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Review Article

Animal Models in Periodontology: A Review

Abdul Naeem[1,*], Vinita Boloor[2], K S Rajesh[3], Shashikanth Hegde[4], Anupama Rao[2]

[1]*Postgraduate, Department of Periodontology, Yenepoya Dental College, Yenepoya (Deemed to be University), Deralakatte, Mangalore, Karnataka, India*
[2]*Additional Professor, Department of Periodontology, Yenepoya Dental College, Yenepoya (Deemed to be University), Deralakatte, Mangalore, Karnataka, India*
[3]*Professor and Head of Department of Periodontology, Yenepoya Dental College, Yenepoya (Deemed to be University), Deralakatte, Mangalore, Karnataka, India*
[4]*Professor, Department of Periodontology, Yenepoya Dental College, Yenepoya (Deemed to be University), Deralakatte, Mangalore, Karnataka, India*

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[*] *Corresponding author.*
Abdul Naeem
dr.abdulnaeem92@gmail.com

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ABSTRACT

In periodontal research, animal studies are complementary to *in vitro* experiments prior to testing new treatments. Animal models should make possible the validation of hypotheses and prove the safety and efficacy of new regenerating approaches using biomaterials, growth factors or stem cells. Rats, hamsters, rabbits, ferrets, dogs, and primates are just a few of the many kinds of animals that have been utilised as models for human periodontal illnesses and therapies. However, animal anatomy and physiopathology differ from those of humans, making it challenging to assess novel treatments. Major periodontal diseases (gingivitis and periodontitis), their development, and innovative surgical procedures have all been studied using experimental models. This review's objective is to draw attention to the animal models that are available for dentistry research.

Keywords: Periodontal disease; Animal models; Biomaterials; Periodontal surgery

1 INTRODUCTION

Periodontitis is a highly prevalent, chronic immuno-inflammatory disease of the periodontium that results in progressive loss of gingival tissue, the periodontal ligament, and adjacent supporting alveolar bone[(1)].The deterioration of the tooth-supporting structures caused by the biofilm and the host reaction to it eventually results in the clinical indications of periodontitis, with the teeth eventually becoming loose in their sockets. Scaling and root-planing are used in conjunction with strict dental hygiene to stop the disease's progression. Regenerating periodontal tissue through non-surgical or surgical methods should be the ultimate goal of periodontal treatment. Although human cell cultures were found to be useful models for replicating some aspects of the periodontal disease process at the cellular level, information about the complex host response was not prominent[(2)]. As a result, animal models have been used to evaluate the pathogenesis of periodontal diseases and various periodontal treatment modalities. Wessler in 1983 defined an animal model as "a living organism with an inherited, naturally acquired, or induced pathological process that in one or more respects closely resembles the same phenomenon in men." The Institute of Laboratory Animal Resources (ILAR) of the National Academy of Sciences adopted and modified Wessler's definition as follows: "An animal model is a living organism in which normative biology or behaviour can be studied, or in which a spontaneous or induced pathological process can be investigated, and in which the phenomenon in one or more respects resembles the same phenomenon in humans or other species of animal"[(3)]. Animal models have undergone extensive research in order to understand specific biological phenomena, with the hope that findings from these studies would provide light on

how other organisms function. Animal models have proved indispensable in the advancement of science, especially in the biomedical field, with various diseases, including periodontal disease being studied extensively. Periodontal disorders may be carried on experimentally, spontaneously, or both depending on the species. Large animal models have been chosen in the context of regenerative medicine employing biomaterials due to the reproducibility and surgical accessibility of experimental abnormalities. Dogs have been extensively utilised for modelling the regeneration of periodontal abnormalities with biomaterials, in addition to monkeys, which are the perfect model in pre-clinical trials. Rats, miniature pigs, sheep, rabbits, and cats have all been employed in several research. In order to guarantee reproducible models that enable statistical analysis, various techniques have been proposed [4].

Prior to conducting clinical trials on people, it is crucial to do experimental research to determine the cause and pathophysiology of the illness process in animal models. Therefore, before being utilised on humans, animal models are used to assess the success of innovative surgical procedures, the efficacy and impact of restorative materials on dental pulp, the etiopathogenesis, clinical characteristics, and histological and immunologic components of periodontal disease [4,5].

