Systematic Review of the Effects of Excessive Occlusal Mechanical Load on the Periodontium of Rats

Abstract

Objective: This study aims to systematically evaluate the effects of traumatic occlusion on the periodontal tissue of rats. The set of questions to be answered were—Can traumatic occlusion acting on a healthy and an unhealthy periodontium cause periodontal destruction? Design: The protocols for systematic review were all developed, following the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement and applied to animal research. Reporting of In vivo experiment guidelines for reporting animal research to assess the risk of bias of the studies. Materials and Methods: A literature search was conducted using MEDLINE through PubMed and manual search from the reference lists of main articles related to the theme. Results: This search strategy identified 65 references, of which 33 were considered inappropriate. The full texts of 32 articles were read, 31 of which did not meet the eligibility criteria and were excluded. The final selection included 1 article for which data was extracted for further evaluation. The article included shows a strongest reaction in the periodontium in front of a secondary occlusal trauma as inflammation and apical migration of the junctional epithelium, bone degradation, and decrease in the quantity of collagen fiber. However, primary occlusal trauma also presents these alterations, with the exception of apical migration of the junctional epithelium. Conclusions: Although only one study was included in the systematic review of traumatic occlusion, there is some evidence from experimental studies on animals that shows a coherent picture of the effects of traumatic occlusion on the periodontium. However, new studies are needed to fully answer the questions posed by this systematic review.

Keywords: Alveolar bone, animal models, occlusion, periodontal ligament, systematic review

Introduction

Normal occlusal function is a mechanical stimulus necessary for the maintenance of periodontal tissue homeostasis, whereas the absence or excess of occlusal load results in disharmonic functioning of periodontal tissue.[1,2] In the face of occlusal force, the mechanism for transmission and neutralization of occlusal forces consists of several elements that work to prevent the occurrence of excessive occlusal pressures on the periodontium. These elements are the following: periodontal ligament fibers; fluids present in the periodontal ligament (hydraulic sustentation system); proprioception of the periodontal ligament; amorphous ground substance and blood vessels of the periodontal ligament; trabecular bone architecture; and tooth root shape.[3]

Histological studies have revealed that several morphofunctional alterations occur when excessive occlusal force is applied, such as disorientation and a decrease in collagenous fibers,[4,5] changes in the alignment of periodontal fibers,[1,6] an increase in the number of fibroblasts,[4] elevated osteoblast activity,[1,4,5,7,11] decreased osteoblast activity,[8,11,12] venous thrombosis,[9,4] cell necrosis in the periodontal ligament,[9,4] and absence of inflammatory cell infiltration.[7,9,11]

In the first 7 days following traumatic occlusion, a pressure increase in the interstitial fluid of the periodontal ligament was observed after 48 h.[4] Until the 5th day the width of the periodontal ligament space decreased, to return to normality between day 14 and 120,[8,13] likely as a result of bone remodeling.[1] However, traumatic occlusion does not alter the clinical probing depth.[14-16]

The bone is constantly being remodeled to guarantee correct mineral homeostasis and maintain structural integrity.[17] Osteoclasts

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reabsorb the mineralized matrix, while osteoblasts form new bone matrix in a rigidly coordinated sequence of events.\cite{18} Several regulatory systems, both systemic and local, exist that are responsible for maintaining the equilibrium between these two processes.\cite{19}

Discussion centers on the question if traumatic occlusion is a co-destructive factor of periodontal disease,\cite{11,20,21} or if it is a modality of periodontal disease itself and how it can affect the periodontium. This is however still controversial.\cite{14-16}

Preclinical research is used to create a better understanding of physiological and pathological processes. In many cases, it can also influence patient care.\cite{22} Systematic reviews are a cornerstone in evidence based medicine.\cite{23,24}

In addressing these issues, a key consideration is the type of evidence that is sufficient to guide different approaches that suit individual cases. Ideally, these issues would be addressed by conducting experimental trials in rats with traumatic occlusion and periodontal changes. Against this background, though, the definition of sufficient evidence is not always clear.

