

Animal Model Used in Dentistry-A Review

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Abstract

The main aim of the study was to know about the various dental studies carried out on animal models. Animals have been targeted for various medical investigations for human observations. From the early nineteenth century, there was a significant increase in the use of animals for scientific experiments. Compared to small animal models like rodents, large animal models are superior in many aspects for the study of human diseases and pre-clinical therapies. This is significant to develop new medicines for newer diseases emerging day by day in the current world. Animals are also used for the safety test to know the potential of medicines before they are being clinically introduced in suffering patients to make sure it doesn't show adverse effects and to check the safety of other chemicals as well. A review is done on different dental studies carried out in animal models which were collected from search engines like pubmed, google scholar, google chrome and from various research articles. Quality analysis was done using the ideal method. The review helps in attaining complete knowledge about dental related studies on animal models. Studies like these can prove to be helpful in further development concerned with humans. This review gives a clear view about the different dental studies carried out in animal models and its observation and outcomes.

Keywords: Animal models, dental study, development, procedures

Introduction

Animals are used in scientific research to help us understand our own bodies in a better way and how they work. This is significant to develop new medicines for newer diseases emerging day by day. Animals are also used to safety test potential medicines before they are tested in people to make sure it doesn't show adverse effects and to check the safety of other chemicals as well. Animals, right from the fruit fly to the mouse, are widely used in scientific research occurring in numerous platforms¹. They are very crucial for allowing scientists and researchers to learn more about human biology and health, and for multiple developments. The use

of animals in scientific research has always been the subject of heated debate for the longest time. On the one hand it is considered morally wrong to use animals in this way solely for human benefit which is painful. But, removing animals completely from the lab would impede the understanding of health and diseases, and consequently affect the development of new and vital treatments. Although sometimes these studies can reduce the quality of life of these animals, thorough regulations are in place appropriately to ensure that they are carried out in a proper way. To help minimise the harm animals usually experience while being studied in the laboratory, researchers are required to follow a set of these protocols which include the 'three Rs'.

These are

Replace: Replacing, where and whenever possible, experiments using animals with alternative techniques such as cell culture in microbiology labs, computer modelling or human volunteers instead of animals, everytime².

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Reduce: Reducing the number of animals being used and by improving experimental techniques and sharing information with other researchers so that the same experiments aren't being done by the other fellow researchers.

Refine: Refining the way the animals are being taken care of. To help minimise any kind of stress or pain, by using less invasive techniques wherever possible and improving medical care and living conditions for such animal models³. Animals have been targets for investigations and observations for mankind. Animal research has been important in the development of many major medical advances. Studies that use animals have played a role in the prevention or treatment of conditions as diverse as tuberculosis, diabetes, polio, parkinson's disease, muscular dystrophy and high blood pressure⁴. From the early nineteenth century, there has been a significant increase in the use of animal scientific experiments⁵. Studies carried out in ex-vivo i.e. procedures done in animals for research are mainly done before performing them in-vivo. The most preferred animals used for medical and dental studies are rats, mice, guinea pigs, rabbits, beagle dogs, goats, and nonhuman primates⁶. The selection of an experimental model is determined according to research objectives, as well as constraints such as housing of large or nonstandard animals^{7,8}. Small animal models generate substantial and relevant data on the interactions between the soft and hard tissue, especially during inflammation⁹.

On the other hand, the major drawback of using small animals is that they show very limited similarity in dentins of humans when dental experiments are concerned¹⁰. Compared to small animal models like rodents, large animal models are superior in many aspects for the study of human diseases and pre-clinical therapies but their usage is difficult¹¹. The dental anatomy of larger species of animals resembles human dentoalveolar architecture more closely than that of smaller species¹². They allow a more direct interpretation of the data and translation of the knowledge to clinical settings. Several large-animal species, such as nonhuman primates, dogs, sheep and miniature pigs, have been traditionally used in periodontal research. Nonhuman primates have oral structures and teeth similar to those of humans and have naturally occurring dental plaque, calculus, oral microbial pathogens and periodontal disease¹³. Mice are

the smallest species used extensively in dental studies. There are several advantages of a mouse as a model. They are extremely cost-effective when compared to larger animals. Rabbits are also preferably good small animal models for studying the impact of inflammation on periodontal wound healing and regeneration. However, with the new advancement of ex vivo animal models, it has become easy to investigate disease pathogenesis and to test the efficacy of newer therapeutic modalities with the reduced usage of animal models¹⁴.

