Original Article

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Dentistry Section

Long- and Short-term Effects of Corticosteroids on the Rate of Orthodontic Tooth Movement and Associated Histological Changes in Animal Model: A Systematic Review

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ABSTRACT

Introduction: Orthodontic Tooth Movement (OTM) involves a multifaceted process intricately linked to the remodelling of bone and tissue subsequent to the application of orthodontic forces on teeth. Various factors, such as age, gender, root morphology and the administration of medications like Corticosteroids (CS), can affect the remodelling of alveolar bone and the pace of OTM. The influence of CS on the rate of OTM has been reviewed in animal studies with conflicting results.

Aim: To systematically investigate the effect of CS (duration) on the rate of OTM in animal models (rats).

Materials and Methods: A sytematic review was conducted at the Department of Dentistry, Faculty of Dental Sciences, IMS BHU, Varanasi, Uttar Pradesh, India. A total of five databases (PubMed, Google Scholar, Wiley Library, Cochrane Library, Scopus) were searched without restrictions until March 5, 2024, using the following keywords: CS, orthodontic, tooth movement and bone remodelling. All in-vivo experimental animal studies assessing the rate of OTM following the administration of CS were included. The Systematic Review Centre for Laboratory Animal Experimentation (SYRCLE) risk of bias tools were utilised. The reporting of the present review was based on the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. The protocol was registered with the number CRD42024441077 in the Prospective Register of Systematic Reviews (PROSPERO) database (http://www.crd.york.ac.uk/PROSPERO).

Results: The results of all five studies (all five studies being in-vivo experimental animal studies) concluded that CS causes suppression of osteoclastic activity histologically. The dosage and duration of steroids used in the studies showed a significant influence on the extent of OTM. Nevertheless, histological examinations revealed changes indicating suppression of osteoclastic activity, as evidenced by reduced activity of Tartrate Resistant Acid Phosphatase (TRAP), a major cytochemical marker of osteoclasts and a decrease in the length of root resorption.

Conclusion: The CS induces alterations in the rate of tooth movement. However, intervention studies have concluded that the effect on OTM depends on both the dose and duration (≤3 weeks=short-term and ≥7 weeks=long-term) of administration.

Keywords: Alveolar bone turnover, Orthodontic forces, Steroids

INTRODUCTION

The OTM is a dynamic biological process that results in the resorption of alveolar bone and remodelling of the periodontal ligament, involving cellular differentiation through various signalling pathways [1]. Optimum orthodontic forces produce inflammation in periodontal tissues. Prostaglandins, lipid mediators derived from arachidonic acid, play a role in the pathogenesis of inflammation. Studies have shown that tooth movement increases with prostaglandin injection [2]. OTM is influenced by several factors, including the magnitude and duration of the orthodontic force applied, the shape of the roots, the mechanical characteristics of the periodontal ligament and the use of pharmaceutical drugs [1].

The CS are anti-inflammatory agents that are relatively inexpensive and commonly used to treat various conditions. The anti-inflammatory effect of CS is associated with inhibiting the synthesis of prostaglandins and leukotrienes by blocking phospholipase A2 and suppressing the production of cyclooxygenase 1 and 2 [1]. The widespread effects of these drugs cause profound alterations in carbohydrate, protein, lipid metabolism and water balance [1]. Molecules of these drugs consumed by patients can reach the site of bone turnover through vascular channels, where they may interact with cells, causing enhancement, delay, or synergistic actions. These effects impact all the major systems in the body, including the cardiovascular, musculoskeletal, nervous and immune systems [1].

Chronic CS therapy inhibits calcium absorption, which induces hypercalciuria and may increase parathyroid hormone levels [1]. According to a clinical review by Mitra R (2011), the chronic use of steroids greatly influences bone metabolism, leading to bone resorption, which in turn causes osteoporosis [3]. CS can be classified into two categories: glucocorticoids (which affect intermediary metabolism, inflammation, immunity, wound healing, myocardial integrity and muscle integrity) and mineralocorticoids (which regulate salt, water and mineral metabolism) [3].