**Objectives**

This study aims to systematically evaluate the effects of traumatic occlusion on the periodontal tissue of rats.

The questions set to be answered were as follows:

a. Can traumatic occlusion acting on healthy periodontium cause periodontal destruction?
b. Can traumatic occlusion acting on unhealthy periodontium increase periodontal destruction?

c. Can traumatic occlusion acting on unhealthy periodontium increase periodontal destruction?

**Materials and Methods**

**Protocol and registration**

The systematic review of the literature was conducted by following the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement.\cite{25} Animal Research: Reporting of In vivo Experiments (ARRIVE) guidelines for reporting animal research\cite{26} were used to assess the risk of bias in individual studies.

**Eligibility criteria**

The search strategy was designed to identify original articles of experimental research in rats that focused on the effects of traumatic occlusion on the periodontium.

Studies presenting any of the following outcomes were eligible for this systematic review:

a. Clinical outcomes: The clinical outcome measures that will be assessed are changes in probing depth, clinical attachment level, bleeding on probing, and mobility.
b. Histomorphometric and histological outcomes: Any change from cells, the distribution and localization of biomarkers and proteins in the alveolar bone, periodontal ligament fibers, nerves, amorphous ground substance, collagen fibers, blood vessels, and tooth root shape.
c. Radiographic outcomes: Any results from radiography and tomography.

**Search strategy**

A literature search was conducted using MEDLINE through PubMed. A manual search from the reference lists of main articles related to the theme was also conducted to guarantee that all available evidence was found and revised. This encompassed all articles that were published in English, Spanish, and Portuguese between 1 January 1965 and 10 March 2015.

Terms and other free terms from the Medical Subject Headings (MeSH) were used for searching, and Boolean operators (OR, AND) were used to combine searches. The following search terms were applied: dental occlusion, traumatic (MeSH), periodontium (MeSH), occlusal trauma (Majr), animal study (Majr), and rats (MeSH) (i.e., 1. periodontium AND traumatic dental occlusion) AND rat, (i.e., 2 traumatic dental occlusion [MeSH Terms] AND periodontium [MeSH Terms] AND occlusal trauma [MeSH Terms] AND animal study[MeSH Terms] AND traumatic dental occlusion) AND periodontium) AND occlusal trauma) AND animal study) OR traumatic dental occlusion) AND periodontium) AND animal study) AND occlusal trauma).

**Data collection process**

Primarily, two reviewers (DAB and MFA) screened the titles and abstracts of articles according to the inclusion and exclusion criteria. All articles that indicated a possible match, or could not be excluded from the information given in the title or abstract, were considered and evaluated.

Further, the selected studies were submitted to quality assessment and data extraction.

To minimize bias during the studies review, in case of disagreement, a decision was reached by consensus of the majority of the authors.

**Inclusion criteria**

Studies that reported data about the clinical, radiographic, and histological evaluation of teeth subjected to excessive occlusal loads were considered eligible for inclusion.

Data on clinical and experimental signs, such as changes in the alveolar bone and tooth root shape; periodontal ligament fibers, nerves, amorphous ground substance, collagen fibers, and blood vessels were included.

**Exclusion criteria**

The following studies will be excluded: reports in which the relationship between mechanical overload and periodontitis was not explicit or could not be determined from the data as: methodology, animal model (other animals than rats), sample size (minimum 3 animals per group of analysis);
control group (absent or made in the opposite side of the same population of the experimental group), no application of continuous force on molars, and updates or dual publications by the same author.

Assessing risk of bias and methodological criteria of animal studies

The risk of bias was assessed using the ARRIVE questionnaire. Table 1 presents the individual quality criteria for each included study.\(^{[26]}\)

### Results

This search strategy identified 65 references, of which 33 were considered inappropriate for this review owing to the fact that their title and/or abstracts did not match in the inclusion criteria. The full texts of 32 articles were read, 31 of which did not meet the eligibility criteria and were excluded [Table 2]. The final selection included 1 article [Table 3] from which data was extracted for further evaluation [Tables 1, 3, and 4] [Figure 1].