2 NEED FOR ANIMAL MODELS

- Animal data can provide us with models of biologic trends before proceeding to human application.
- Since there are no accurate clinical signs for continuing tissue degradation (disease activity), periodontal disease can only be investigated retrospectively in humans. Therefore, it is desirable to have an animal model that allows for the prospective study of particular microbiological and immunological parameters.
- Proper evaluation of a new therapy necessarily involves the use of treated and untreated controls which are difficult to obtain in the human.
- The testing of potentially harmful new devices and drugs may be unethical in man prior to thorough evaluation in higher animals.

3 CLASSIFICATION OF ANIMAL MODELS

1. **Davidson et al. (1987)** [6]

   (a) **Induced/Experimental models**: These make an effort to mimic the characteristics of the actual species.
   (b) **Spontaneous/Natural models**: Recognised as sharing certain characteristics with the original species.
   (c) **Negative/Non-reactive models**: They are the normal counterparts of the disease model.
   (d) **Orphan models**: Animal disease for which no human or animal counterpart exist.
   (e) Over the years, a fifth category of a **genetically modified model**, in which the genetically modified animal can be coordinated to mimic the human disease in various specific aspects, has been added and is gaining a clear importance in the field of experimental animal models.

2. **Page and Schroeder (1982)**

   (a) **Small Rodents** (mice, rats, hamsters, minks)
   (b) **Larger animals** (dogs, sheep)
   (c) **Non-human Primates** (macaca, baboons, chimpanzees)
   (d) **Others** (cats, horses, guinea pigs, etc.)

4 SELECTION CRITERIA

For selection of suitable animal; specific anatomical, physiological, pathological, and/or psychological characteristics need to be considered based on current scientific literature as under [7].

1. **Factors related to the species :**

   (a) Availability
   (b) Characteristics:

      i. Size, body conformation, and anatomic characteristics
      ii. Age and life expectancy
      iii. Feeding habits
      iv. Genetic characteristics
      v. Polymorphism
      vi. Reproduction
      vii. Health status
      viii. Indigenous factors

   (c) Requirements:

      i. Nutrition
      ii. Environment
      iii. Space and caging

2. **Factors related to the research project:**

   (a) Type of agent being investigated
   (b) Dosage of the drug and route schedule of administration

3. **Factors related to the investigator(s) :**

   (a) Past experience and existing knowledge
   (b) Field of interest on practical basis, the size and configuration of the animal may be an important parameter.

5 BENEFITS OF ANIMAL MODELS IN RESEARCH

The following are the benefits of the use of animal models in research:[8–10]

1. The use of animals in research has made a substantial contribution to the understanding of biological processes.
2. It has been responsible for many important biomedical discoveries.
3. It is used in the development of a great number of therapies and preventative treatments, such as antibiotics, insulin, vaccines, and organ transplantation.
4. Moreover, animal models provide an opportunity to investigate discrete steps of periodontal disease.

6 ETHICAL GUIDELINES

Before initiating their research projects, all scientists using experimental animal models should abide the national or institutional ethical standards. Everyone should completely abide the recommendations of the animal ethics committee.

1. The three Rs concept is the most crucial rule to follow while conducting research using experimental animals as models. Replacement, reduction, and refinement are the three Rs that Russell and Burch introduced. The goal of the three Rs when using experimental animals for research is to employ them only when absolutely required, keep the number of animals used for study purposes to a minimal, and limit the suffering of the animals while they are being studied.[11]
2. The Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) in India also propagated the 4 Rs, which stands for replacement, reduction, refinement, and rehabilitation of animals used in experiments. The rehabilitation of animals after experimentation must be a component of the research, according to CPCSEA's national policy. The fourth R, which is added to the research field, directs the researcher to take extra care when employing animal models postoperatively.[12]

Many regulatory organisations are concerned about the welfare of the animals, which results in the development of policies governing the proper handling and use of animals in research. Five basic principles were developed by the regulatory authorities' advisory committee for the use and treatment of animals employed in research and testing.