The appropriate guidelines to use animals in researches is as follows :

- Depending only on the need, one should allow and provide facilities to use animal models for all kinds of research purposes.
- It is recommended for all the researchers that one should not use animals unless it is an unavoidable situation and circumstance.¹⁵
- It should be ensured that unnecessary pain or injury to the animals should be evaded.
- It should provide adequate care, housing, and make sure that the animal models used for research purposes are physically comfortable and in good state of health.
- Sources of experimental animals for research should be from recognized animal facilities where there will be availability of genetic, health, and nutritional status of each animal model.¹⁶
- It should provide training facilities to the scientific researcher and the supporting staff those who take care of the animals during experiment.¹⁷
- Alternative animal models should be used to replace experimental animals wherever possible and least usage should be kept in mind.¹⁸
- Procedures which are painful should ensure appropriate use of anesthesia.
- Forming ethical committees will ensure the minimal usage of animal models.¹⁹

Different animal Profiles

It is extremely important to know about animal

profiles prior their use in any field of research. Animal profile includes physiological norms of commonly used laboratory models like mouse, rat, hamster, guinea pig, rabbit, cat, dog, and monkey etc. Maturity of age, adult weight, respiratory rate, rectal temperature, pulse rate per minute, and life span are some of the physiologic norms of the healthy animal models to follow during selection of research.²⁰²¹

Table 1.1 Different animal profiles used in various fields of research

Animal	Age at maturity:	adult weight:	respiratory rate:	rectal temperature:	pulse rate per min:	life span:
Mouse	6–8 weeks	25–30 g	90–180 per min	37.4°C	600 on average	1.5–2 years
Rat	10–12 weeks	200–300 g	80–150 per min	37.5°C	300 on average	2.5–3 years
Hamster	6–8 weeks	80–100 g	40–120 per min	37.6°C	450 on average	1.5–2 years
Guinea pig ²²	16–20 weeks	400–500 g	60–110 per min	38.6°C	150 on average	4–5 years
Rabbit	24–32 weeks	2–2.5 kg	35–56 per min	38.7°C	133 on average	4–5 years
Dog ²³	1–1.2 years	12–15 kg	14–28 per min	38.6°C	95 on average	10–15 years
Monkey ²⁴	4–5 years	10–12 kg	30–54 per min	38.4°C	200 on average	15–20 years
cat	30–35 weeks	3–5 kg	20–30 per min	39.5°C	110 on average	8–12 years

The current study discusses the various researches in the field of dentistry and related areas of interest. This study would enable one to know about procedures carried out in animal models and its outcome as well (figure 1).

Materials And Methods

A review literature was done on different dental studies carried out in animal models. The system and data based searches for the relevant articles were done

and collected from search engines like pubmed, google scholar, google chrome and from various research articles. The articles were primarily dated back till 2000 but few references were dated even earlier. About 50 articles were collected, analysed and reviewed. Quality analysis was done using the ideal method using the health evidence (quality analysis tool) and it was scored as weak, moderate and strong and also by grading them on various levels from level 1 to 5.

