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When will RNA-based tests similar to Oncotype DX be used for oral cancer?

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Abstract

Methods for detection, diagnosis and predicting treatment outcomes for oral squamous cell carcinoma (OSCC) have not changed in decades. Information from studies about molecular changes that occur with these tumors are not useful in the clinic. This is in contrast to breast cancer where global gene expression analysis in the form of the Oncotype DX and Mammaprint tests are used routinely to determine ideal treatment for a large subset of breast tumors. While the first large scale studies of gene expression in both cancer types were done over a dozen years ago, research on OSCC has not led to gene expression profiles that are useful in the clinic. Global gene expression data for well over a thousand breast tumors linked to clinical outcomes has been available online for nearly ten years. This accelerated the development and validation of multiple RNA classifiers used to predict breast cancer treatment outcomes. Molecular characterization of oral and head and neck cancer research has been handicapped primarily due to low sample numbers. The recent release from The Cancer Genome Atlas of global gene expression analyses of over 500 head and neck tumors, including 308 oral tumor samples, obtained by standardized methods, along with linked clinical outcome data, should change this. It makes the vision of including gene expression analysis in OSCC treatment planning an obvious and attainable goal that could occur in the next five years.

Key words: Treatment outcome; Oral squamous cell carcinoma; Gene expression classifier

Core tip: Methods for characterizing oral squamous

cell carcinoma have not changed in decades. This is in contrast to breast cancer where global gene expression analysis is often used to determine ideal treatment. Studies focusing on molecular changes in oral cancer have suffered from lack of uniformity and small size. The recent release from The Cancer Genome Atlas of global gene expression analyses of over 500 head and neck tumors, including 308 oral tumors, should bring to the clinic in the next few years gene and gene expression analysis, and improved outcomes.

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INTRODUCTION

Detection and diagnosis of oral cancer is done today largely the same way it was done 30 years ago. White light is used to visually scan the oral cavity for unexplained lesions, followed by cervical lymph node visual examination and palpation. Suspicious oral lesions are then surgically biopsied and, after sectioning and staining, the pathologist provides a diagnosis based on tumor cell nuclear size and stain intensity, cell morphology and an examination of the mucosal architecture. While vital stains such as Toluidene blue can be used to stain the oral cavity, making lesions more easily detectable, and brush cytology is available to noninvasively assay cell and nuclear size and shape, these adjunct methods themselves are decades old and have not gained widespread usage[1]. Unlike detection, diagnosis, and even treatment planning with other cancers, measurement of molecular changes are seldom done with oral cancer.

In 2002, just two years after the original global gene expression analysis of breast tumors was published[2,3], one of the first relatively large scale studies of global gene expression in 26 head and neck tumors was revealed[4] (Table 1). At that time there was great optimism that those types of studies would provide gene expression signatures that could be used to diagnose and type oral tumors. However, there were problems early on including the usage of non-ideal statistical methods for studies with low sample numbers that often resulted in over-fitted data. The inclusion of multiple tumor subtypes compounded the problem of insufficient sample numbers and also made interpretation complex[5]. Finally, comparisons were often done between RNA from tumor and healthy mucosa; and not tumor *vs* benign lesions that can be mistaken for oral squamous cell carcinoma (OSCC)[6]. One way to rectify these problems is to study a subgroup of tumors in a single high risk group, such as tobacco or betel nut users, and to compare these tumors to benign pathology[5]. Until these factors are considered, improved detection of head and neck cancer using gene expression based methods will not move to the clinic and even then there is unlikely to be a single genetic classifier for all OSCCs.

Another potential role for gene expression analysis of OSCC is in the prediction of treatment outcomes. Currently OSCC staging is based on the universally used TNM system of the Union International Contre Ie cancer and the American committee on cancer. TNM staging is based on anatomic extent of the tumor only. Specifically T stands for tumor size, N indicates nodal involvement and M indicates presence or not of distant metastasis. The shortcomings of the currently used TNM staging system for head and neck and OSCC are elegantly discussed by Takes *et al*[7]. It is unfortunate that despite these limitations OSCC staging plays a key role in treatment decisions that ultimately impact survival. Studies have indicated that tumor specific histopathologic characteristics impact on outcomes and survival, such as depth of invasion, tumor volume and thickness, presence of extracapsular extension, perineural invasion, pattern of invasion, lymphovascular invasion, but these research findings are not routinely included in staging or treatment decision-making for multiple reasons[8-14]. Typically, early stage tumor patients are treated with single modality therapy, surgery alone or, rarely, radiotherapy alone, while more advanced stage tumors receive multimodality treatment with surgery and adjuvant therapy such as radiation with or without chemotherapy. The rationale is that stage Ⅰ or Ⅱ tumors, which are by definition without lymph node involvement, can be reasonably controlled with surgery or localized irradiation. Systemic genotoxic treatment provides no advantage and has potentially more toxic side effects. While this approach has spared patients unnecessary adjunctive treatment, it would be better to know which tumors have a propensity to progress and need multimodality treatment. Much effort has been made to develop a gene expression-based classifier for OSCC that does not just stage the tumor but also predicts aggressiveness. For example, this was attempted by recording changes in gene expression pattern in tumor tissue that correlate with lymph node invasion and/or tumor recurrence[15-19]. A problem in these studies may have been insufficient sample numbers. A second lesser problem was the seeming paradox that there was very little overlap between marker RNAs identified by one group and that of another, the latter creating a level of doubt about the methodology (needs a period).