- It is permissible to conduct animal experiments to increase our understanding of physiological processes that have a major positive impact on people's well-being.
- When conducting animal testing, one should take into account the lowest creatures on the evolutionary tree that produce meaningful data.
- If animals are to be utilised in research techniques, avoid or reduce pain and misery. Each procedure must be carried out under sufficient sedation, analgesia, or anaesthesia.
- The postoperative treatment of the experimental animals is the responsibility of the researchers.
- Care should be made to ensure that animals have a comfortable environment to live in.

7 ANIMAL PROFILE

It is important to know the animal profile prior to the use in research.[13] Table 1

8 LIMITATIONS OF ANIMAL MODELS

1. There is ongoing debate over the utility of animal research for human experience. No matter how much information is available, it is impossible to predict that various species will react to a challenge in the same way or even in a comparable way except within extremely specific bounds.
2. There are huge financial incentives to use computers or other alternatives in place of animals. Only because there are now no alternatives are research animals utilised, which are highly expensive to obtain and maintain.
3. Depending on the type of illness present and the stage of development, the characteristics of periodontal diseases in humans and animals differ significantly.
4. Numerous of the animals' genetic backgrounds are unknown
5. Wild animals that have been captured for use in study frequently vary in age, body weight, dental health, and other health issues.

9 ALTERNATIVES TO EXPERIMENTAL ANIMAL MODELS

Alternative models have been developed to address the drawbacks and unethical practice of utilising experimental animals as models. Alternative approaches have the benefits of speed, requiring less labour, and being economical. In biomedical research and testing, anything that completely or partially replaces the use of live animals is regarded as an alternative or substitute. A few examples of alternatives to animal testing include stem cells, microdosing, DNA chips, microfluidics chips, human tissue, novel imaging technologies, and post marketing drug surveillance[14]. The majority of experimental animal models can be replaced with computer simulations, cell and tissue cultures, and different alternative creatures like invertebrates, lower vertebrates, and some microorganisms like prokaryotes, protists, and fungus. No doubt that these alternatives will minimize the usage of animal models, but they cannot

Table 1: Animal profile

Animals	Age	Weight	Respiratory Rate	Rectal Temperature	Pulse/Min	Life Span
Mouse	6-8 weeks	25-30 g	90-180 per min	37.4°C	600	1.5-2 years
Rat	10-12 weeks	200-300 g	80-150 per min	37.5°C	300	2.5-3 years
Hamster	6-8 weeks	80-100 g	40-120 per min	37.6°C	450	1.5-2 years
Guinea pig	16-20 weeks	400-500 g	60-110 per min	38.6°C	150	4-5 years
Rabbit	24–32 weeks	2–2.5 kg	35–56 per min	38.7°C	133	4-5 years
Cat	30-35 weeks	3-5 kg	20-30 per min	39.5°C	110	8-12 years
Dog	1-1.2 years	12-15 kg	14-28 per min	38.6°C	95	10-15 years
Monkey	4-5 years	10-12 kg	30-54 per min	38.4°C	200	15-20 years

completely eliminate their usage in pre-clinical studies.

10 FUTURE PERSPECTIVES

The research carried out using animal models are indicated as biomedical research since the fundamentals of biology have now reached the molecular level and different phenomena of life are now reliant on genes. For instance, current animal models for human diseases are enhanced by the coordinated use of genetic, cellular engineering, and embryonic manipulation principles in accordance with the needs or study objectives.

Following are the objectives to follow during the usage of animal models.[15,16]

1. Replace the animal models in non-animal-based experimental researches
2. *Ex vivo* models or in vitro procedures must be employed to reduce the number of animals used to the absolute minimum.
3. Once all prerequisites are met, as set forward by regulatory agencies, animal research can begin.
4. The studies must be more credible and informative, and animal models should be regularly enhanced to keep up with biomedical research breakthroughs.
5. Animal protection is always a concern when using animals in research

11 CONCLUSION

Periodontal disorders, and particularly the severe types of periodontitis, have long been and are a mystery to both individuals who experience them and those who work to understand and avoid them. Since more than a century ago, efforts have been made continually and with varied degrees of success to comprehend these disorders through clinical and experimental study. In addition to humans, a number of other mammals, especially those raised in captivity or in the home environment, acquire periodontitis on their own as they get older. In order to discover an answer to the subject that has perplexed us for a long time, a variety of mammals and animals' periodontal tissues as well as the safety and effectiveness of new biomaterials and treatments have been thoroughly researched.

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