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[REVIEW ARTICLES]

The effect of Ethanol intake during orthodontic tooth movement: A systematic review of experimental studies

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ABSTRACT

Background and Objectives. Consumption of toxic substances like alcohol is widespread in the general population and thus also in patients receiving orthodontic treatment. Considering the effect of alcohol on bones, consuming alcohol may have some consequences on orthodontic tooth movement (OTM). Several recent improvements in science to accelerate orthodontic tooth movement. Though the ethanol content of alcohol has been shown in multiple studies to accelerate the formation of orthodontic teeth, the results of these investigations remain conflicting. The aim of this research is to investigate in a systematic way and appraise the quality of the available evidence from studies regarding the effect ethanol intake on the rate of OTM.

Materials and Methods. A comprehensive literature search was conducted using databases; an electronic search for relevant randomized controlled trials (RCTs) using PubMed, Cochrane, Plos one, Wiley, and hand searching with a publication period from 2012-2022. The quality of available evidence was assessed using the selection criteria established in the PRISMA.

Results. A total of 343 titles and abstracts were identified. After the review process, 10 full-text articles met the inclusion criteria. The results show that ethanol affect bone mass and there was no statistically significant difference observed between ethanol and the group control of tooth movement.

Conclusions: Alcohol can have an effect on bone remodeling during OTM.

Keywords: Orthodontic tooth movement (OTM); Ethanol, Bone remodeling; Osteoblast; Osteoclast

Abbreviations:

OTM = Orthodontic Tooth Movement

RCTs = randomized Controlled Trials

INTRODUCTION

The result of a biologic response to interference in the physiologic equilibrium of the dentofacial complex by an externally applied force" is the definition of orthodontic tooth movement (OTM). Numerous studies have been conducted on the order of cellular, molecular, and tissue-reaction processes during OTM. The rate of movement may be impacted by changes in bone turnover and density, which may occur alone or in combination with other factors to influence remodeling processes and eventual tooth displacement. In this way, a variety of biological substances contribute to the inflammatory process and modify the pathways involved in the remodeling of the bone that occurs along with OTM [1].

When a regulated mechanical force is applied, OTM takes place. OTM is characterized by changes in cellular activity and collagen fiber stretch and compression brought on by the movement of the tooth inside the periodontal space when the regions of the compression side that are hyalinized (cell-free) as a result of inflammatory cytokines and blood flow disturbance are eliminated [2,3]. Changes in the distribution of stress and strain in the periodontium cause the alveolar bone to undergo (re)modeling, which is the process through which orthodontic teeth shift [4,5].

The connection of resorption and creation is a key notion in bone remodeling. It has been suggested that coupling mechanisms prevent bone from being acquired or lost during healing. Though the precise process through which coupling occurs is unclear. The presence of various paracrine factors

(e.g., IGF-II, IGFBP-5 or -6) in cementoblasts and lacunae during the early phases of tooth movement healing implies that they may be involved in regulating this remodeling sequence [6]. Alcohol has bioactivity that surpasses its nutritional worth, making it a significant non-essential component of diet. In many nations, the amount of alcohol consumed per person accounts for five to ten percent of daily energy needs [7,8].

An optical densitometric assessment was done to determine how bone density and alcohol-induced OTM are connected. According to several research shows alcohol consumption affects bones, alcohol causes rats' cortical and cancellous bone mass to decrease, a reduction that persists throughout the animal's lifetime [9,10].

Contradictory benefits of alcohol in bone remodeling have been outlined in various journals. Therefore, it is necessary to re-analyze whether alcohol consumption has an effect on OTM. The purpose of this systematic review was to examine and evaluate the quality of the scientific data from research that was currently available about the impact of alcohol consumption during OTM.

MATERIALS AND METHODS

Determination of journals collected with inclusion criteria: (1) Research journals related to effect ethanol intake during OTM. (2) English-language research journals (3) Year of Publication 2012-2022.

Search Method Data was collected through electronic search. Sources of data search conducted included Google Scholar, PubMed, Wiley, Ebsco with a publication period from 2012-2022.