### Study characteristics

**Type of selected study and population characteristics**

The studies selected for this review were experimental research in rats (≥3 animals per group). The primary and second occlusal trauma case was assessed by Nakatsu et al. 2014\(^{[27]}\) in an age range of 8 and 9 weeks. Periodontitis was induced by topical application of lipopolysaccharide into rat gingiva [Tables 3 and 4]. The diagnostic criteria to identify periodontitis were anti-LPS IgG serum levels.

**Characteristics of the traumatic occlusion induction**

Traumatic occlusion was induced in one tooth by placing a metal wire (1.0 mm in diameter) bonded with resin cements on the occlusal surface of the lower right first molar\(^{[27]}\) [Table 4].

**Type of diet**

The type and consistence of food was not specified in the article selected for this systematic review.

**Direction of the applied force**

The selected article used a method to create occlusal trauma, aimed at applying axial forces to the teeth.

**Time of study, material of analysis, and gender**

Nakatsu et al. 2014\(^{[27]}\) registered the effects of traumatic occlusion on the periodontium with periodontitis in the upper jaw 5 and 10 days post-surgery, using male rats for the experiment [Table 4].

### Types of outcome measured

The outcomes observed in the included study were as follows:

1. **Histomorphometric and histological outcomes:**
   - Periodontal ligaments
     - Loss of attachment
   - Alveolar bone
     - Bone surface irregularity
   - Osteoclasts – TRAcP
   - Gingiva
     - Immunohistological findings of C1qB

### Histomorphometric and histological outcomes

- Periodontal ligament fibers
Hyalinization areas of the periodontal ligament

Histological analysis in hematoxylin and eosin (HE) was carried out. Hyalinized tissue was a histological finding observed in the furcation region of teeth submitted to traumatic occlusion.\cite{27}

Organization of collagen fibers

Under the microscope, polarizing sections of picrosirius red-staining were used to analyze collagen fibers. The collagen fibers oriented from the root surface toward the alveolar bone crest were partially decreased or absent in the experimental traumatic occlusion (T); traumatic occlusion and periodontitis (T + I); and non-immunized rats without traumatic occlusion and periodontitis (n-(T + I)) groups on day 5 and 10.\cite{27}

Loss of attachment

Nakatsu \textit{et al.}, 2014\cite{27} calculated the loss of attachment by measuring the distance between the cementoenamel junction and the coronal position of the junctional epithelium and showed that the occlusal trauma alone caused a slight inflammatory infiltration in adjacent junctional epithelium and connective tissue but caused no apical migration of the junctional epithelium, or loss of attachment. However, inflammation in conjunction with traumatic occlusion caused inflammatory cells to infiltrate in the junctional epithelium and adjacent connective tissue; also, apical migration of the junctional epithelium ($P < 0.001$).

Gingiva

Through analyses of immunohistochemical marker C1qB (immune complex), Nakatsu \textit{et al.}, 2014\cite{27} showed that it was not detected in the phosphate-buffered saline (PBS) and n-(T + I) groups. In Groups I and T + I on day 5, C1qB reactive cells were present in the junctional epithelium and adjacent connective tissue. The location of C1qB in Groups T + I and T, on day 10 was similar to Group T + I on day 5.

Alveolar bone

Irregular bone surface and TRAcP positive cells

Nakatsu \textit{et al.}, 2014\cite{27} did not observe TRAcP-positive cells in the alveolar bone crest in the groups PBS palatal and n T (I + T). Few TRAcP-positive cells were observed in group I on days 5 and 10; in group T + I on day 10 had a greater increase than the other groups ($p < 0.001$).

No TRAP-positive cells were observed in the palatal alveolar bone crest in PBS, T and n-(T + I) groups; and few TRAP-positive cells were observed in group I on days 5 and 10. T + I group, on day 10 showed a significantly greater increase than the other groups ($p < 0.001$). There were no significant differences in the number of TRAcP positive cells among the groups on day 5 in the alveolar bone crest and palatal alveolar bone crest\cite{27}.