ORAL CANCERS LIKE BREAST CANCERS ARE NOT ALL ALIKE

The state of the gene expression-based staging of breast cancer offers a contrast in clinical value[20,21]. The Oncotype DX treatment response predictor has been used over one-half million times for breast cancer

Table 1 Major events in global gene expression analysis of breast and head and neck cancer

Breast cancer	Events	HNSCC
2000 (Perou *et al*[2])	First large scale global gene expression analysis	2002 (Méndez *et al*[4])
2001 (Sørlie *et al*[3])	First identification of tumor subtypes based on global gene expression analysis	2004 (Chung *et al*[22])
2002 (van de Vijver *et al*[35])	First published classifier to advise treatment based on global gene expression analysis	2005 (Roepman *et al*[18])
2003 (Sorlie *et al*[34])	First confirmation of tumor subtypes based on global gene expression analysis	2013 (Walter *et al*[23])
2006 (Paik *et al*[28])	First validated classifier to advise treatment based on global gene expression analysis	Still waiting
2006 (1200 samples)	More than 1000 samples global gene expression analysis data available	2013 (1200 samples)

HNSCC: Head and neck squamous cell carcinoma.

staging. This gene expression-based test fills a void left by the uncertainty over which stage Ⅰ and Ⅱ breast cancers require chemotherapy after surgery. It was known early on that a subset of early-stage estrogen receptor positive breast tumors tended to progress if chemotherapy was withheld[20,21]. In 2000 and 2001, it was first noted that breast cancer could be divided into more than 4 subtypes based on gene expression analysis[2,3]. These groups roughly coincided with the older histological classifications. The realization that breast tumors were a heterogeneous group made it clear in the beginning that studies of gene expression in breast tumors would require large numbers of samples or a focus on one subtype, or both, to produce meaningful results. An effort was made to maximize the number of cases in studies and to make data available to multiple groups *via* the web. By contrast, in 2004 Chung *et al*[22] made the observation that head and neck tumors fell into 4 groups, but there was no clear association with etiology or histology. Attempts to link gene expression with targeted treatment were unsuccessful[23]. And the only accepted subgroup of head and neck cancers, oral pharyngeal cancers with transforming human papillomavirus (HPV) was not linked to a specific gene expression subtype till years later[23-25]. In short, it was difficult to discern how real the subgroups were and what the gene expression similarities meant until two gene expression studies done about a decade later on 138 and 279 head and neck tumors respectively showed the same head and neck squamous cell carcinoma (HNSCC) subtypes based on gene expression and/or DNA alterations[23,24]. A meta-analysis published in 2015 after 9 years and over 20 studies totaled 1300 samples and revealed a further subdivision of two of the subtypes[26]. This evidence shows that HPV-negative HNSCC and OSCC are not homogenous cancers but fall into separate subtypes.

Starting in the early 2000s, several groups sought to design a gene expression-based classifier that could aid in diagnosis and treatment decisions for breast cancer (Table 1). The group that ended up producing the Oncotype DX gene expression-based classifier made several decisions that probably facilitated their dominance in the United States market for breast cancer analysis[27]. First, they largely focused on genes already shown to be important for cancer, thus reducing the number of samples required for a statistically valid analysis. Next, they optimized analysis of RNA from fixed tumor tissue in paraffin blocks, already the standard method for storage of biopsy material. Finally, they used large numbers of samples and focused on one subset of breast tumor patients, those with estrogen receptor enriched but lymph node negative breast cancer. Finally, their test answered an important clinical question: Which patients with node negative tumors that were estrogen receptor positive would best be helped by being treated with genotoxic chemotherapy after surgery[28]? Research on head and neck and oral cancer did none of these things. Typically, frozen tissue was required and low numbers of samples were used so while classifiers for head and neck and oral cancer were produced they were not validated for clinical usage. For example, early work suggested a role for the epidermal growth factor receptor in the oral cancer process and treatments that target this protein have been tested but there has been little success[29]. The lack of targeted therapies for oral cancer is likely due to the lack of sufficient numbers of molecularly well characterized oral cancer tumor samples.