Animal studies conducted by Ashcraft MB et al., (1992) and Kalia S et al., (2004) reported an increase in the rate of OTM following the administration of cortisone acetate in rabbits treated for four days before and for 14 days during the experimental period, with an application of an orthodontic force of approximately 100 cN [4,5]. However, Ong CK (2000) and Yamane A et al., (1997) reported no increased rate of OTM when CS prednisolone was administered at a dosage of 1 mg/kg/day to rats for an induction period of 12 days, followed by an experimental period of 12 days [6,7]. Additionally, Gonzales C et al., (2008) reported less tooth movement and root resorption in the test group administered with CS [8].

Conditions such as asthma, hay fever, eczema and allergic diseases are common in orthodontic practice and are treated with various forms of CS. The exact physiological basis for CS affecting total bone formation or resorption is not completely understood. Regarding bone formation, the effects of CS appear

to be multidimensional. Evidence indicates that CS directly inhibits osteoblastic function. This inhibition is mediated through direct effects on osteoblasts and osteoblastic precursors, resulting in a decrease in total bone formation. Animal intervention studies have not clearly identified the effect of CS on the rate of OTM and other studies have provided mixed opinions that do not adequately describe the effects on OTM. Therefore, a systematic review of the effects of long- and short-term therapy with CS on animal models (specifically rats) for assessing the rate of OTM was necessary.

Fixed orthodontic treatment typically takes approximately two years. Patients' medical histories may indicate long-term or short-term steroid therapy for various reasons, or they might undergo steroid therapy during active orthodontic treatment. Hence, it is imperative to determine the short-term and long-term effects of CS on the rate of OTM and its effect on alveolar bone structure.

The present systematic review aimed to identify the effects of steroids on the rate of OTM, particularly CS that have been administered clinically in experimental animals (adult rats) in the literature and to decipher their effectiveness. Additionally, the goal was to critically evaluate the dosages used, the effects of long-term and short-term interventions and the changes observed histologically.

MATERIALS AND METHODS

The systematic review was performed at the Department of Dentistry, Faculty of Dental Sciences, IMS BHU, Varanasi, Uttar Pradesh, India, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The main research question was formulated according to the population, intervention(s), comparator(s)/control and outcome(s) (PICO) framework. The protocol was registered with the number CRD42024441077 in the PROSPERO database (http://www.crd.york.ac.uk/PROSPERO) [9,10]. The present systematic review was conducted in accordance with the SYRCLE guidelines [11].

Eligibility criteria: The eligibility criteria for the participants, intervention, comparison, outcomes and study design domains (PICOS) are presented in [Table/Fig-1]. The authors reviewed in-vivo experimental animal studies involving healthy rats subjected to active orthodontic force. The rate of OTM had to be investigated after the administration of CS and comparisons were made with a placebo intervention.

Domain	Criteria
Participants	• Healthy animals (rats) irrespective of age and gender applied with orthodontic force.
Interventions	• Administration of any form of Corticosteroids (CS) orally or systemically in animal models (rats) to know the rate of Orthodontic Tooth Movement (OTM) and bone remodelling. • No restrictions applied on dosage, timing, or frequency of administration of CS.
Comparisons	• Healthy animal models (rats) that are not exposed to corticosteroid drugs.
Outcomes	• Rate of Orthodontic Tooth Movement (OTM) after administration of CS in animal models (rats). • Histological changes associated with it.
Study design	• In-vivo, experimental studies included all types of healthy rats with the control group.

[Table/Fig-1]: Eligibility criteria for present systematic review.

Information sources and search strategy: A health sciences librarian conducted a comprehensive search of five databases (PubMed, Google Scholar, Wiley Library, Cochrane Library, Scopus) until March 5, 2024. All articles published in English were searched. The reference lists of the included and excluded studies, as well as retrieved reviews and other relevant articles, were also searched manually.

