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Cytotoxicity and Genotoxicity Effect of Orthodontic Brackets on Oral Mucosal Cells.

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ABSTRACT

To review the literature on the implications and possible effects of fixed orthodontic brackets on the oral mucosa. The PubMed, Google Scholar, NCBI and Medline databases were searched for articles on "orthodontic brackets, appliances, metallic ion release, cytotoxicity, genotoxicity and oral mucosa". Only articles published from 2000 to 2017 were used. The search was augmented by screening the references cited in each paper for additional articles that might have been missed by the electronic search. Fixed orthodontic appliances decreased cellular viability, and the amount of nickel and chromium contents increased in the buccal mucosal cells. These changes still under normal values and revert upon the removal of the appliances.
Keywords: Orthodontic brackets, cytotoxicity, genotoxicity, oral mucosa, metal ions release.

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INTRODUCTION

Dental orthodontic appliances materials should be able to assure absolute safety and healthy biocompatibility in either short or long term of use. The orthodontic appliances comprise a number of deferent components. An orthodontic bracket is one of the essential components, which is defined as a small metal attachment welded or soldered to an orthodontic band or attached directly to the teeth, for fastening the archwire to the band or tooth [1].Uses of these brackets which are available in different commercial types and material composition for over years may cause intraoral problems or disorders. The oral cavity environment had many factors like saliva or microbial activity in addition to food and drinks, which enhance the biodegradation of orthodontic materials[2]. So, that makes the oral cavity acts as a corrosion area for bracket materials. For this reason, the concern of cytotoxicity and genotoxicity have increased. The purpose of this review is to evaluate the biocompatibility of orthodontic bracket materials. The article is not planned to be an extensive literature review, but somewhat an evidence-based review to state a knowledge in this area.

MATERIALS AND METHODS

A review was performed on studies in English using PubMed, Google Scholar,NCBI and Medline databases; only articles published between 2000 to 2017 were used. By manually searching reference lists of selected studies, we identified additional articles that might have been missed by the electronic search. The articles were chosen based on specificity about “metal ions release from orthodontic brackets; cytotoxic and genotoxic effects of metal bracket appliances”.

RESULTS

Metal ions release from orthodontic appliances

Fixed orthodontic brackets are made from alloys that composed of wide arrays of metallic, ceramic, or polymeric materials [3]. These materials have a combination of different percentages. Most of these brackets which were usually used during orthodontic treatment period are made from alloys that contain cobalt (Co), chromium (Cr), iron (Fe), nickel (Ni), and titanium (Ti); among them, Ni and Cr have a great concern [4].Metal-based orthodontic appliances averagely contain 8–50 % nickel and 17–22 % chromium [5]. Remaining of these bracket materials intra orally force it to start to the gradual release of their ion into that intraoral environment, which considered as an important issue in the biosafety of orthodontic treatment [6]. Previous investigations have revealed the corrosion and metal ions release from orthodontic brackets through emission of electro-galvanic currents with saliva which acting as the medium for continuous erosion over time [7]. Most of these investigations measured ion release during exposure to a biological medium, such as blood, urine or saliva, for periods ranging from 1 day to 1–2 months. In general, following the fixed orthodontic bracket insertion there is Ni and Cr concentration upsurge in saliva[6]. Some studies have shown that more amounts of these ions with high concentrations are released immediately after placement of brackets[8]. One of the studies demonstrated that the induction of stress can lead to a significant increase in nickel release from orthodontic brackets into saliva, but for the salivary chromium content was not significantly altered[5]. Another study done showed that no significant differences were found in Ti concentrations, but significantly higher values of Co, Cr, Cu, Ni metals considered were detected in patients under orthodontic treatment [9].