WHAT NEED DO THE ONCOTYPE DX, MAMMAPRINT AND OTHER SIMILAR GENE EXPRESSION-BASED TESTS FILL?

Breast cancer diagnosis routinely entails histology, histochemistry to measure estrogen, progesterone and estrogen receptors, and finally the FISH assay to directly measure *HER2* gene amplification. In addition, immunohistochemistry measures the Ki-67 level, which is proportional to tumor proliferation and correlates with responsiveness to genotoxic chemotherapy[20,21]. By contrast, tumors that show low proliferation rates seldom recur and do not respond to genotoxic chemotherapy. This makes measuring cell proliferation rates in tumors crucial, but Ki-67 immunohistochemistry is prone to variation depending on tissue preparation, antibody staining, and pathologist quantification. As a result, Ki-67 protein is a poor marker. Tumor grade, which is a measure of how differentiated the tumor cells appear and correlates with Ki-67 levels and is also a predictor of recurrence, is also difficult to quantify accurately and consistently between laboratories. As is now well understood, Oncotype DX and the 16 cancer genes it measures[27], Mammaprint with the 70 genes it measures[30], and the Genomic Grade Index

that originally measured 96 genes[31], include a large percentage of genes that vary with cell proliferation rates. Because so many genes change in expression levels with changes in proliferation rates, it is possible to have 3 different working gene expression tests-Oncotype DX, Mammaprint, and the Genomic Grade Index - for prediction of treatment response of node negative estrogen receptor positive tumors, with little overlap in the markers that are measured. Remarkably, the markers for the different tests were selected based on different criteria such as their ability to predict survival or differentiate early *vs* late stage tumors among different subsets of breast cancer groups, yet they all contain a large percentage of markers for cell proliferation[27,30,31]. While they also can predict estrogen receptor status, it is now recognized that their ability to more accurately and reproducibly quantify tumor cell proliferation than Ki-67 immunohistochemistry and tissue grade is what makes them valuable in the clinic.

CONCLUSION

The Oncotype DX and other tests all address an important and frequent question about treatment in a common cancer: When to use conventional chemotherapy in early breast cancer? While there are newer gene expression-based tests that better address questions of optimal treatment for longer survival (10 years *vs* 5 years) and that may help more patients, the current tests now help many patients and that is why they exist[20,21]. There is a similar clinical question for OSCC patients, in that clinicians have to make decisions about which patients will get adjuvant therapy with radiotherapy or chemoradiotherapy after surgery. Recent work by The Cancer Genome Atlas (TCGA) will help to address this. TCGA has characterized over 500 head and neck tumors in regard to genomic changes, miRNA and mRNA expression changes, along with large amounts of clinical information including treatment follow up and cancer recurrence[32]. Genetic studies from TCGA allow the identification of pathways that are altered with OSCC[24]. For example there is a subgroup of tumors that lack HPV but have an intact *p53* gene and have long recurrence-free survival times. TCGA work also confirms the 4 gene expression based subgroups of head and neck cancer and for oral cancer. This will make easier the identification of targeted and conventional genotoxic-based chemotherapies that will show efficacy with individual subgroups of tumors but not all OSCCs. It is not hard to believe that a validated classifier for OSCCs that respond best to treatment will be in the clinic before long, simply because the numbers to begin these studies in earnest are beginning to be available to researchers[26,33]. While the heterogeneity of OSCC makes the development of a single classifier for OSCC difficult, it makes the vision of including gene expression analysis in OSCC treatment planning an obvious and attainable goal that could occur in the next five years if enough tumor samples are characterized using standardized methods.

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About gravity and occlusal forces in the jaws: Review

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Author contributions: Ben Yehuda A performed literature review and wrote the paper; Singer C helped in study design, literature search and writing the paper; Katz J wrote the paper.

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Abstract

Mechanical forces resulting from gravitation seem to be essential for structural adaptation and remodeling of skeletal bones. These forces have the capability of delivering powerfully distorting stimuli to skeletal bones in a very short time, several times a day, in a uniform direction. Facial and jaw bones are not subjected to gravity impact forces. These bones need a mechanism of "compensation" for this deficiency. The goal is achieved by a unique mechanism that substitutes for gravity impact forces - the mechanism of occlusal load transmission to the bone *via* the periodontal apparatus space. In cases of early loss of teeth and loss of periodontal ligament this mechanism will be missing resulting in premature bone aging.

