of metabolic syndrome in an animal model: bibliographic review

Inducción y evaluación del síndrome metabólico en un modelo animal: revisión bibliográfica

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Abstract:

The metabolic syndrome includes several systemic conditions and is widely associated with chronic diseases that can be the cause of mortality due to its increasing prevalence in people of all ages and all continents. Scientific efforts to study this syndrome have used tools such as animal models, mainly rats and rabbits, which allow obtaining valuable information on the early stages of the metabolic syndrome.

Keywords:

Metabolic syndrome, animal model, rabbits, investigation.

Resumen:

El síndrome metabólico abarca una serie de afecciones a nivel sistémico y está ampliamente relacionado con enfermedades crónicas que pueden ser causa de mortalidad, debido al aumento de su prevalencia en individuos de todas las edades y de todos los continentes los esfuerzos científicos para la investigación de este síndrome han utilizado herramientas como los modelos animales principalmente ratas y conejos los cuales permiten obtener información valiosa de las etapas tempranas.

***Palabras Clave**:*

Síndrome metabólico, modelo animal, conejos, investigación,

1. Introduction

The prevalence of chronic non-communicable diseases has increased over the past century, due to changes in human lifestyles. Obesity, diabetes and hypertension are examples of diseases associated with the metabolic syndrome, which is not considered a disease because it is a grouping of biochemical and physiological metabolic abnormalities at the systemic level that cause mortality [1].

The metabolic syndrome (MS) has become one of the major public health problems of the 21st century and is associated with increased food intake, saturated fat, high calorie levels and refined sugars. Various animal models have been used in an effort to expand the study of MS [6].

The study of animal models involves the intervention and handling of live animals in order to gain scientific knowledge, and their importance is essential for the development of aspects related to human life [3]. The experimental models allow a deeper understanding of MS at early stages of its development, thus making it possible to generate diagnostic and therapeutic alternatives [16].

2. Metabolic Syndrome

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The metabolic syndrome is a group of metabolic abnormalities and risk factors that increase an individual's likelihood of developing high mortality diseases. The risk factors that make up MS include obesity, hypertension, insulin resistance and dyslipidemia, which predispose to cardiovascular disease and diabetes. These chronic degenerative diseases that make up MS progressively deteriorate the body of the person affected [10].

The WHO describes the risks associated with overweight and obesity as heart disease, stroke, musculoskeletal disorders and cancer; obese children suffer from respiratory problems, increased risk of fractures and high blood pressure; and psychological effects, including an increased risk of premature death and disability in adulthood. MS is a global problem involving lifestyle choices such as sedentary lifestyles, increased consumption of saturated fats, reduced intake of fruit and vegetables, and increased leisure time activities [9].

To understand the behaviour of MS, information related to lifestyle, diet and physical inactivity is addressed, within metabolic issues, the literature describes the release of insulin by the pancreas when certain foods are eaten. Insulin is a hormone that helps the body's cells to accept glucose, which provides them with energy; if the cells develop resistance to insulin, more insulin is needed to get glucose into the cells, so the body increases its production. The insulin is distributed in the bloodstream, giving rise to a state of hyperinsulinemia, which triggers the activation of alternative metabolic pathways and therefore gluconeogenesis, all of which leads to an increase in the concentrations of triglycerides and cholesterol, hypertension and the likelihood of vascular risk. The above is related to other factors, such as those of genetic origin, and for this reason MS is not considered an isolated disease, but rather a set of problems of biological and socio-cultural origin [13].

This syndrome has been described in adults, adolescents and children and has become a current issue in Mexico, where at least a quarter of the young population with obesity have developed a disease such as MS, so one of the aims of the research is to work on reducing the rate of obesity in the young population and therefore the development of MS and its future complications [11].