Cytotoxic effects of metal release from orthodontic brackets

The term “cytotoxicity” is used to describe the cascade of molecular events that interfere with macromolecular synthesis and lead to unequivocal cellular, functional and structural damage[10].There are different studies that assess the cytotoxicity of orthodontic materials. The approach consists of the extraction of epithelial buccal cells from orthodontic patients, then the viability of the cells is evaluated during or after orthodontic treatment. These studies are few and have contradictory results [6]. In a study done in 2001 found the cytotoxicity of the ternary alloy is higher than that of the binary alloy, this is related to the release of Cu [11].A study at 2002 done by Mockers et al. using 28 new and 9 clinically used materials, including brackets, molar bands, and arch wires found that the metallic and non-metallic materials were almost similar in terms of cytotoxicity, except in 6 cases the cytotoxicity of the 3-day results were different from the 14-dayresults. The materials, in general, can be considered as non-cytotoxic [12]. In 2003 a study was done by Faccioni et al. on epithelial cells of buccal mucosa on 55 orthodontic patients with fixed appliances in both arches. The fixed

appliances consisted of an average of 4–8 bands and 20 bonded brackets and found a significant decrease in cellular viability [7]. After that, a series of studies conducted and found that NiTi alloys do not have cytotoxic effects if the Ni content up to of 50% [13] One study demonstrates that the orthodontic therapy with metallic brackets was not able to increase nuclear alterations related to cytotoxicities such as karyorrhexis, pyknosis and karyolysis[14]. For the stainless steel brackets and archwires, wires showed the least biologic damage, whereas titanium brackets and arch wires produced the greatest cytotoxicity [2]. In another study it was found that the stainless steel was the material that induced a decrease in cellular viability[15], but another study found that the stainless steel arch wires have the highest cellular viability and nickel-titanium produced the highest inhibition of cell growth [16]. In one of the recent studies in 2014 done by Papageorgiou et al. investigated how the therapeutic effects and side effects of brackets used during the fixed-appliance orthodontic treatment are affected by their characteristics. They included 25 trials on 1321 patients, with most comparing self-ligated and conventional brackets and reported that there is no clinical recommendation can be made [17].

Genotoxic effects of metal release from orthodontic brackets

The term Genotoxicity is defined as a detrimental cellular effect causing disintegrity on its genetic material such as DNA and RNA [18]. Various base metal alloys are used for fabrication of different orthodontic appliances and were assessed for their genotoxic effects where some metals showed positive results. It should be noted that no single genotoxic test is actually competent in determining all compatible genotoxic agents. International Standard ISO-10993, proposed the following battery in-vitro and in-vivo genotoxic test-1)Ames test, (OECD 471), 2) In-vitro assay such as-the Mouse Lymphoma gene mutation assay (MLA) (OECD 476), chromosomal aberration (CA) assay (OECD 473), micronucleus assay (MN) (OECD 487) 3) In-vivo assays such as- a) a bone marrow micronucleus (MN) Assay (OECD 474) b) a bone marrow chromosomal aberration (CA) assay (OECD 475), c) a peripheral blood MN assay. Also, some studies have been found that used both alkaline and enzyme modified version of comet assay.

The first genotoxicity test using comet assay to see effects of fixed orthodontic appliance found that there are potential genotoxic effects of nickel and cobalt by producing breakage of DNA in oral mucosal cells[7]. Enzyme modified comet assay has become a favoured method for detecting different types of DNA damage such as oxidative damage caused by ROS[19]. This method was used only once in orthodontics research for assessing oxidative DNA lesions from both silver soldered band (SSB) and non-soldered band on HepG2 and HOK cell lines[20]. The author concluded that both orthodontic bands showed increased release of toxic metals where NSB were less genotoxic than SSB on both cell lines. A study done on four different commercial orthodontic brackets with a comet assay in mammalian cells concluded that no genotoxic induction was done by the brackets[21].

CONCLUSION

All the previous studies suggest the importance of further evaluations of orthodontic appliances because the compositions of materials have a role in the cytotoxicity result. According to the above reviews, we can conclude:

(1) The alloy components of orthodontic brackets considered safe to use.
(2) Nickle, Chromium and stainless steel have most cytotoxicity effect on oral mucosal cells which need further future study.
(3) The orthodontic bracket components show some levels of genotoxic effects initially after placement but subside in longer time use.
(4) The rest component of orthodontic appliances alloy is biocompatible.

Declaration of conflict of interest

The authors have no conflict of interest and no financial or personal relationships with other people or organizations that inappropriately influence (bias) this paper.

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