Search Details Journal searches used keywords: orthodontic tooth movement (OTM), ethanol, alcohol consumption, bone remodeling, osteoblast, osteoclast.

Data Collection and Data Analysis The author obtained research journal articles through electronic databases according to keywords of 343 journals. The author selects the research journals that result from searches based on the title and abstract of the research, in order to obtain relevant titles and abstracts of 55 journals. Authors read full-text journal articles to determine that the study met the

criteria. Studies that met the criteria then underwent quality assessment and data extraction. The author reviews and selects 10 journal articles that are included in the synthesis table.

RESULTS

Table. A Synthesis of Literature Review

DISCUSSION

There exists only a single report regarding the effects of ethanol during orthodontic movement, despite numerous research suggesting that it may have a detrimental effect on alveolar bone and the periodontum [11].

Mild and continuous EtOH exposure may interfere with the generally long-lasting orthodontic treatments by altering the aforementioned proteins and genes, which could result in orthodontic failure or other undesirable outcomes [12].

Ethanol had no effect on bone metabolism in the current investigation, regardless of tooth mobility. Despite progress in comprehending the intricate effects of alcohol on bone, numerous questions remain [13,14].

Research on the skeletal effects of persistent high alcohol drinking has been conducted in elderly rats. In one rare instance, giving 8-month-old female rats as low as 3% of their calories in the form of alcohol decreased the production of bone in the rats [15].

In summary, ethanol did not cause any cytotoxicity or affect apoptosis or necrosis in hPDL fibroblasts, suggesting that this cell type is very resistant to ethanol [16,17]. Although ethanol demonstrated anti-inflammatory properties, it also heightened prostaglandin induction, which causes pain, inflammation, and osteoclastogenesis and it might also raise the chance of undesired root resorption or periodontal bone loss [18,19].

Low to moderate level alcohol use may benefit the cardiovascular system, but everyday large-scale alcohol consumption over time may have disastrous consequences for tissue systems used in orthodontic treatment, such as the skeletal system [20,21].

The alteration of the surrounding bone architecture is one recognized biological reaction to orthodontic stresses. This may stimulate osteoclastogenesis in compression areas of the periodontal ligament during OTM, impact on hPDL fibroblasts may therefore contribute to the restoration of the circulation at compression sites, which is disrupted during tooth movement [22,23].

Following alcohol delivery, osteocalcin levels were shown to significantly decrease in both investigations. During abstinence, a noteworthy rise in the carboxy-terminal propeptide of type I procollagen was observed by everyone [24,25]. On the other hand, the majority of data regarding the relationship between bone density and alcohol use point to a linear relationship between increased alcohol consumption and decreased bone loss over time [26,27].

There is currently not enough data to pinpoint a specific level of alcohol consumption that is linked to increased bone density because studies on the relationship between bone density and alcohol consumption only involved a small number of heavy drinkers [28,29].

Our findings are consistent with those observed in humans, suggesting that the mature rat is not only a useful model for adult alcohol misuse but also potentially predictive of the skeletal effects of moderate alcohol consumption. Adolescents who consume ethanol may, on the one hand, have lower peak bone mass, which puts them at risk for osteoporosis [30,31].

Alcohol consumption may not have an impact on the active ingredient or the study rate of tooth movement because a balance between the apoptotic impact on the osteoclasts and the osteopenic effects has been obtained [32,33].

Osteocytes, which resorb bone, osteoblasts, which create bone, and osteoclasts, which resorb bone, are the three main cell types involved in bone remodeling. Early researchers analyzed osteocalcin, a protein created by osteoblasts that is assumed to be a marker of their function and is dependent on vitamin K, to ascertain whether ethanol had a direct effect on osteoblasts [25,27].

This study revealed that alcohol exposure did not appear to have an impact on orthodontic therapy. As a result, our results cannot be directly applied to clinical situations. These variables may eventually impact OTM and have a connection to bone remodeling. Orthodontists ought to focus more on their patients problematic alcohol consumption habits [32,34].

However, a different study found a dose-dependent link between ethanol use and bone loss. Additionally, they discovered that alveolar bone loss is not considerably impacted by low ethanol concentrations [14,16].