Key words: Gravity; Occlusal; Forces; Bone; Implant; Periodontal ligament

Core tip: The anatomy and physiology of the periodontal ligament is structured to oppose occlusal forces that impact facial bone in multidirectional vectors. This mechanism is different from the long bones that oppose only vertical forces. Dental implants planning and placement should be compatible with these principles.

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INTRODUCTION

The masticatory system is challenged on a daily bases by a variety of high magnitude mechanical forces resulting from occlusal contacts. Occlusal loads are transmitted to jaw and facial bone by a special organ: The periodontal attachment apparatus; root cementum, periodontal fibers, alveolar bone, and gingivae.

In the recent years implantology has revolutionized dentistry and has significantly improving the quality of life of many dental patients. However, in spite of the

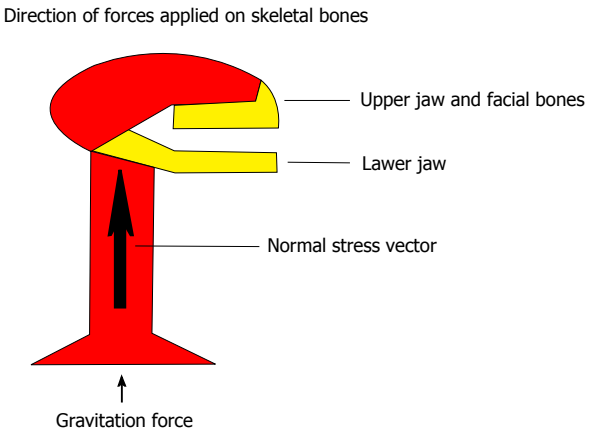

Figure 1 Vertical forces applied to the long bone are negated by the strength of bone trabecula rearranged along the long bone axis.

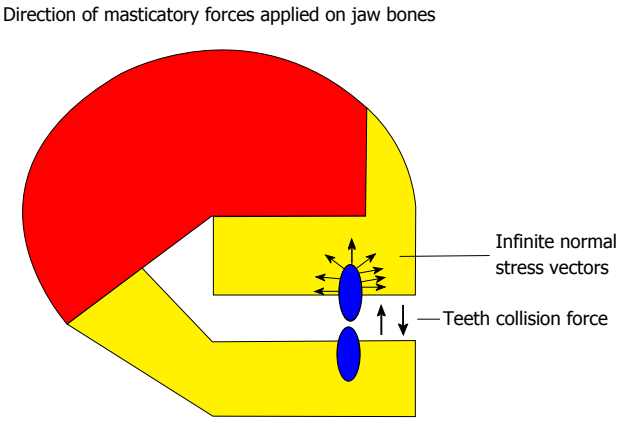

Figure 2 Occlusal loads in the jaw are converted into compressing vectors around the root surface of the tooth.

great successes in patient's oral rehabilitation, some implant procedures are failing mainly because the basic principles of oral occlusion are not adhered to. The magnitude the occlusal force in the jaws is enormous and their direction and counter balancing are significantly different from the forces applied on the skeletal bones.

The purpose of the present manuscript is to review the literature that is pertinent to the basic principles of occlusal forces in the facial bone compared to the skeletal bone. In a consecutive manuscript (part Ⅱ) we plan to describe an implant based on these principles and describe cases associated with this technique.

LITERATURE REVIEW AND DISCUSSION

We have used the PubMed website to search for publications with the following key words: Occlusal, forces, balanced, periodontal ligament, jaws skeletal. The search was limited to the English literature and the time frame used was 1900 to present. We have also cited classic text books that are considered to pioneer the field.

The gravity force that affects our skeleton is the result of acceleration of our body against the ground. The outcome of this force over the small area of the feet reveals an intensified stress that is applied to the skeleton. The result is a prominent stress vector (Figure 1) with uniform direction that repeats itself several times a day for short period intervals. The importance of this vector is in the fact that it is turned into a principle stress vector[1]. To negate this force of the bone, trabeculae rearrange along the axis of this vector and build the long bones. The new architecture enables the bone not only to resist compressive stress but also to minimize shear stress according to Mohr's circle[2]. Compressive stress is a most effective stress for bone remodeling. While this kind of stress activates bone remodeling, it needs a relatively high threshold to become a destructive stress[1]. The more intense the stress, the thicker and closer the trabeculae will become. The most hazardous stress for the bone is shear stress that stimulate bone degradation (law threshold is needed for destruction). Obviously, shear stress demands increased density to protect the bone. Torsion and bending, which comprise shear stresses, cause the bone to protect itself by intensifying bone mineralization density (BMD) and thickening compact bone[1,3]. The greater these stresses, the thicker the compact bone. The impact gravity activities are shown to increase cortical thickness in long bones of athletes[4]. This is done in addition to increasing BMD. Non-impact horizontal activities (like swimming) do not cause thickening of the bone's cortex and cause a lesser degree of BMD. Most of the actions like walking result in reduction of the risk of hip fractures[5,6]. When these activities are intensified, the risk for hip fractures decreases even more. Non-gravitational activities like swimming do not reduce the chances of hip fractures[5,6].

