Neuropathic pain: An animal model of diabetic peripheral neuropathy and its mechanism

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ABSTRACT

Diabetic peripheral neuropathy (DPN) is one neuropathic pain caused due to chronically high sugar levels in the blood, which damages the peripheral nerves. It carries signals between the brain and other body parts, causing numbness and loss of sensation in feet, legs, or hands. Through several decades various animal models were used for mimicking DPN, rodents being one of the most common among them. The first-ever rodent model for DPN was streptozotocin (STZ) induced rats and mice models. Many models and methods have emerged, and some are still in trial. In this review, the different animal models of diabetic peripheral neuropathy are discussed, and recent animal model techniques are reported. Experiments with rat models include the streptozotocin-induced rat model, Otsuka Long-Evans Tokushima Fatty (OLETF) rats model, L-fucose induced neuropathic rat model, spontaneously diabetic WBN/Kob rat model, partial sciatic nerve ligated rat model, and genetically modified SDT fatty rat model. Though many such models are available, certain limitations often reduce their effectiveness.

BACKGROUND

- Neuropathy caused by high blood glucose levels in the body which leads to sensory abnormalities best describes diabetic peripheral neuropathy (DPN). DPN can be either polyneuropathy or mononeuropathy.
- The higher the age the more you are prone to DPN. Often seen in diabetic people over 50 years. Individuals more than 61 years of age are considered to be at high risk.
- While the exact cause of diabetic peripheral neuropathy is still unknown, two things may explain it: - high blood glucose levels for a long time can interfere with the signaling of nerves and can also cause the weakening of blood capillary walls which supplies the nerves with oxygen and nutrients.
- Being one of the common and often most painful complication of a diabetic person, the risk of diabetic neuropathy rise with age of the person, duration of diabetics, smoking, body mass index and diabetic retinopathy.

OBJECTIVES

- To show the pros and cons of with rodent models includes its more time-consuming, and most of them are not validated either by antidiabetic or anti neuropathic drugs.
- To discuss the different animal models of diabetic peripheral neuropathy and recent animal model techniques have been reported.
- Hence, it is an attempt to provide a better and more efficient model for DPN and has integrated all the information

METHODS

- The authors followed the PRISMA guidelines and retrieved the information from the various electronic databases.
- The articles were selected from 2005 to 2021 published papers in the peer reviewed journals.

ANIMAL MODELS IN DPN

Animal models, mainly rodents, which mimic the clinical aspects of DPN, can be of two types:-

Drug induced DPN models:-

- Certain drugs are induced into rodent models to make them diabetic. Such two drugs are streptozotocin and alloxan.
- If we take the working of each drug separately then STZ mainly harms the pancreatic β-cells by making them toxic through alkylation and in case of alloxan (ALX), it toxicates the β-cells by producing free radicals of oxygen.
- Examples of drug induced rodent models that we are going to come across this study are:-
  - Streptozotocin-induced rat model (classic),
  - Streptozotocin-induced rat model (recent),
  - Streptozotocin-induced mouse models.
  - Alloxan induced models.

Genetically modified animal models:-

Bio-breeding/Worchester (BB/Wor), Evans Tokushima lean rat (LETL), Otsuka Long-Evans Tokushima Fatty rats model (OLETF), Non-obese diabetic (NOD) mice model etc are few of the genetically modified models we are going to come across through this study.

There are also drug induced models that are modified genetically such as:-

- Streptozotocin-induced mouse models(genetic)
- Swiss Mice
- C57BL/6
- ICR
- NOD (Non-obese diabetic)
- C57BL/6
- Swiss Webster
- Swiss Wistar

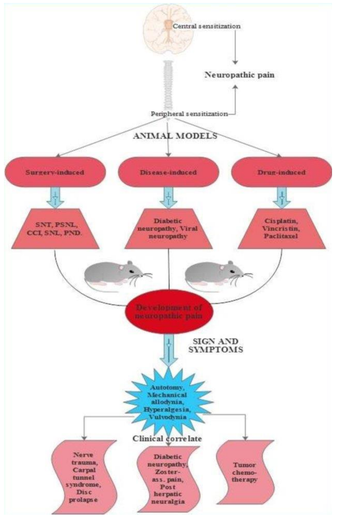

Figure: Diagram representing animal models of DPN.

DIAGNOSIS AND REDUCTION

- The diagnosis of DPN can be done by various physical examinations and a close evaluation of the outcome produced and medical history.
- Some of the tests being: - filament test, sensory test, nerve conducting test, muscle response test and autonomic test.
- One of the frequent and best reduction method for DPN is to maintain the blood sugar level at a healthy rate by making balanced and healthy life choices (balanced diet, exercise, quit smoking). This in turn will help ease the symptoms and also aid in improving overall health of an individual.

SIGNIFICANCE OF ANIMAL MODELS

- **Animal models are used to obtain information about:**
  - Brain physiology and disease progression
  - Understand the molecular mechanism of DPN
  - Disease prevention and diagnosis
  - Develop the treatment strategies
  - Drug testing and discovery

SCOPE AND FUTURE STRATEGIES

- As for the future strategies zebra fish and drosophila melanogaster, both which has a high genetic similarity to humans, cheap to maintain than rodent models and robust can be altered to mimic DPN which may turn out to be a more efficient and popular animal model for DPN.

CONCLUSIONS

- Finding the best model for DPN which perfectly mimics the disease is difficult because of it being a multifactorial disorder. Still some of the models are considered best than other models.
- Among rodents mice were observed to be better models for DPN.
- The following features of them contributes in being a better model for DPN:- has discrete genetic backgrounds, the impacts of gene knockouts and overexpression can be studied, it can develop hyperglycemia for a long span of time and also other features of human DPN.
- Although we have a vast variety of best and effective models, more experiments should be conducted with different models as DPN in each person can act differently cause of our heterogeneous population.

ACKNOWLEDGEMENT

The authors thank Chettinad Academy of Research and Education for constant support and encouragement.

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