The contrast in weight increase between the control and experimental groups may have been influenced by the animals exposed to ethanol eating less and by the ethanol's direct impact on rats' capacity to convert dietary nutrients into body weight. Although opinions on how ethanol affects bone remodeling are still divided [17,20].

However, we discovered that ethanol encouraged an unbalanced resorption of bone. Additionally, as tooth mobility is a process that depends on bone, its consequences must be carefully taken into account from an orthodontic perspective [10].

The mechanisms of collagen deposition and bone neoformation are unaffected by ethanol because ethanol intake at the end of OTM encourages a reduction in resorption. Because ethanol alters bone metabolism, it may cause an OTM delay [13,33].

The decrease in indicators of bone resorption suggests that the reduction in bone remodeling that we observed in alcohol drinkers in our study may be the primary cause of their increased BMD, because creation and resorption are intertwined, serum osteocalcin, a marker of bone formation released by osteoblasts, has a strong correlation with resorption [14,33].

In skeletally adult rats, the main consequence of long-term heavy alcohol consumption is a remodeling imbalance that causes progressive but gradual bone loss. Studies have also been conducted on the impact of alcohol use on estrogen levels. Estrogens affect how bones are metabolized, controlling the activation of bone remodeling units and preserving the ideal ratio of osteoblast to osteoclast activity [8,9].

CONCLUSION

Alcohol can have an effect on bone remodeling during OTM.

CONFLICT OF INTEREST

There is no conflict of interest.

AUTHOR'S CONTRIBUTIONS

All authors are contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript.

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FIGURES, TABLES AND SCHEMES

TABLES

Table 1. A Synthesis of Literature Review

NO	JOURNAL (YEAR)	AUTHOR	TITLE	OBJECTIVE	METHOD	RESULT
1	Alcohol Clin Exp Res, 2016	Gino W. Gaddini, Russell T. Turner, et al.	Alcohol: A Simple Nutrient with Complex Actions on Bone in the Adult Skeleton	To describing the complex effects of alcohol on the adult skeleton.	Assessing the effects of alcohol on bone in adult humans as well as skeletally mature animal models published since the year 2000 are emphasized	Light to moderate alcohol consumption is generally reported to be beneficial, resulting in higher bone mineral density (BMD) and reduced age-related bone loss, whereas heavy alcohol consumption is generally associated with decreased BMD, impaired bone quality, and increased fracture risk. Bone remodeling is the principal mechanism for maintaining a healthy skeleton in adults and dysfunction in bone remodeling can lead to bone loss and/or decreased bone quality. The specific effects of alcohol on bone remodeling in heavy drinkers are even less certain because the effects are often obscured by unhealthy lifestyle choices, alcohol-associated disease, and altered endocrine signaling.
2	Arterioscler Thromb Vasc Biol. 2021	Andrew M. Cobb , Syabira Yusoff, Robert Hayward, et al.	Runx2 (Runt-Related Transcription Factor 2) Links the DNA Damage Response to Osteogenic Reprogrammin g and	The development of ectopic vascular calcification is strongly linked with organismal aging, which is primarily	The isolates used in this study were as follows; 35F (04:35F:11A), 20M (05:20M:18A), and 54M (05:54M:20). Cells were maintained in M199 medium (SigmaAldrich)	We found genotoxic stress-stimulated Runx2 accumulation and transactivation of its osteogenic target genes, leading to enhanced calcification. Inhibition of DNA damage signaling