Study selection: The electronic database search was conducted by two review authors independently using the keywords: CS, orthodontic, tooth movement and bone remodelling, up to March 5, 2024, as listed in [Table/Fig-2]. All articles published in English were included. The two reviewers independently read the titles of the retrieved studies and subsequently read the abstracts, considering predetermined exclusion and inclusion criteria based on the PICOS framework.

S. No.	Search engines	Result
1	Pubmed	13
2	Google scholar	2250
3	Wiley library	57
4	Cochrane library	0
5	Scopus	57

[Table/Fig-2]: List of search engines and their results.

Inclusion criteria: The inclusion criteria included healthy animals (rats) of any age and gender that were subjected to orthodontic force to assess the rate of OTM and bone remodelling, comparing them with healthy animal models (rats) that were not exposed to CS drugs. All in-vivo experimental studies were included.

Exclusion criteria: The exclusion criteria comprised animals other than rats, rats with co-morbidities or systemic diseases, as well as non randomised controlled trials, cohort studies, case series, case reports and expert opinions. The same procedure was applied to the full texts of potentially included studies, evaluated independently by both reviewers. Any disputes regarding the selection of an article as relevant were resolved by a third reviewer with more than ten years of experience.

Study Procedure

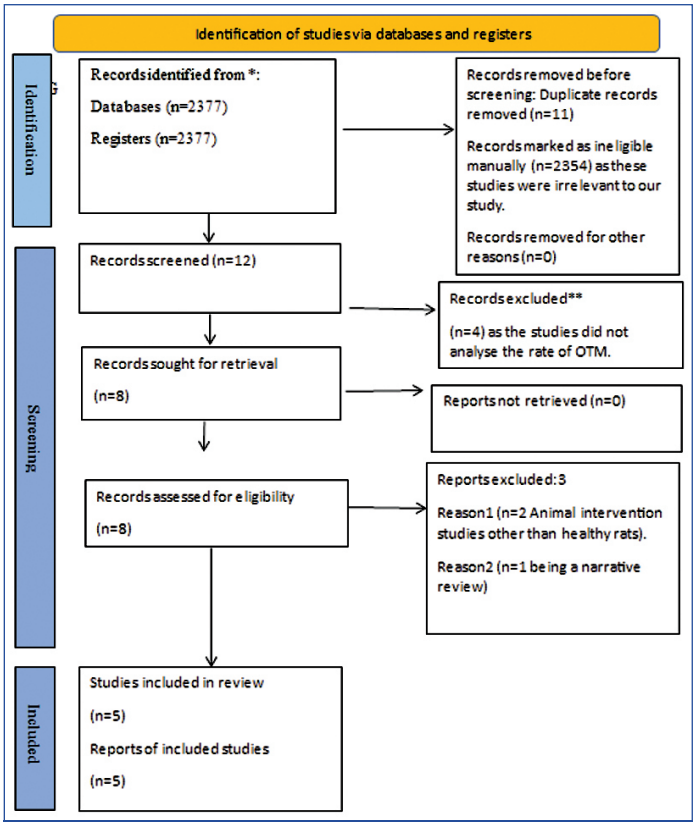
Data collection and data items: The full texts of the relevant studies were analysed in the second stage, which is the final stage and were relabeled according to the same exclusion and inclusion criteria and desired outcomes. The extracted data were organised in a Microsoft Word file. In case of any discrepancies, they were resolved by a third reviewer (AP) through discussion.

The information included the author, year of publication, intervention methods, sample size, species, gender, average weight, age of the animal models (rats) and the magnitude of orthodontic force applied. Missing data were requested from the study authors via email (two attempts maximum).

