Mansoura University
Faculty of Dentistry
Department of Orthodontics

“ Evaluation of the Antibacterial Efficacy and Stability of Strontium Incorporated Hydroxyapatite [Sr-HA] Coated Mini-screws Used for Maxillary Canine Retraction: A Randomized Clinical Trial “

Protocol of Thesis

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Submitted By

Hind Hussein Jasim Mohammed Al-Khazraji

BDS [2012]

Faculty of Dentistry University of AlYarmouk,Iraq,Baghdad

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Supervisors

Dr. Ahmad Mohammed Hafez

Professor of Orthodontics Department OF Orthodontics

Faculty OF Dentistry-Mansoura University

Dr. Nehal Fouad Albelasy

Assistant Professor of Orthodontics Department of

Orthodontics Faculty of Dentistry, Mansoura University

Dr. Waleed Mahmoud Eldars

Professor of Medical microbiology and Immunology
Department of Medical microbiology and Immunology
Faculty of Medicine, Mansoura University

Introduction

Orthodontic mini-screws (OMS) play an important role in orthodontic treatment as they represent an absolute skeletal anchorage, especially in difficult cases that require high orthopedic forces such as expansion, distalization, intrusion and even with skeletally anchored fixed functional appliances [1]. The retention of orthodontic mini screws depends mainly on two different mechanisms, namely, primary stability and partial osseointegration [2]. The former depends on three main factors, which are summarized as follows:

- Mode of insertion.
- Surface texture and configuration of the orthodontic mini screw, and;
- Quality of bone [3].

On the other hand, partial oseointegration relies on direct functional and structural connections between the outer surface of the mini screws and the jaw bone [4]. Despite the great success rate of orthodontic mini screws as absolute anchorage devices with different cases of malocclusion, there is about a 30% failure rate due to bacterial infections and soft tissue and bone inflammation surrounding the orthodontic mini screws . So Some problems may occur during the use of mini-screws, such as peri–implant mucositis, mobility, and postoperative pain. Moreover, with the application of heavy forces, there is a weak connection between bone and the surface of the mini-screw [4,5] . Finding a solution to the failure of orthodontic mini screw has attracted the attention of many researchers, and some studies reported possible solutions, including different modalities and techniques for the method and angle of insertion of the mini-screw more recently, the application of different surface coatings to orthodontic mini screw has been investigated [6,7].

Strontium compounds have demonstrated varying antibacterial effects against different bacterial strains making them suitable for enhancing the antimicrobial properties of medical devices. These compounds can inhibit

bacterial growth, impede the permeability of the cytoplasmic membrane, and slow the replication of bacterial chromosomes and cell metabolism [8,9]. In recent years, Sr has been incorporated into dental and orthopedic biomaterials to minimize the risk of secondary caries in dental restorations [10]. It has also been used in injectable bone cement for minimally invasive delivery of Antimicrobials in vertebral compression fractures, aiming to inhibit microbial contamination and prevent implant-related infections [11].

Furthermore, Sr- coated implants have been explored for the prevention of peri-implantitis [12] As The major components of the bone extracellular matrix (ECM) are collagen types I, III, and V, as well as hydroxyapatite (HA). HA, also known as calcium apatite, contains Ca minerals within the matrix. Sr is an important trace element found in the body and shares similar chemical properties and structure to Ca. As a result, Sr can actively incorporate into the crystal lattice of HA [13,14].

Divalent cation have captured the interest of researcher's biomedical and dental fields due to their beneficial effects on bone formation. These metallic elements are similar to trace elements found in human bone. Strontium is divalent cation commonly found in various biomaterials. Since strontium has a radius similar to calcium, it has been used to replace calcium in any calcium-containing biomaterials. Strontium has the ability to inhibit bone resorption and increase bone deposition, making it useful in treatment of osteoporosis. Strontium has also been used as a radio pacifier in dentistry and has been incorporated into a variety of dental material to improve their radiopacity.

Furthermore, strontium has been shown to improve the antimicrobial and mechanical properties of dental materials promote enamel remineralization , alleviate dentin hypersensitivity, and enhance dentin regeneration [15].

In vitro study [16] outlines a method for coating temporary orthodontic titanium mini-screws with two biocompatible nanoparticles, silver/ hydroxyapatite (Ag/HA) and zinc oxide nanoparticles (ZnO NPs), with the aim

of reducing inflammation around the mini- screws. Among the two coatings, ZnO NPs demonstrated superior antimicrobial activity, better cytocompatibility, and lower cytotoxicity on all tested cell types, including oral epithelium, bone cells, and fibroblasts, compared to the Ag/HA NPs coating.

In another study [17],fluorohydroxyapatite(FHA)and fluorohydroxyapatite/ strontium (FHA–Sr) coatings were synthesized using the sol–gel method and applied to Ti6Al4V alloys via dip coating. Anodization by the MAA process and subsequent hydrothermal treatment improved coating morphology, creating dense, sphere-like particles with the addition of Sr^{2+} ions .Strontium doping enhanced crystallinity, shifted peaks to lower angles, and increased peak intensities due to its higher atomic weight compared to calcium. The FHA–Sr coatings exhibited higher shear bond strength (43 MPa) compared to FHA coatings (38 MPa), attributed to compact morphology, covalent bonding, and better diffusion at the coating-Ti interface MTT tests confirmed non-toxicity of both coatings to MG63 cells, with consistent cell viability over 3 and 7 days. Cell adhesion studies showed more elongated pseudopodia on FHA–Sr surfaces, indicating enhanced osteoblast interaction. ALP activity on FHA– Sr samples significantly increased by 105% over 14 days, compared to a 43.28% increase in FHA samples , suggestion that Sr^{2+} ions enhance bone mineralization and support osteoblast proliferation and differentiation by interacting with calcium-sensing receptors.