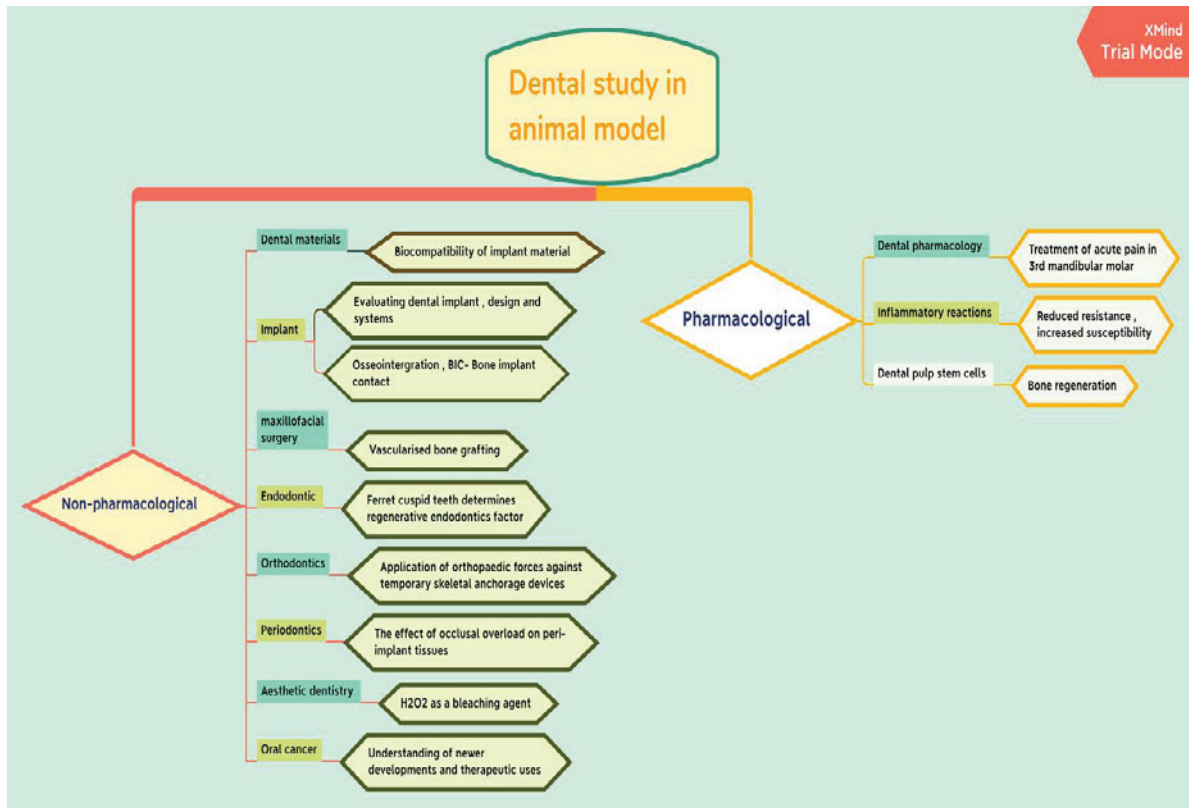


Figure 1: Flow chart describing the branches of studies involved.

Discussion

Dental pharmacology and animal model

Treatment of acute pain after the removal of mandibular 3rd molars can be used to study in a dental pain model and compared to the analgesic efficacy of a new, orally administered NSAID, lornoxicam, with another potent NSAID in a double-blind. Placebo-controlled randomized was used in the previous literature.²⁵

Oral and maxillofacial surgery

The oral maxillofacial region of miniature pigs is similar to the ones seen in humans. The similarities include anatomy, physiological development, pathophysiology and the disease occurrence as well^{26,27}. Reaction of bone tissue was determined after placement of two different types of in vascularised bone grafting, the results revealed that a hydroxyapatite-coated implant as well as a titanium screw-type implant might be applied with a vascularized bone graft for jaw reconstruction.

Relationship between dental erosion and GERD

GERD-Gastro esophageal reflux disorder is a condition where the mucosal layer gets eroded due to stomach acid reflux into the esophagus. The study reveals the fact that there is an existence of a relationship between the dental erosion and GERD. Dental erosion was only detected in the reflux rats first. Relationship between dental erosion and GERD was observed First step of dental erosion caused by GERD is the loss of surface enamel induced by regurgitation of an acidic liquid and acidic gas²⁸.