The authors used the following search Medical Subject Headings (MeSH) terms for PubMed: {"bone remodelling" (All Fields) OR "bone remodelling" (Mesh Terms)} OR {"bone" (All Fields) AND "remodelling" (All Fields)} OR {"bone remodelling" (All Fields)} AND {"adrenal cortex hormones" (Mesh Terms)} OR {"adrenal" (All Fields) AND "cortex" (All Fields) AND "hormones" (All Fields)} OR "adrenal cortex hormones" (All Fields) OR "corticosteroid" (All Fields) OR "corticosteroids" (All Fields) OR "corticosteroidal" (All Fields) OR "corticosteroide" (All Fields) OR "corticosteroides" (All Fields)} AND {"tooth movement techniques" (Mesh Terms) OR {"tooth" (All Fields) AND "movement" (All Fields) AND "techniques" (All Fields)} OR "tooth movement techniques" (All Fields) OR {"tooth" (All Fields) AND "movement" (All Fields)} OR "tooth movement" (All Fields)} AND {"orthodontal" (All Fields) OR "orthodontic" (All Fields) OR "orthodontical" (All Fields) OR "orthodontically" (All Fields) OR "orthodontics" (MeSH Terms) OR "orthodontics" (All Fields)}.

The PRISMA flow diagram is presented separately in [Table/Fig-3] [11].

Risk of bias in individual studies: An independent quality assessment of the included studies was performed by a pair of observers using the SYRCLE Risk of Bias (RoB) tool for animal intervention studies. This tool is based on the Cochrane Collaboration RoB Tool [11]. A total of 10 domains of bias were assessed under the following headings: a) Selection bias; b) Performance bias; c) Detection bias; d) Attrition bias; e) Reporting bias; f) Other bias. The studies were categorised as follows: a) Low risk of bias; b) High risk of bias; c) Unclear risk of bias.



[Table/Fig-3]: PRISMA 2020 Flow diagram for new systematic reviews which included searches of databases and registers only [11].
*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers)
**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools

RESULTS

Study selection: A total of 2,377 articles were retrieved through electronic searches in various search engines, including PubMed, Google Scholar, Wiley Library, Cochrane Library and Scopus. A total of 11 articles were eliminated due to duplication and 2,354 articles were deemed ineligible through a meticulous scrutiny process. A total of 12 articles were selected for phase I screening (title and abstract reading). Of these, eight articles were chosen for phase II screening (full-text reading). Four articles were excluded because they did not analyse the rate of OTM. Out of the eight articles, two were studies involving animals other than healthy rats and one was a narrative review; therefore, five articles were selected for qualitative review to maintain homogeneity.

Study characteristics: The basic characteristics of the included studies, which include the author, year of publication, study subjects, mean age, dosage of CS, study duration, magnitude of orthodontic force applied and evaluation of orthodontic force is represented in [Table/Fig-4] [5,6,8,12-14]. All in-vivo studies used experimental animals (rats) and applied orthodontic force for OTM while administering CS. All studies included male rats with a mean age ranging from nine to 24 weeks, with a magnitude of orthodontic force applied between 25 and 50 grams on the left side. The evaluation of tooth movement was measured using vernier calipers in three studies [5,6,12]. Bony changes were observed histologically in the same studies [5,6,12,13]. One study utilised digitalised lateral cephalometric radiographs for evaluation [8]. The dosage of corticosteroids was 1 mg/kg in two studies [6,12], while other studies [5,8] included dosages ranging between 0.67 and 8 mg/kg. In all five studies, closed coil springs were used to apply orthodontic force for a mean duration of 11 to 21 days.

Results of individual studies: The results of all studies are included in [Table/Fig-5] [5,6,8,12,13]. Despite the differences in type, dosage and frequency of corticosteroids, all studies concluded that there was suppression of osteoclastic activity histologically. However, to affect the magnitude of the rate of orthodontic movement, both the duration and dosage of steroids were necessary. Kalia S et al., reported a significant change in the rate of orthodontic movement in the chronic group (which received pharmacological treatment for seven weeks and orthodontic treatment for three weeks). In contrast, Gonzales C et al., concluded that there was less tooth movement in the test group administered with CS [5,8].