3. Animal models and metabolic syndrome

Human studies of MS treatments are scarce compared with those conducted in animal models, and with very different methodologies, particularly in terms of pharmacological dose management [7]. While animal models in research are considered the most complete of all experimental models, as they are the closest to the real conditions, they are considered par excellence the main source of knowledge of pathophysiology and surgery, their use requires facilities and specialised personnel, in addition to handling care, equipment and knowledge of techniques; providing an appropriate environment is one of the responsibilities that must be made clear to the research team, as when they need the animal, it must be respected because it is endowed with sensitivity and memory [14].

Various species such as primates, pigs, dogs, fish and even rabbits have been used to study MS induced by hyper-caloric diets rich in carbohydrates or fats [16].

Some species, such as guinea pigs, have several similarities with humans in the metabolism of lipoproteins and cholesterol and are therefore considered an ideal model for the study of diseases such as diet-induced atherosclerosis, in contrast to mice and rats, which are used for the study of dyslipidaemia and treatments to reduce cholesterol levels [7].

These experimental models as a research tool allow us to increase our knowledge of MS, particularly of the cellular and molecular mechanisms involved [16]. There are animal species that have been studied for similarities to the human prototype, often by inducing metabolic and biological processes in the chosen model in order to extrapolate the results. Extensive studies of obesity have mainly used rodents, as obesity is associated with MS and there is a cause-and-effect relationship [21]. At the time of using animal models for the study of MS evaluation it is possible to carry out an assessment of changes that occur at the histological, physiological and biochemical level during different stages of development, although there are several and all contribute knowledge it is important that when choosing a model it adapts to the lines of research [16].

Among the characteristics that an experimental model must have are that the course of the disease develops in a shorter period of time than in humans, that it is easy to maintain and work with [7]. Considering the short lifespan of some species, such as rats, compared to humans, it would be impractical to conduct chronic use studies in humans as the results would take longer [20]. When choosing a model, scientific, practical and ethical considerations must be taken into account, including the definition of the hypothesis to be tested [14]. Regarding what has been written previously about bio-models, it is important to emphasise that whenever they are to be used in research, their use must be justified [21].

4. Induction of metabolic syndrome in the animal model.

In animals, food intake is determined by the satisfaction of energy needs, however, some recent literature suggests that the degree of satiety can vary depending on the proportion of macronutrients present in the food (lipids, proteins or carbohydrates), the regulation of ingested food depends not only on the caloric content of the food but also on the origin of the energy, overfeeding results in the storage of excess energy from carbohydrates and fats [21].

Therefore, different diets are used to induce the development of obesity, diabetes mellitus and MS in animal models, some examples being hypercaloric diets with high amounts of carbohydrates and easily digestible fats. The aim of using food as a method of inducing MS is to develop chronic non-communicable diseases and alterations in glucose homeostasis, the use of sugary solutions simulating the consumption of juices and soft drinks by the population has been documented [16].

The induction of the first phase of MS by the administration of drinking water containing 35% sucrose has been carried out using rats as an animal model, other research describes that fasting glycaemia determines a predictive parameter for the onset of MS, in addition the hyperglycaemic environment in the prenatal stage of animal models condition the response to develop MS, these results have been observed in animals subjected to diets containing 10% fructose [2], [6].

In Mendoza's research, the administration of glucose in the drinking water together with a non-nutritive sweetener has been shown to cause a greater increase in body mass and a slight increase in food consumption in male rats, compared to the situation in real life where the diet of some people is unbalanced, with an excess of ultra-processed foods and soft drinks containing sweeteners, but the authors believe that it is not only sweeteners that cause obesity and therefore this problem must be addressed in a multifactorial manner [20].

While other high-fat diets have a variety of effects, they do not always produce signs associated with MS; this is due to the amount of total calories from fats, whether they are of animal or vegetable origin, so variations such as origin and caloric intake need to be considered when choosing high-fat diets [16].

The effects of diets rich in different fatty acids using lard, shear butter, olive oil, safflower oil and soybean oil have been studied in mice, the diets were designed to resemble human diets, results showed differences in body weight after twelve weeks, the animals consuming diets with soybean oil and lard [15].