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**Table 3:** Characteristics of the studies included in traumatic occlusion with and without periodontal disease

| Authors          | Year | Language | Type of study          | Sample size (n) | Groups comparison                                                                 |
|------------------|------|----------|------------------------|-----------------|-----------------------------------------------------------------------------------|
| Nakatsu \textit{et al.}, 2014\cite{27} | 2014 | English  | Qualitative and quantitative | 60 rats | PBS group: Treated topically with PBS vehicle                                   |
|                  |      |          |                        |                 | T group: Experimental occlusal trauma                                              |
|                  |      |          |                        |                 | I group: Experimental periodontitis                                                |
|                  |      |          |                        |                 | T + I group: Combination of experimental occlusal trauma and periodontitis         |
|                  |      |          |                        |                 | n-(T + I) group: Non-immunized rats without occlusal trauma and periodontitis     |

PBS=Phosphate-buffered saline

**Table 4:** Methodological aspects of the studies included in traumatic occlusion

| Author          | Nakatsu \textit{et al., 2014}\cite{27} |
|-----------------|-----------------------------------------|
| Gender          | Male                                    |
| Age (week)      | 8-9                                     |
| Method used to induce TO | The occlusal surface of the lower right first molar was raised by placing a metal wire (1.0 mm in diameter) bonded with resin cements |
| Analyzed jaw    | Upper                                   |
| Analyzed areas  | Bucco-palatal sections                  |
| Analyzed periods (days) | 5 and 10                                |
| Parameters analyzed | Collagen fibers: picrosirius red-polarization method |
|                  | Bone surface irregularity               |
|                  | The numbers of TRAcP-positive multinuclear cells |
|                  | Immunohistological staining for C1qB   |

TO=Traumatic Occlusion
However, the standard deviations observed in these studies were a factor of interest because of their large range.

Sample size calculation was not present in any of the articles assessed. In a sample size calculation conducted with pre-existing data, we found that the ideal number of rats per group to study the number of TRAcP positive cells is 18. Large sample sizes contradict universal ethical norms regarding animal testing and are therefore undesirable. According to Damy et al., 2010, animal health and care during the experiment, in combination with well-planned research projects, the use of appropriate techniques for detecting biological differences, data collection, and statistical analysis, are all pre-requisites for reducing the number of animals used in a study and reaching better results.

**Age**

Alveolar bone turnover maintains the integrity of the tooth function, especially in young rats. With the advancing of age it tends to decrease, rapidly from week 6 to 30–40, and slightly between weeks 50 to 100. Osteoclasts are most seen on the distal side of the roots; the continuous growth of rat jaws and their posterior site of lengthening may be responsible for the distal movement of the teeth. Rats aged 20 weeks are particularly suitable for the study of occlusal trauma considering biological and economical aspects.

**Control group**

The control group is an important part of the study design because it is necessary to accurately evaluate the effects of the experiment. There is much research which does not follow a number of important principles that ensure more reliable results, such as treating the control and experimental group independently; presenting a negative control group without any intervention; selecting animals of similar age and weight for the control group; and ensuring that the sample size is equal to that of the experimental group.

The use of opposite sides of the jaw as a control group to reduce the difference between individual animals is not recommended in this kind of experiment because the control side also suffers changes in muscle activity and occlusion.

**Differences between the lower and upper jaw**

The alveolar bone and jaw region are important factors to consider when analyzing the results of traumatic occlusion on the periodontium, as mandibular bone density is different from that of the maxilla, and although in the same jaw, the bone density is not consistent in all areas. With regard to bone quality, the maxilla is mainly characterized by a thin layer of cortical bone that surrounds trabecular bone with a lower density, classified as bone type III and IV. In the mandible, there is a predominance of a thick
layer of cortical bone that surrounds dense trabecular bone with more corticalization in some areas and little medullary bone tissue, classified as bone type I and II. The resistance of bone tissue to compression forces is proportional to the square of its density; the elasticity module. Consequently, the mechanical resistance of the cortical bone can reach 10 times that of the trabecular bone. However, the trabecular bone occupies approximately 20 times more surface area per volume unit than cortical bone, and therefore, its cells can be more easily and directly influenced by medullary bone cells. Owing to this fact and its organizational structure, spongy bone has a higher metabolic capacity and remodeling activity. Therefore, it responds quicker to mechanical, chemical, and hormonal stimuli.