Facial and jaw bones are in an exceptional geographic position, as they are not on the principle stress axis (Figure 1). This group of bones is not prone to gravity collisions and need a substitute to compensate for this deficiency. According to analysis done for occlusal loads, it has been shown that transmission to the alveolar bone occurs *via* the periodontal ligament space[7]: Occlusal loads are converted into normal compressing vectors all around the root surface of the tooth. These vectors are perpendicular to the root surface (Figure 2) and are equal in their magnitude. Bone distortion is accepted as a result of a spherical stress tensor that compresses the bone all around the root surface. Arrangement of trabecullae during remodeling is done along the principal vectors which in this case are an eigenvector[1]. The result is that the trabecullae are radiating from the root. This arrangement helps in limiting shear stress and turns the alveolar bone into a cushion hammock that absorbs occlusal loads on one side and transmits them in a radiating direction to distal bony structures on the other side. Macro structure of facial bones is constructed in a way that enables maximal strength with minimal mass[3]. According to this principle, facial and jaw bones have air spaces and get their strength from the bone that border them. Impact loads that hit the maxillary tooth will cause deformation not only in the

alveolar bone nearby the root, but also in other supra alveolar structures like the orbits, nasal meatuses and the paranasal sinuses, and the partitions in-between them. As maxillary occlusal impact loads may regulate upper jaw facial and forehead bone adaptation, it is done in a dual action; mechanical compression that aims at trabecular bone remodeling and bending or torsion stress that is responsible for remodeling and maintenance of the cortical surfaces[1].

Mandibular bone, unlike the upper face bones, is a modification of long bone and is more prone to bending and torsions distortion. Therefore, the mandible will express a thicker compact bone. The fact that edentulous mandibles were shown to have thinner cortical bone in contrast to dentulous mandibles support this thesis[8]. In skulls affected by early loss of teeth, facial bones express early aging appearance[9]. According to this theory, the stress tensor that acts directly on the alveolar bone influences also distant bony structures. Early loss of teeth may explain premature aging and deformation of the face because of loss of bone mass. Installation of dental implants is aimed to partially delay facial aging. Dental implants were an obvious outcome of harnessing of orthopedic screws in an attempt to reconstruct artificial dental roots. While orthopedic screws are meant for fixation of bone fractures for at least the period of bone repair, dental implants are intended to permanently replace natural dental roots. Contemporary implants are aimed mainly for retention and stabilization of the bone, and osseous integration is used to substitute for attachment by periodontal ligament (PDL).

Dental implants transmit stress to bone by a stress tensor that includes compressive but also shear stress vectors. Obviously the suggested mechanism of the PDL apparatus does not exist and implants are prone to shear stress and bone degradation. This is supported by clinical observations and retrospective studies that demonstrate bone loss along dental implants during the years[10-12]. Bone degeneration and perimplantitis around dental implants is reported to be up to 28% of the cases. Furthermore, the older the implant, the greater the rate of bone absorption.

Nevertheless, dental implants have a high rate of survival and are usually the better solution for reconstruction of missing teeth. It is suggested that in cases of plastic facial rejuvenation, attention would be directed to occlusion rehabilitation before any procedure is done in an attempt to achieve more efficient and long lasting results.

CONCLUSION

Impact forces are essential for mechanical bone adaptation and for achieving bone strength. The impact gravity loads serve the goal of strengthening skeleton bones. Impact occlusal loads are suggested to serve the same aim for facial and jaw bones. The impact of occlusal forces depends on their magnitude, frequency, and direction.

The result is a clear strain vector signal that leads to forming bone cells. Dental implants lack the ability to compress purely nearby bone; they serve merely to preserve reservation facial bone.