The use of 20% palmitic acid in the feeding of young rabbits has shown an increase in triglyceride levels, cholesterol levels, as well as the presence of dyslipidaemia, a condition in which oxidative stress due to peroxidation of lipids has been reported, when there is an overproduction of reactive oxygen species and the capacity of antioxidant systems is exceeded, an alteration in cellular functions is generated later organs and tissues [5].

Diets in rabbits with cholesterol administered in the form of simple syrup for 4 weeks have been sufficient to study atherosclerosis in the aorta, rabbits are reported to accept the different doses without problems, probably due to the sweet taste of the syrup. Similarly, rabbits given cholesterol developed hepatic steatosis, an injury associated with elevated levels of alanine transferase and aspartate aminotransferase; in humans, elevation of these enzymes is associated with liver disease, including steatosis induced by MS components [18].

5. Assessment of metabolic syndrome

Some of the clinical criteria for the diagnosis of metabolic syndrome in humans are: increased waist circumference, increased triglycerides, decreased HDL, increased blood pressure and increased fasting glucose [17].

The anthropometric parameters studied in animals are weight, abdominal circumference and body mass index. The assessment of basal glycaemia, cholesterol and triglycerides allows the onset of MS to be determined in groups of induced animals by comparing the biochemical parameters with groups of healthy animals [6].

For animal nutrition issues, weekly weight records of the animals are included to calculate weight gain and average daily gain, records of feed consumption, as well as necropsy characteristics; in addition, samples for haematological biometry and lipid profile are taken at sacrifice [22].

For this reason, studies on New Zealand rabbits mention that, after the diet has been provided for the specified period, metabolic pro-life assessment is carried out by taking blood samples and, finally, by determining lipid and blood parameters, including glucose levels, total cholesterol, high-density lipids (HDL), triglycerides and low-density lipids (LDL) [4].

Thus, alterations in plasmatic lipoproteins are associated with dyslipidaemia and an increased risk of developing cardiovascular disease, issues closely related to MS, highlighting the importance of these biochemical parameters for diagnosis in research [23].

Therefore, to determine the presence of dyslipidaemia in young fat-fed rabbits, lipid profiles have been obtained comparing the average values of these in animals fed a normal, fat-free diet and in rabbits fed a high fat diet, elevated triglyceride levels and a decrease in HDL being the most indicative of the presence of MS [5].

In addition, research in mice has documented the collection of blood by intracardiac puncture at the end of treatment after a 12-hour fast. The selected parameters are processed with a blood chemistry analyzer, the lipid pro-life values are the same as mentioned above [23].

6. Treatment of metabolic syndrome

Due to the high prevalence of MS, research has focused on the search for alternative treatments, some of which suggest physical training, mainly aerobic training, observing a significant improvement in body composition measurements, this is associated with improved changes in the metabolism of lipids and lipoproteins, however exercise is not enough as it must always be accompanied by dietary changes [17].

Pharmacological treatment should be considered for people whose risk factors are not adequately reduced by the indicated measures; it is worth mentioning that the management of MS is difficult because there is no recognized method of prevention, so the emphasis must be on treating each component separately, starting with weight reduction, followed by other conditions such as dyslipidemia, hypertension, etc. [24]. [24] The optimal diet is controversial; scientific evidence recommends a regular daily intake of fiber, omega-type polyunsaturated fatty acids for their anti-inflammatory benefits, and regular physical activity [19].

7. Conclusions

Metabolic syndrome includes a large number of interrelated conditions, with a high prevalence worldwide in people of all ages, as written in this review, animal models are an excellent option in the field of research, especially rats and rabbits; the recent information on the variety of diets that have been used for its induction open the way to obtain more information about MS, however it is

important to carefully choose the animal model, an adequate study protocol and consider the ethical issue, the latter taking into account the importance of continuing to investigate alternatives that can provide information for its treatment and prevention.

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