Author name	Year	Study subjects	Mean age	Study groups	Dosage of steroids	Study duration	Magnitude of orthodontic force	Evaluation of OTM
Ong CK et al., [6]	2000	12 male rats	9-week-old	Experimental group n=6 (prednisolone-treated) OF (Orthodontic force) Control group n=6 (saline-treated) OF	1 mg/kg	2 days of prednisolone treatment and 11 days of OF. (short-term)*	30 grams of OF on the left-side	Vernier calliper and histological examination
Ong CK et al., [12]	2001	12 male rats	9-week-old	Experimental group: n=6 (1 mg/mg/kg) OF Control group: N=6 (saline-treated) OF	1 mg/day	Experimental group: 12 days of prednisolone and OF. Control group: 12 days of saline and OF. (short-term)*	30 grams of force on the left-side	Vernier calliper and histological examination
Kalia S et al., [5]	2004	64 male rats	6 month old	Experimental group: group A n=23 (chronic treatment of methylpredisolone received pharmacological treatment for 7 weeks and OT for 3 weeks) Group B n=22 (acute treatment of methylprednisolone received pharmacological treatment and OT simultaneously for 3 weeks) Control group n=19 (OF)	8 mg/kg/day	Experimental group: Group A: 7 weeks of methylpredisolone and OF for 3 weeks. (long-term)** Group B: Methylpredisolone and OF simultaneously for 3 weeks. (short-term)*	25 grams of force left-side	Electronic Calliper and histological examination
Gonzales C et al., [8]	2008	60 male rats	10 week-old	Experimental group: n=5 (prednisolone treated for 2 weeks and OF) Control group: N=5 (orthodontic force)	0.67-0.13 mg/kg	Administration of steroids and OF for 2 weeks. (short-term)*	50 grams of OF on the left-side	Digitalised lateral cephalometric radiographs
Karakida LM et al., [13]	2017	100 male rats	9 week old	Experimental group: N group (Nebido Experimental group) N=35 (anabolic androgenic steroids) Nebido was administrated for 20 days and OF D group (n=35 AAS Deposteron for 20 days and OF)	1.25 mg/kg per dose (2.5 mg/week)	20 days of administration of steroids. (short-term)*	30 grams of OF	Histological examination

[Table/Fig-4]: Basic characteristics of included studies [5,6,8,12,13].
OF: Orthodontic force; OTM: Orthodontic tooth movement; OT: Orthodontic treatment
*3 weeks=short-term; **7 weeks=long-term *[14]

Author name (year)	Orthodontic appliance	Duration of OTM	OF	Type of CST	Dosage	Delivery method	Duration of CST	Primary outcome	Histological examinations reported
Ong CK et al., (2000) [6]	Closed coil spring	11 days	30 grams	Prednisolone	1 mg/day	Oral	12 days	No significant change in magnitude of OTM	PDL compression=ns Width PDL tension=ns Length hyalinised zone=ns Root resorption compression=s p<0.01. More on non-steroid appliance group TRAP activity=reduction in steroidal appliance group than non appliance group
Ong CK et al., (2001) [12]	Closed coil spring	11 days	30 grams	Prednisolone	1 mg/kg	Oral	12 days	No significant change in rate of tooth movement	Histologically low dose steroids caused reduced GHR and IGF-IR immunoreactivity
Kalia S et al., (2004) [5]	Closed coil spring	21 days	25 grams	Methylprednisolone	8 mg/kg	Subcutaneous injection	21 for acute and 49 days for chronic	Significant change in rate of tooth movement. More tooth movement in chronic group	Area of alveolus=chronic>acute group>control group. Extension of mineralising surface of alveolar wall=chronic>acute>control group
Gonzales C et al., (2008) [8]	Closed coil spring	14 days	50 grams	Prednisolone	0.13-0.67 mg/kg	Oral	Unclear	Less amount of tooth movement in test group	Reduced root resorption in test group administration of celecoxib causes less tooth movement and root resorption
Karakida LM et al., (2017) [13]	Closed coil spring	14 days	30 gF	Anabolic androgeic steroids nebido and deposteron	2.5 mg/ week	Intramuscular injection	20 days	No clinical change in rate of tooth movement	Nebido and deposteron groups showed accelerated number of osteoclasts and howship's lacunae [13] Increase in the number of fibroblasts, synthesis of collagens and underlying substance in steroids groups