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MINIREVIEWS

Laser assisted periodontics: A review of the literature

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Abstract

Over the years, the use of the laser within health field and more particularly dentistry has been increasing and improving. The application of laser in the periodontal treatment takes part of a non-surgical and surgical approaches, is used for the decontamination of periodontal pockets due to its bactericidal effect, and the removal of granulation tissues, inflamed and diseased epithelium lining, bacterial deposits and subgingival calculus. However in spite of all the marketing surrounding, the use of laser highlighting its beneficial effect, the capacity of laser to replace the conventional treatment for chronic periodontitis is still debatable. In fact there is no evidence that any laser system adds substantial clinical value above conventional treatments of chronic periodontitis. Some studies showed a significant positive effect on clinical attachment level gain and probing depth reduction. In the other hand, several articles demonstrated no evidence of the superior effectiveness of laser therapy compared to root planing and scaling. Our aims is to review the literature on the capacity of erbium:Yttrium-aluminum-garnet and neodymium: Yttrium-aluminium-garnet laser to either replace or complete conventional mechanical/surgical periodontal treatments.

Key words: Laser; Review; Scaling and root planning; Erbium:Yttrium-aluminum-garnet; Neodymium:Yttrium-aluminium-garnet; Periodontitis

Core tip: Faced with the increased use of lasers in dentistry, we tried to demystify, in this review, the real benefits and disadvantages of the use of the neodymium:Yttrium-aluminium-garnet and erbium: Yttrium-aluminum-garnet lasers in periodontics. Many trials showed that the use of lasers is an effective and safe method of root planing in periodontal non-surgical treatment of chronic periodontitis. However, due its possible side effects and less effective results when used alone, lead some authors to state that the use of lasers as a replacement of the conventional mechanical treatment is still doubtful.

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INTRODUCTION

Chronic periodontitis is defined as inflammation of the gingiva extending into the adjacent attachment apparatus. The disease is characterized by loss of clinical attachment due to destruction of the periodontal ligament and loss of the adjacent supporting bone[1]. Clinical findings include attachment loss, gingival recession, alveolar bone loss and pocket formation. Although chronic periodontitis is the most common form of destructive periodontal disease in adults, it can occur over a wide range of ages. It usually has slow to moderate rates of progression, but may have periods of rapid progression. Clinical features may include combinations of the following signs and symptoms: Edema, erythema, gingival bleeding upon probing, and/or suppuration[1]. The development of periodontitis appears to be associated with a shift from a predominantly Gram-positive flora to a predominance of anaerobic Gram-negative rods[2].

Several characteristics can be observed in contaminated periodontal pockets. Usually, biofilm deposits, calculus and bacterial endotoxins infiltration into the cementum of root surfaces are reported. Mechanical scaling and root planning with manual and/or ultrasonic instruments represents the initial phase of periodontal non-surgical therapy. However, this therapy is not always effective for complete removal of bacterial and their endotoxins deposits. In fact, complex root anatomy makes access to areas such grooves and furcations difficult[3]. Although systemic and local administration of antibiotics into periodontal pockets is occasionally effective for disinfection, but risk of producing resistant microorganisms limits this approach.

Furthermore, conventional mechanical therapy is often uncomfortable for both patients and operators. Indeed, this time - consuming technique depends on the operator's dexterity. The power and the curette's angulation vary form one operator to another and can give totally different results. In addition, noises and vibrations of ultrasonic instruments are often source of stress and fear in some patients. All these constraints led searchers to explore other therapeutic approach to replace or complete the conventional periodontal mechanical therapy, such as lasers. Recently, the application of laser - assisted treatments for removal of granulation tissues, inflamed and diseased epithelium lining, bacterial deposits and calculus has been proposed as alternative or as adjunctive treatment to the more conventional periodontal mechanical therapy[4].

The word Laser is the acronym for light amplification by stimulated emission of radiation. Lasers can be distinguished from other light sources by their coherence, allowing lasers to be focused to a tight spot[5]. Since Albert Einstein's theory of stimulated emission of electromagnetic radionation and Maiman's first functioning laser using a synthetic ruby crystal in 1960[5], laser research has produced a variety of improved and specialized laser types, optimized for different application such as dentistry. In fact dental lasers are recognized today for their ability to ablate hard and soft tissues, to reduce bacteria counts and even to provide hemostasis of soft tissues during their use with minimal anesthesia[6]. Lasers used in dentistry emit wavelengths between 377 nm and 10.6 μm. The most common types are CO_2, diode, erbium:Yttrium-aluminium-garnet (Er:YAG) and neodymium:Yttrium-aluminium-garnet (Nd:YAG) lasers.

The use of lasers in periodontal therapy has evolved since a laser for periodontal applications was first introduced in 1985[7,8]. Initially, most articles that advocated the use of lasers for soft tissue surgery were anecdotal. Nowadays, it appears that research in soft tissue applications is increasing exponentially, and the claims of decreased bleeding, swelling, pain, and bacterial populations are being referenced in several publications[6].