Type of occlusal trauma induction and number of overloaded teeth

Some clinical findings should be considered to select the appropriate force and type of load for inducing traumatic occlusion. The excessive occlusal load that causes occlusal trauma is mostly intermittent and strong enough to allow for detailed investigation of periodontal ligament breakdown following mechanical overload. Various methods have been applied to induce traumatic occlusion, using materials that include amalgam, resin, a pin, a palatal arch, gold crowns, steel wire, and others.

The composite filling is a technique that is suitable for many animal models and large populations. However, it is too sensitive with regard to dental bonding, standardized filling performance, and wear. To minimize errors, restorations should be performed by a single trained dentist, taking utmost care to prevent moisture during the composite filling performance. In addition, this method should only be used in short term studies because filling wear can influence the forces applied to teeth. Occlusal interference performed by placing metal wire and metal casts bonded with resin cement is easier and better maintains the force applied to teeth. This enables studies that encompass a longer time frame (15 to 60 days). Furthermore, it causes major destruction in the periodontal ligament and provokes more acute tissue damage, which directly influences lesion progression, leading to faster periodontal response.

Occlusal overload applied to one tooth causes a stronger mechanical force on the periodontium than methods that spread the force for two or more teeth. As such, it may induce a stronger reaction in the periodontium, involving bone turnover and breakdown.

The study of the effects of traumatic occlusion (TO) in the periodontium may yield better results when analyzing the opposite molar, considering that induction of TO using adhesive methods can generate some adhesion with the adjacent tooth.

Force direction can also modify the results. The application of axial forces causes greater osteoclasts activity, which is concentrated on the distal side of the roots. Lateral forces, however (normally induced by palatal arch), result in more bone turnover on the side opposite to where the force was applied.

Direction of section surfaces

The direction of section surfaces may be a reason behind discrepancies in the results. Bone remodeling sequences are more marked in the mesial-distal and horizontal sections than in the buccolingual sections of the tooth socket because molars tend to drift distally toward the mandible.

Knowledge gaps knowledge and research directions needed

Radiographic observation during our clinical experience has revealed that teeth overloaded by occlusal forces, without the presence of bacterial periodontal disease, suffered much bone thinning in the interdental septum and interradicular space, even before bone height decreased. This situation can be reversed by the appropriate distribution of occlusal forces and dental containment in cases marked by higher tooth mobility. It was also found that male patients represent a larger number of occlusal overload cases that involve dental and periodontal damage. This damage occurs in adults and senile patients, perhaps as a result of bone characteristics or even the time needed for the development of the lesion. In addition, the presence of C1qB reactive cells strongly suggest that immune system was involved in the periodontal destruction.

Further research is needed to clarify the role of distant bone remodeling, the reversibility of occlusal trauma, and the influence of sex hormones on periodontal bone turnover in the face of traumatic occlusion. It should focus on factors that influence the activation or recruitment of osteoclasts, in particular stress factors. Immunohistochemical evaluations such as heat shock protein, periostin, osteoprotegerin, RANK, RANKL, and RUNX 2, as well as micro CT, are a great help in evaluating bone resorption around teeth and in the center of the alveolar septum. Bone mineralization/demineralization is also an import factor to be explored, through chemical and molecular properties in the bone sample.

Conclusion

Although only one study was included in the systematic review of traumatic occlusion, there is some evidence from experimental studies on animals that shows a coherent picture of the effects of traumatic occlusion on the periodontium. However, new studies are needed to fully answer the questions posed by this systematic review.

Acknowledgment

We are grateful to Ana Paula Rímoli de Oliveira for assistance with the search strategy.

This study did not receive any financial support.
Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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