[Table/Fig-5]: Other characteristics of included studies [5,6,8,12,13].
OTM: Orthodontic tooth movement; OF: Orthodontic force; CST: Corticosteroid therapy; ns: Non significant; GHR: Growth hormone receptor; IGF-1R: Insulin like growth factor-1 receptor; TRAP: Tartrate resistant acid phosphatase

Risk of bias within studies: A summary of the risk of bias assessment using SYRCLE's RoB tool for animal intervention studies is provided in [Table/Fig-6] [5,6,8,12,13]. This tool is based on the Cochrane Collaboration RoB tool and aims to assess methodological quality, having been adapted to evaluate aspects of bias that influence animal experiments. The resulting RoB tool for animal studies contains 10 entries related to six types of bias: selection bias, performance bias, detection bias, attrition bias, reporting bias and other biases [11].

In the animal intervention study conducted by Ong CK et al., the effect of prednisolone on OTM was examined in 12 male rats [6]. He concluded that prednisolone therapy demonstrated no impact on the extent of OTM when compared to the non steroidal control groups. Nevertheless, it did influence the length of root resorption. Changes were apparent along the mesial compression and there was a decrease in TRAP activity within the periodontal ligament, indicating a decline in clastic activity [6].

Author et al., (year)	Sequence generation (Selection bias)	Baseline characteristics (Selection bias)	Allocation concealment (Selection bias)	Random housing (Performance bias)	Blinding (Performance bias)	Random outcome assessment (Detection bias)	Blinding (Detection bias)	Incomplete outcome data (Attrition bias)	Selective outcome reporting (Reporting bias)	Other source bias (other bias)
Ong CK et al., (2000) [6]	-	+, -, +	-	?, -	?	?	?	-	+	+, +, +, -
Kalia S et al., (2004) [5]	+	+, -, +	?	-, -	-	?	-	+	+	+, +, +, +
Ong CK et al., (2001) [12]	-	+, -, +	-	?	-	+	-	-, +	+, +	+, +, +, -
Karakida LM et al., (2017) [13]	-	+, -, +	-	-	-	+	-, +	+	+, +	+, +, +, -
Gonzales C et al., (2008) [8]	-	+, -, +	-	?	-	?	?	+, +	+, +	+, +, +, +

[Table/Fig-6]: Summary of risk of bias assessment (SYRCLE's risk of bias tool for animal studies) [5,6,8,12,13].
'+' (yes)=indicates low risk of bias, '-' (no)=indicates high-risk of bias, '?'=indicates unclear risk of bias

DISCUSSION

Summary of evidence: The effect of corticosteroids on OTM was studied in all intervention studies. Methodological heterogeneity was noted across all studies, with some authors using different methods for evaluating orthodontic force. In-vivo studies in animal models have reported mixed results. The set of retrieved data was limited and the observed level of confidence was variable due to the small number of studies found in the literature, small sample sizes, varying magnitudes of OTM, high risk of bias in some studies and different observation periods.

Five different animal intervention studies (in rats) were considered for this systematic review, which was assessed and analysed to evaluate the effect of corticosteroids on the rate of OTM.

Kalia S et al., studied how tissues responded to orthodontic force when corticosteroids were administered over short and long periods [5]. Histomorphometric examinations verified that glucocorticoid medication induces a significant alteration in bone turnover speed. In the short-term drug regimen, OTM remained unaffected; however, tissue-level remodelling appeared delayed, as evidenced by reduced remodelling without mechanical loading. Conversely, in the chronic treatment group, the tooth movement rate escalated, potentially due to the initiation of secondary hyperparathyroidism.