Biocompatibility between dental materials

The impact of bone compression on bone to implant contact of an osseointegration is called bone impact contact The biocompatibility of two implant materials, vitallium and poly-methyl methacrylate (PMMA), was evaluated in an animal model in which bone formation and resorption are independent of each other. Neither material accelerated resorption, but formation was inhibited 12% by vitallium and 38% by PMMA²⁹.

Endosteal dental implants

One-hundred and twenty endosteal dental implants were inserted bilaterally in the mandibles of 30 adult mongrel dogs after bilateral extraction of all premolars. describes an animal model that is useful in evaluating dental implant designs and compares the results with those from humans³⁰.

Regenerative endodontics

Study was done to investigate ferret cuspid teeth as a model to investigate the factors involved in regenerative endodontics. Each animal was anesthetized and perfused with 10% of buffered formalin³¹. Block sections including the mandibular and maxillary canine teeth and their surrounding periapical tissues were obtained then radiographed, decalcified, sectioned, and stained with the H and E (hematoxylin-eosin) to determine and study the various stages of apical closure in these teeth. Thus the study concludes that ferret cuspid teeth can be used to investigate various factors involved in regenerative endodontics that cannot be tested in human subjects easily³².

Speed surgical orthodontics(SSO)

Speedy surgical orthodontics (SSO), which is an innovative orthodontic treatment, involves the application of orthopedic forces against temporary skeletal anchorage devices following the suprasedgmental corticotomy to induce movement of specific dental segments³³. For the study 5 beagle dogs were divided into 2 groups and their 6 maxillary incisors were retracted en masse by applying 500 g orthopedic force against a single palatal mini-plate. All animals were killed on the 70th day, and their periodontal structures were processed for histologic analyses and scanning electronic microscopy (SEM)^{34,35}.

Effect of occlusal load

Evaluates the effect of occlusal overload (OV) on peri-implant tissue health in animal studies. Data on OV on stable implants are limited and conflicting. OV may lead to bone loss in the presence of dental plaque and to an increase in BD in areas where plaque control is performed³⁶.

The complex microenvironment of any periodontal wound creates many challenges linked with multi tissue regeneration of periodontal lesions. Recent characterization of mesenchymal stem cells-like populations residing in periodontal ligament tissues has shown that these cells exhibit features of postnatal stem cells. The aim of this study was to assess the regenerative potential of (PDLSCs) also called allogeneic periodontal ligament stem cells in a rat periodontal fenestration defect mode and to identify an optimal end time-point suitable for quantitative assessment of tissue regeneration³⁷.

Radiology

Hepatic cryoablation was done in rabbits with VX2 tumors and in two healthy rabbits. Nonenhanced and dynamic contrast material-enhanced computed tomography (CT) and magnetic resonance (MR) imaging and power and color Doppler flow ultrasonography (US) were performed 7–8 days after cryoablation. In this animal model, recurrent tumor typically appeared as focal nodules at the cryolesion periphery. The rim and central foci of enhancement, doppler flow, and increased signal intensity on T2-weighted MR images can be normal findings after hepatic cryoablation³⁸.

Implantology

Development of optimal interface between bone orthopaedics and dental implants has been taking place for many years and animal models are often an essential step for testing of orthopaedic dental implants prior their use clinically in humans³⁹. Some of the more commonly available and frequently used models are of the dog, sheep, goat, pig, rabbit for evaluation of bone-implant interactions^{40,41}. Insertion Torque Resonance Frequency, Analysis of dental Implant systems in animal Model Loaded with Implants⁴². Thirty-two implants were placed in 16 beagle dogs maximum insertion torque values were recorded. After a healing period of 8 weeks the implants were loaded for 3 months, the animals were then sacrificed⁴³. Studies from animal subjects indicate that irradiated bone has a greater risk of implant failure than non-irradiated bone⁴⁴. Animal clinical studies differ on the importance of dose effect on implant location regarding implant survival^{45,46}. Influence of multiple variables with different animal models monkeys, dogs, pigs, rats, rabbits, sheep leading to results that might not be comparable reliably on clinical implications on