Also another study[18] found that Titanium implants capable of releasing strontium and silver ions demonstrated outstanding in vivo bone- bonding properties and effective antimicrobial activity against MSSA both in vitro and in subcutaneous pockets in vivo. These results highlight the potential of this novel material as a promising solution to address challenges related to bone fragility and surgical site infections (SSI).

There are several studies [19,20,21] discussing the coating of orthodontic mini-screws, including The modification of orthodontic mini-screw surfaces plays a crucial role in enhancing both their stability and antibacterial properties, the bioactive Ti-6Al-4V mini-screws demonstrated improved osseointegration and mechanical retention, particularly when coated with Ca-P via cyclic pre-calcification after TiO_2 nanotube formation , this surface treatment accelerated bone integration and enhanced stability[19]. Similarly, the incorporation of antibacterial agents, such as Ti-BP-AgNP and Ti-BP-SeNP, provided strong antimicrobial effects, with SeNP offering a promising alternative due to its lower cytotoxicity[20]. Additionally, coating orthodontic micro-implants with TiO_2 and ZnO NPs proved effective in preventing biofilm formation, reducing microbial infections, and minimizing peri-implant inflammation. Collectively, these findings emphasize the importance of surface modifications in improving the performance, stability, and antibacterial properties of orthodontic implants .

Aim of study

The aim of this study is to evaluate the antibacterial efficacy and stability of strontium- incorporated hydroxyapatite (Sr-HA) coated orthodontic mini-screws used in maxillary canine retraction in comparison to uncoated mini-screws.

Material and Method

Study Design:

This is a double-blind, split-mouth, randomized controlled clinical study with a 1:1 right-to-left allocation. The clinical study aimed at comparing the effects of Strontium hydroxyapatite coating and uncoating the orthodontics mini-screws and assessment the stability, antimicrobials in addition measurement gingival blood flow. The study will include (40) mini-screws, divided equally into two groups: one group without coating by Strontium Incorporated Hydroxyapatite and the other coating by Strontium Incorporated Hydroxyapatite .

Sample Size:

A total sample size (20) patients will be included in this study and (40) mini-screws, divided equally in to two groups:

- **Group 1 [Control]:** (20) uncoated orthodontic mini screws .
- **Group 2 :** (20) coated orthodontic mini screws .

Inclusion Criteria

- Adult patients within an age range (16-20) years.
- Orthodontic treatment plan requiring the extraction of the upper first premolars.
- Patients have fully permanent teeth are erupted (third molars are not included).
- No previous orthodontic treatment.

- No medical problem that could interfere with treatment.

Exclusion Criteria

- Presence of problematic healing such as, compromised immune defense, bleeding disorder, pathological bone quality, and xerostomia.
- Inadequate oral hygiene.
- Heavy smoking.

Ethical Consideration:

All selected patients will be informed about the aims and characteristics of the study, the potential risks and benefits and the Option of withdrawing from it whenever they desire. Then all patients will sign the informed consent document. All patients will be informed about the results after finishing. All selected patients' personal data and details will be held and handled confidentially and privately in the orthodontic department, faculty of dentistry, Mansoura University, the study will follow the guidelines of the ethical committee of Faculty of dentistry,Mansoura University.

Methods:

- All patients will be treatment with fixed appliance and Roth type brackets where leveling and alignment will be done utilizing nickel titanium.
- Extraction the upper first premolars and retraction the canine will be done using 17 ×25 SS wire.
- A periapical X-ray will be taken to confirm the orthodontic miniscrew position to avoid interference with adjacent root and to ensure that there are no periapical lesion.

- Symmetrical orthodontic mini screws will be inserted between the second premolar and first molar.
- The orthodontic mini screws that will be used in this study will be self-drilling, conical in shape, 1.6 mm in diameter, and 8 mm in length, constructed of titanium alloy, i well be purchased from Dentaurum company [Germany].
- The orthodontic mini screws were loaded with a 150 g NiTi coil spring.
- On one side, a coated will be inserted, and on the other side, an uncoated orthodontic mini screws will be used for the same patient.
- Coated materials will utilize Strontium incorporated Hydroxyapatite applied by electrochemical deposition and concentration percentage about 5 % .
- No mucoperiosteal flap will be raised, and no pilot hole will be made during the procedure.
- Will be assessed throughout follow-up periods of up to four months.

Outcome Measurement:

Assessment Orthodontic mini-screws stability (coated and uncoated) using Periotest device , Evaluate antimicrobial effect of Strontium incorporated Hydroxyapatite using Enzyme -Linked Immunosorbent Assay technique , and Evaluate the gingival health and blood flow .

Statistical analysis

Data will be analyzed using SPSS (statistical package for social sciences) version 26. Qualitative data will be presented as number and percent, Quantitative data will be tested for normality by Kolmogrov-Smironv test then described as mean and standard deviation for normally distributed data and median and range for non-normally distributed. The appropriate statistical test will be applied according to data type with the following suggested tests: Chi-Square for categorical variable Student T test, Mann Whitney U test and Spearman correlation is used to assess correlation between continuous variables.

Duration of the study:

- This study is suggested to be finished in one year.

Cost:

- 150,000 Egyptian pounds.

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