Ong CK et al., conducted a study to investigate how prednisolone influences the expression of GHR and IGF-IR in dental tissues after OTM. OTM seemed to increase the immunoreactivity of GHR and IGF-IR, but this increase was diminished after prednisolone administration

[12]. The decrease in GHR and IGF-I immunoreactivity in animals treated with steroids suggests a mechanism through which prednisolone may hinder the bone resorption and deposition essential for OTM. Nevertheless, at 12 days after appliance insertion, there was no discernible variance in OTM following low-dose prednisolone treatment.

Karakida LM et al., studied the interaction between tooth movement and two anabolic steroids, Deposteron and Nebido [13]. Excessive doses of the anabolic and androgenic steroids Nebido® and Deposteron® caused changes in the number of osteoclasts, Howship's lacunae and blood vessels, hastening the reorganisation of the periodontal ligament. This led to an accelerated biological response to the induced tooth movement in rats. Gonzales C et al., [8] conducted a study to determine the effect of prednisolone on tooth movement and root resorption. The study concluded that prednisolone suppressed both tooth movement and root resorption.

Various animal intervention studies revealed that corticosteroid administration affected the rate of tooth movement and bone turnover rates, which were assessed histochemically in studies [15,16]. They advocated that the effect of corticosteroids is dependent on dosage and duration. The studies by Gonzales C et al., [8], Kalia S et al., [5] and Ong CK et al., [6,12] concluded that bone resorption and deposition, necessary for tooth movement, are inhibited by corticosteroids [16]. However, the effect on OTM is dependent on the orthodontic force applied, dosage, potency, duration of corticosteroid administration, duration of the experiment and the time interval of administration.

Thus, in all animal intervention studies, the primary aim was to determine the rate of OTM following the administration of CS. The results of all studies concluded that CS does cause suppression of osteoclastic activity; however, to affect the magnitude of OTM, the dosage and duration of steroid administration play a role [17]. Kalia S et al., concluded that the tooth movement rate increased with chronic administration of CS [5]. Verna C et al., in his study, also concluded that short-term therapy with CS causes more root resorption than long-term therapy [14]. Since short-term therapy with CS is often prescribed for conditions such as asthma, hay fever, or other allergic reactions, orthodontists should keep in mind that short-term therapy (less than or equal to 3 weeks) leads to more root resorption compared to long-term therapy (7 weeks).

Low-dose CS does not cause a significant change in the rate of OTM; however, histologically, they induce changes that suppress osteoclastic activity, as evidenced by decreased activity of TRAP, a major cytochemical marker of osteoclasts and a reduction in root resorption length. Changes in blood vessels, Howship's lacunae and alterations in fibroblasts were also reported after the administration of steroids in these intervention studies [18]. In the present systematic review, the authors found that long-term CS therapy leads to increased tooth movement with an average dosage of 8 mg/kg/day over an average treatment duration of seven weeks. In contrast, short-term CS therapy (less than or equal to 3 weeks) does not cause significant changes in OTM, as inferred from the studies by Ong CK et al., [6,12] and Kalia S et al., [5].

Limitation(s)

Varying results were reported due to differences in the orthodontic force applied, the duration of the experiment, the dosage and timing of administration and the potency of the steroids used.

CONCLUSION(S)

The rate of OTM following the administration of CS has been studied by several authors. The rate of OTM is significantly observed during long-term CS therapy, while short-term CS therapy does not result in significant changes in the rate of OTM. However, histologically, suppression of TRAP activity and GHR and IGF-IR was observed, indicating that CS does cause histological changes that result in the suppression of osteoclasts.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jul 27, 2024
- Manual Googling: Feb 15, 2025
- iThenticate Software: Feb 18, 2025 (15%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

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