			Apoptosis of Vascular Smooth Muscle Cells	caused by the accumulation of DNA damage over time. As Runx2 (Runt-related transcription factor 2) has been identified as a regulator of vascular smooth muscle cell osteogenic transition, a key component of vascular calcification, we examined the relationship between DNA damage and Runx2 activation	supplemented with 20% fetal bovine serum at 37°C and 5% CO2 and used between passages 9 and 20. Control mouse VSMCs (Runx2f/f) and Runx2 KO VSMCs (Runx2ΔSM) were cultured in the same media.	attenuated this response. Runx2 localized to sites of DNA damage and participated in DNA repair by regulating phosphorylation events on histone H2AX, with exogenous expression of Runx2 resulting in unrepaired DNA damage and increased apoptosis. Mechanistically, Runx2 was PARylated in response to genotoxic stress, and inhibition of this modification disrupted its localization at DNA lesions and reduced its binding to osteogenic gene promoters
3	European Journal of Orthodontics, 2017	Eliane H. Dutra , Ahmad Ahmida , Alexandro Lima, Sydney Schneider, Ravindra Nanda , and Sumit Yadav	The effects of alveolar decortications on orthodontic tooth movement and bone remodelling in rats	To determine the effects of AD in the amount of OTM and on alveolar bone remodelling in a rodent model, after 7 or 14 days.	A total of 32 15-week-old male Wistar rats were used in four treatment groups: (1) orthodontic spring only (7 days), (2) orthodontic spring only + AD (7 days), (3) orthodontic spring only (14 days), and (4) orthodontic spring only + AD (14 days). A closed coil nickel–titanium spring delivering 8–10 g of force was used to move the molar mesially. Alveolar	The spring + AD group presented with a significant increase in the rate of tooth movement when compared with spring only group, 7 and 14 days after the beginning of the experiments. In addition, the spring + AD group had a significant decrease in bone volume and tissue density and a significant increase in the trabecular spacing and the number of osteoclasts at 7 and 14 days. Furthermore, a

					decortication was done using a high speed, quarter round bur adjacent to the left first maxillary molar, on the palatal alveolar bone. At each endpoint, rats were sacrificed and microfocus computed tomography and histological analysis were performed.	fibrous tissue was found to replace the alveolar bone in the spring + AD group at day 14
4	Frontiers in Physiology, 2017	Jorge M. Barcia , Sandra Portolés , Laura Portolés , Alba C. Urdaneta , Verónica Ausina , Gema M. A. Pérez-Pastor , Francisco J. Romero, et al.	Does Oxidative Stress Induced by Alcohol Consumption Affect Orthodontic Treatment Outcome?	To known about the potential role of the oxidative conditions induced by ethanol intake as a possible setback for orthodontic treatment in adults.	A literature review with keyword : ethanol, oxidative stress, orthodontic movement, periodontal ligament, orthodontic treatment.	Orthodontic treatment implicates mechanical forces on teeth. Interestingly, the extra- and intra-cellular responses of periodontal cells to mechanical movement show a suggestive similarity with the effects induced by ethanol metabolism on bone and other cell types.
5	Int J Clin Exp Pathol, 2015	Jinyou Han, Hong He	Expression and function of osteogenic genes runt-related transcription factor 2 and osterix in orthodontic tooth movement in rats	To investigate the expression and function of osteogenic genes osterix (OSX) and runt-related transcription factor 2 (RUNX2) in the rat periodontal tissues under orthodontic force for the remodeling of	24 Wistar rats were randomly divided into 4 groups of OTM.for 1, 3, and 7 days (experimental groups) and control group (without orthodontic force). The expression of RUNX2 and OSX in the periodontal tissues was analyzed using real time PCR for mRNA and	The mRNA levels of RUNX2 and OSX increased in the periodontal tissues after subjected to the orthodontic force for 1 to 7 days, with the highest level occurring at day 7. The relative expression levels of RUNX2 and OSX mRNA were 1.85±0.12, 304±0.06 and 4.16±0.068, and 1.52±0.09, 1.83±0.03