performance in humans, estimate percentage of patients who would experience different amounts apical root shortening⁴⁷. Diamond coated titanium dental implant used in nanodentistry: Nano-crystalline diamond-coated titanium dental implants – A histomorphometric study in adult domestic pigs⁴⁸. Twenty four MWP-CVD diamond-coated and twenty four un-coated dental titanium-alloy implants were placed in the frontal skull of eight adult domestic pigs. To evaluate the effects of the nano-structured surfaces on bone formation, a histomorphometric analysis was performed after 2 and 5 months of implant healing.⁴⁹

Aesthetic dentistry

Hydrogen peroxidase, commonly known as H₂O₂ is a bleaching agent used in aesthetic dentistry. It possesses bleaching efficacy due to its ability of penetrating the tooth structures and oxidized organic molecules. The inflammatory tissue response in rats teeth after dental bleaching is performed and seems to be greater in diabetic rats. Reproducible Experimental model that directly relates Kronick biphosphate administration development, osteonecrosis with and without the extraction with no drug involved. New animal models of BRONJ after zoledronic acid administration, dental extractions achieving bone changes are similar or superior⁵⁰.

Inflammatory reaction infection

Diabetes mellitus is a complex multisystemic disorder with elevated prevalence. Patients' diabetes with reduced resistance to bacterial infection and decreased tissue repair ability will eventually contribute to an increased susceptibility to inflammatory reactions infections⁵¹.

DPSCs- Dental pulp stem cells:

Evaluating frequency of dental pulp stem cells for bone regeneration. Stem cells are the ones with self regenerating ability⁵². They are capable of differentiating into multiple cell lineages as a promising cell-based tissue. Significantly no healing period is generally accepted as a prerequisite for osseointegration of dental implantology^{53,54}.

A histological assessment of intruded teeth:

The study evaluated the histological examination of surgical repositioning of the intruded dog hit upon the pulpal and surrounding tissue. 30 teeth in 10 adult dogs, between the age group of 2 to 4 were used. The observation was done at the seventh, 15th and 30th postoperative days; it was later concluded that the pulpal necrosis, external root resorption and losses were common sequelae to serve traumatic intrusions⁵⁵.

Canine periodontics

Periodontal disease refers to a group of inflammatory diseases caused by bacterial plaque in the periodontium and are ranged in various stages. Periodontal disease had an enormous impact on humans and veterinary medicines due to its high prevalence. The commonest animal as a periodontal disease model is the dog and they are used for having useful approaches for understanding human periodontal diseases in a new therapeutic and preventive measure⁵⁶.

Maxillary sinus floor elevation

The study uses 12 fresh heads of 4 merino sheep, 4 Marciano granadina goats, 4 large white pigs. Two schools from each species were used and several 3-D pictures of them were taken. The study concludes that the approach of maxillary sinus in sheep, goat and pigs from the buckle vestibule required a previous surgical enlargement of the vestibule⁵⁷.

Animal model in oral cancer research

Oral cancer is the world's 11th most common human new place yeah. No animal model, of course, is perfectly applicable to any kind of human cancer. Even so, it is generally agreed that animal model is a virtually inevitable prelude to understanding how new development takes place and helps in assessing efficiency of new therapeutic approaches for such cases⁵⁸.

Conclusion

In conclusion, the review shows that there have been multiple experimental studies that have been carried out in animals and are being done currently as well the main purpose is to make the best out of these places ex-vivo studies. This will make future research easier and simpler by knowing appropriate usage of animal models and different procedures carried out in them.

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Ethical Clearance: As it is a review article so it is not required.

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