9 - Experimental model of induction of *diabetes mellitus* in rats[1]

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ABSTRACT - *Diabetes mellitus* is a potentially morbid condition with high prevalence worldwide, thus being a major medical concern. Experimental models play an important role in understanding such a disease, which is treatable only. This study describes a rat *diabetes mellitus* model induced by administering a reduced dose of alloxan, thus greatly reducing the animals' death rate.

KEY WORDS Alloxan. Diabetes. Rats.

Introduction

Due to its high prevalence and potential deleterious effects on a patient's physical and psychological state, diabetes mellitus, which can result in a morbid condition, is a major medical concern. [1, 2]

According to the World Health Organization (WHO) the number of diabetics has doubled in the past few years and is expected to double once again by the year 2025. Today, there are 160,000 diabetics worldwide, 10,000 in Brazil only, which makes the county the sixth in the world rank.[3]

In humans, *diabetes mellitus* is one of the most prevalent conditions with spontaneous manifestation. In animals, it can be induced by partial pancreatectomy or by the administration of diabetogenic drugs such as alloxan, streptozotocin, ditizona and anti-insulin serum.[4]

These agents selectively destroy the Langerhans islet ß-cells. The best known drug-induced diabetes model is the alloxan diabetes. Alloxan, a derivative of uric acid, as well as of other substances of different chemical groups, cases ß-cells to degranulate and consequently degenerate.[1, 5, 6, 7, 8, 9, 10, 11,12,13]

Alloxan induces irreversible *diabetes mellitus* after 24 hours following its administration and the condition proves to be chronic by laboratory tests after seven days.

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Proposition

This study describes the method of inducing *diabetes mellitus* in rats by alloxan administration.

Method description

The experimental animal in this model is the male, adult Wistar EPM (*Rattus norvegicus alvinus*, Rodentia, Mamalia) weighing 250 to 350 g.

After a 48-hour fast, the rats were weighed and anesthetized by her inhalation in a glass dome. A solution of alloxan at 2% diluted in saline at 0.9% was administered to the animals in a single dose corresponding to 40 mg of alloxan per kg of animal weight injected into their penial vein.

Food and water were presented to the animals only 30 minutes after the drug administration.

From the animals subjected to this procedure, 40% developed chronic *diabetes mellitus*; 20% either developed the condition to a mild or slight degree or did not developed it at all; and the remaining 40% died within the first seek of follow up, probably due to acidosis.

The animals showed the following signs of the condition: polydipsia (abnormal thirst), polyuria (increased urine volume), weight loss (due to lean mass loss), asthenia (weakness due to the inability to use glucose as a source of energy), dehydration (due to the animal body s'attempt to get rid of the excess blood glucose as the normal process of storing glucose in the body cells is impaired).

In order to assess the effect of alloxan and to chemically establish the diabetic condition, an incision was done in any of the four veins in the tail of the rat using a 15 scalpel blade 10 days after induction. A sample of the rat s'venous blood was collected on a reagent strip 10 days after the diabetes induction procedure for blood glucose level determination using a portable glucose analyzer.

The level of serum glucose considered to be normal in *rattus novergicus* ranges from 50 to 135 mg/100ml.[14] In this study, rats with glucose levels above 200mg/dl were considered as having severe diabetes.

Procedure for alloxan induction of diabetes mellitus

Lying on its back, the animal is given an injection of alloxan in its penial vein (Figure 1).

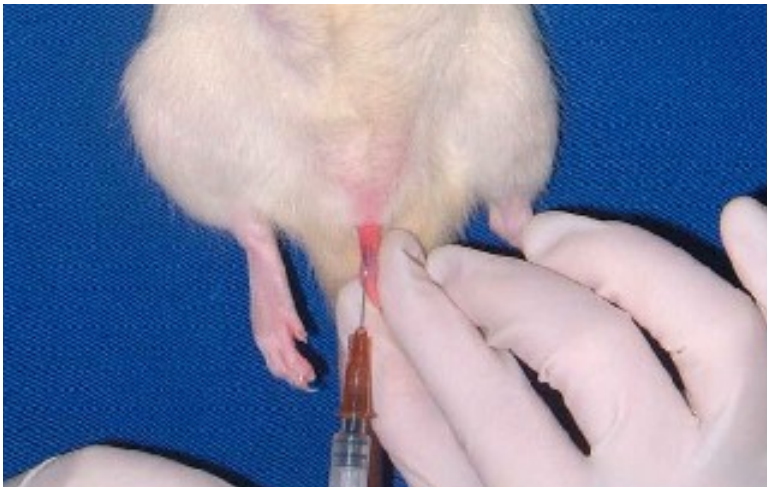

FIGURE 1 Administration of alloxan in the animal s'penial vein.

Incision in a tail vein for determination of glycemia level 10 days after alloxan injection (Figure 2).

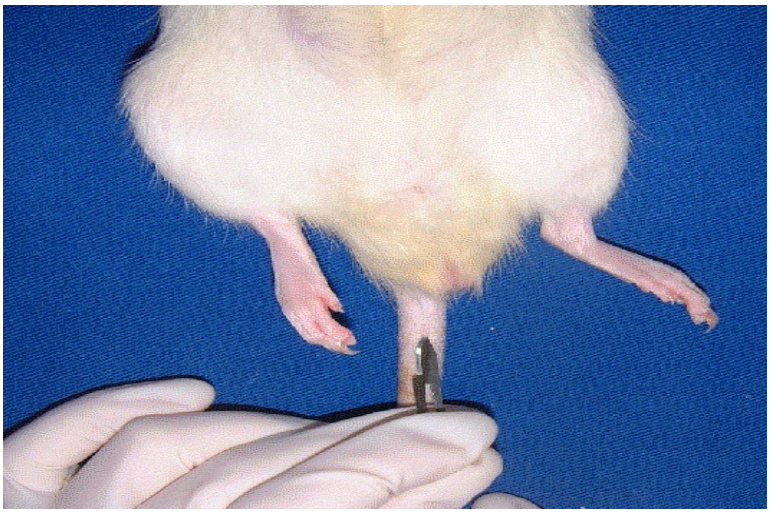

FIGURE 2 Incision in a tail vein of the rat with a 15 scalpel blade.

FIGURE 3 Bleeding resulted from the tail vein incision.

FIGURE 4 Portable blood glucose test device.

Perspectives

The procedure for chemical induction of *diabetes mellitus* proved to be effective. This experimental model adds to various others and can be used as alternative model in studies carried out in several fields such as plastic surgery.

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RESUMO - O diabetes mellitus é uma condição mórbida da maior importância no contexto da medicina. Este artigo decreve um dos modelos de indução do *diabetes mellitus* com aloxano, uma das substâncias que provocam a hiperglicemia permanente em várias espécies. Com base na literatura, tem o intuito de estabelecer esse modelo como uma opção para investigar as complicações do *diabetes mellitus* e seus tratamentos. Tese, ainda, considerações sobre perspectivas de aplicações deste modelo, ainda pouco utilizado.

DESCRITORES Aloxano. Diabetes. Ratos.

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