				the periodontal tissue	Western blot analysis for protein. The data were also analyzed for involvement of the two genes in signal pathways using bioinformatics tools.	and 2.56±0.06 at day 1, 3 and 7, respectively. The results of Western blot analysis were consistent with the mRNA results
6	Indian Journal of Endocrinology and Metabolism, 2022.	Johns T. Johnson, Mohammad Anwar Hussain, Kripa Elizabeth Cherian, et al.	Chronic Alcohol Consumption and its Impact on Bone and Metabolic Health – A Narrative Review	To summarizes the findings from published studies that provide consistent evidence on the various effects of alcohol abuse on the bone health and metabolism	A detailed literature search was conducted utilising Pubmed and the Google search engines using the keywords "Alcohol", "Bone", "osteoporosis", "vertebral fractures" "mechanisms of bone loss", "body composition", "obesity", "diabetes", "obesity". All review articles and original studies describing the effect of alcohol and body composition were appraised in synthesising this review..	The results shows chronic excessive alcohol consumption could result in low bone mass and this may predispose to fragility fractures and an increased morbidity and poor health-related quality of life. Regular alcohol consumption is most common following skeletal maturity, emphasising the importance of understanding the skeletal consequences of drinking in adults.
7	Materials 2021	Kyungjae Hong, Won-Hyeon Kim , Emmanuel Eghan-Acquah , Jong-Ho Lee, et al.	Efficient Design of a Clear Aligner Attachment to Induce Bodily Tooth Movement in Orthodontic Treatment Using Finite Element Analysis	To present an effective attachment design of an attachment that can efficiently induce tooth movement by comparing and analyzing the movement and rotation of teeth between	The 3D finite element modes were constructed from CBCT data and used to analyze the distal displacement of the central incisor using 0.5- and 0.75-mm-thick aligners without an attachment, and with general and overhanging	The aligner with the overhanging attachment can effectively reduce crown tipping and prevent axial rotation for an intended distal displacement of the central incisor. In all models, an aligner with or without attachments was not capable of preventing the lingual

				a general attachment and an overhanging attachment	attachments	inclination of the tooth.
8	Photomedicine and Laser Surgery, 2014	Patricia Carvalho-Lobato, Valentin Javier Garcia, Khaled Kasem, Josep Maria Ustrell-Torrent, et al.	Tooth Movement in Orthodontic Treatment with Low-Level Laser Therapy: A Systematic Review of Human and Animal Studies	To organize the existing published literature regarding tooth movement in orthodontic treatment when low-level laser therapy (LLLT) is applied	Studies in humans and animals in which LLLT was applied to increase the dental movement were reviewed. Three reviewers selected the articles. The resulting studies were analyzed according to the parameters used in the application of laser and existing changes clinically and histopathologically	Out of 84 studies, 5 human studies were selected in which canine traction had been performed after removing a premolar, and 11 studies in rats were selected in which first premolar traction was realized. There were statistically significant changes in four human studies and eight animal studies.
9	Scientific Reports, 2021	Ayumi Shoji-Matsunag, Takehito Ono, Mikihito Hayashi, Hiroshi Takayanagi, et al.	Osteocyte regulation of orthodontic force-mediated tooth movement via RANKL expression	To provide in vivo evidence for the key role of osteocyte-derived RANKL in alveolar bone remodeling, establishing a molecular basis for orthodontic force-mediated bone resorption.	With show that osteocytes are the critical source of RANKL in alveolar bone remodeling during OTM. Using a newly established method for the isolation of periodontal tissue component cells from alveolar bone	The result was osteocytes expressed a much higher amount of RANKL than other cells did in periodontal tissue. The critical role of osteocyte-derived RANKL was confrmed by the reduction of OTM in mice specifcally lacking RANKL in osteocytes
10.	Scientific Reports, 2022	Hirokazu Kamei, Takenobu Ishii, Yasushi Nishii	Semaphorin 3A regulates alveolar bone remodeling on orthodontic tooth movement (OTM)	To observed the regulation of alveolar bone remodeling by Sema3A during orthodontic tooth movement	In vivo, springs were attached to the maxillary frst molars of C56BL/6J mice (OTM model) and the localization of Sema3A was confrmed by immunofuorescent.	Injection of rSema3A into the OTM model increased mineralization on the tension side and decreased the number of osteoclasts on the compression side. In vitro, IL-1β

				(OTM).	Recombinant Sema3A (rSema3A) was locally injected into the OTM model. Infammatory cytokine localization in the OTM model was confrmed by immunohistochemistry. In vivo, more Sema3A was observed on the tension side in the OTM group	signifcantly increased Sema3A mRNA levels. Immunohistochemistry for IL-1β in vivo showed more concentrated staining in the periodontal ligament on the tension side than on the compression side

FIGURES

Figure 1. Diagram of the study selection process