Four types of interactions may occur when biological tissue is irradiated with laser light: Reflection, scattering, absorption, or transmission. Basically, the reflection, scattering and transmission decrease, as the absorption increases. The type of interaction that takes place depends on the wavelength of the laser. For most biological tissues, higher absorption occurs in wavelengths with greater absorbance in water. The lasers with greater absorbance in water are the Er:YAG lasers. Erbium radiation is readily absorbed by most tissues, and this translates into less penetration and a shallower layer of laser-affected tissue[9].

Laser irradiation exhibits strong ablation, hemostasis, detoxification and bactericidal effects on the human body. These effects can be useful during periodontal treatment, especially for handling of the soft tissue as well as for the debridement of diseased tissues. Thus laser treatment may serve as an alternative or adjunctive therapy to mechanical approaches, in periodontal therapy. However, the high cost of laser equipment and the lack of reliable clinical research are a significant barrier for the laser utilization by the dentist. Also, each laser has different characteristics because of their different wavelengths. Thus the operator must be aware of the possible risks involved in clinical applications, and precaution must be exercised to minimize these risks when performing laser therapy. The most important precaution in laser surgery is the use of glasses to protect the eyes of the patient, the operator and the assistants. Protection of the tissues surrounding the target is also recommended. Second, thermogenesis during the interaction of the laser with the tissues must be addressed and well controlled[9].

In lasers that exhibit deep-tissue penetration, such as the Nd:YAG, the thermal injury to the pulp tissue and underlying bone tissue can be a concern during treatment. Also, a root surface that has received major thermal damage could render the tissue incompatible for cell attachment and healing. During treatment of

hard tissue, the use of water spray can minimizes heat generation by cooling the irradiated area and absorbing excessive laser energy. Therefore, thermal injury must be prevented by using irradiation conditions and techniques that are appropriate for the lasers used. In addition, in periodontal applications, there exists the risk of excessive tissue destruction as a result of direct ablation and the possibility of thermal side effects in periodontal tissues during irradiation of periodontal pockets. Improper use of lasers could cause further destruction of the intact attachment apparatus at the bottom of the pocket wall as well as excessive ablation of root surfaces and the lining of the gingival crevice[4].

Damage of the tooth surface should also be avoided during irradiation with Er:YAG lasers, as the enamel and dentin easily undergo melting, carbonization or ablation by these types of lasers. Thus, in order to use lasers safely in clinical practice, the practitioner should have precise knowledge of the characteristics and effects of each laser system and their performance during application, and should exercise appropriate caution during their use[4].

The aim of this study is to review the literature on the effectiveness of Er:YAG and Nd:YAG lasers in periodontics, as either a complete treatment or as an adjunctive treatment. We performed a review of the recent literature in Pubmed and Mesh databases.

POSITIVE EFFECT

The erbium family of dental lasers consists of two wavelengths with similar but not identical properties. The Er:YAG laser produces a wavelength of 2940 nm and the erbium, chromium: Yttrium-scandium-gallium-garnet laser produces a wavelength of 2780 nm. The erbium family of lasers has been used for cavity preparation and caries removal and has shown promise as a laser system for periodontal treatment approaches on hard tissues. The Er:YAG laser has the most shallow penetration into soft tissue of any dental wavelength and can ablate both soft and hard tissues safely with water irrigation and are applicable to periodontal treatments such as scaling, debridement and bone surgery, and have minimal thermal effect[4].

Er:YAG laser seems to be the only laser, used today in dentistry, able to remove calculus and lipopolysaccharides from root surfaces[10]. In fact its wavelengths have the highest absorption in water and hydroxyapatite compared with the diode and Nd:YAG lasers (respectively 10 times and 20000 times greater)[11]. When using the Er:YAG laser, the energy is highly absorbed in water which is then vaporized by thermal effect leading to micro explosions rather than heating the surrounding tissue (resulting in minimal thermal side effects). Theses beneficial properties of the Er:YAG laser and its capacity to ablate both soft and hard tissue led to its approval in 1997 by the Food and Drug Administration in the United States for preparation of dental cavities, for incisions, excisions, vaporization, ablation and hemostasis of soft and hard tissues in the oral cavity[9]. A special optical fiber or a hallow waveguide permit the use of this laser in periodontal pockets.

The Er:YAG can not only be used to remove calculus from root surfaces but also to significantly reduce bacteria load in diseased tissues from root furcations or intrabony pockets. As with other soft tissues lasers, there is a proven bactericidal effect. It can also be used on contact mode to cut or ablate soft tissues with precision with a good hemostasis and almost no need of anesthesia. Because of the potential for possible soft and hard tissue applications, use of this laser has been investigated in periodontal therapy for scaling, root debridement and periodontal and peri-implant surgeries[12].

The Er:YAG laser is capable of easily removing subgingival calculus and root smoothing without a major thermal change of the root surface. The level of calculus removal by this laser seems similar to that of ultrasonic scaling[4]. In fact, in 1994, Aoki *et al*[13] were the first to suggest the use of Er:YAG as an alternative to remove subgingival calculus. The capacity of Er:YAG laser to remove calculus was then examined on human extracted teeth with subgingival calculus. They concluded that the pulsed Er:YAG laser used with irrigation was capable of subgingival calculus removal without damaging the surrounding tissue with an slight increase in temperature during the laser application. Watanabe *et al*[14] showed the safety and usefulness of Er:YAG laser therapy for subgingival calculus removal in nonsurgical pocket therapy. Although some randomized, controlled clinical studies showed improved clinical results following Er:YAG laser irradiation, most failed to show consistently superior and/or additional benefits of the laser therapy. Similar or sometimes better results were obtained with Er:YAG laser therapy than conventional scaling and root planing therapy in terms of reduction of bleeding on probing, pocket depth and improvement of clinical attachment level[15]. In addition, these clinical improvements could be maintained over a 2-year period[16]. Significant clinical improvements were exhibited 6 mo following Er:YAG laser therapy, but they were similar to those obtained using the ultrasonic scaler alone[17]. However, the treatment with the Er:YAG laser resulted in significantly higher pocket depth reduction and clinical attachment level gain at 2 years post-therapy in comparison to treatment with an ultrasonic scaler[18]. One important finding of this study was that at 1 year post-treatment, there was increase of pocket depth and attachment loss in the ultrasonic group, whereas stability of Er:YAG laser-treated pockets was noted until 2 years following treatment[18].

Regarding bacterial reduction no superior reduction in bacterial number was observed following treatment with the Er:YAG laser in comparison to ultrasonic scaling[19]. However, in the same study[19], when the patients perceptions were investigated, ultrasonic scaling was more pleasant than therapy with an Er:YAG laser or hand curet instrument. Furthermore, in a study evaluating treatment of periodontal pockets using an Er:YAG laser, in

a periodontal maintenance program, no differences were reported in the microbial profiles between treatment with the Er:YAG laser and ultrasonic scaling, although faster healing (pocket depth reduction and clinical attachment level gain) and less discomfort during treatment were observed in the group treated with the Er:YAG laser[20].

In 2012, a systematic review and a meta analysis, made by Sgolastra *et al*[21], tried to determine the efficacy of Er:YAG, when used as alternative treatment to scaling root planing (SRP) in the treatment of patients with chronic periodontitis. Five random controlled trials, with a total of 85 patients and 3564 sites, were entered in the meta-analysis to investigate clinical attachment level gain, probing depth reduction, and gingival recessions changes in the Er:YAG laser and SRP groups. The meta-analysis revealed no significant differences for any investigated parameter at 6 and 12 mo and concluded that there was no evidence of the superior effectiveness of the Er:YAG laser compared to conventional SRP.

Lopes *et al*[22] in 2008, in a controlled clinical study with twenty-one subjects evaluated clinical and immunological effect on root surfaces irradiated with an Er:YAG laser with or without conventional SRP. The results pointed out that after thirty days both treatments demonstrated significant reductions in gingival indices and probing depth. An increase of the gingival recession was observed in the both groups. No difference in the interleukin IL-1β, was detected among groups and periods.

In spite of the lack of well-controlled clinical trial with high level of evidence, and all the contradictory results in the literature, the American Academy of Periodontology state in 2011 that: "Erbium lasers show the greatest potential for effective root debridement (SRP)"[23]. At a low energy level, the Er:YAG laser had shown a bactericidal effect against periodontopathic bacteria in addition to its capacity to remove toxins present in the root cementum such as lipopolysaccharides[24-26].

For optimal tissue regeneration and successful surgical procedure, the root surface and the bone defect should be debrided and decontaminated. Lasers in periodontics had shown effective results in debriding intrabony defect and furcation areas where mechanical conventional instruments are less effective. In addition, many studies showed that Er:YAG laser application is effective and easy to use in root surface debridement and granulation tissue removal during surgical procedures[4,9].

Sculean *et al*[27] reported that the Er:YAG laser is an effective and safe method with significant clinical improvement six months after a treatment of periodontal intrabony defect with access flap surgery. Gaspirc and Skaleric[28] compared, in a long term clinical outcome, the conventional method using the modified widman flap to Er:YAG laser assisted flap surgery. Significant reduction of pocket depth and a gain of clinical attachment level were found in the laser group at 6-36 mo after surgery. Therefore, application of the Er:YAG laser for surgical degranulation is a promising approach, and its effectiveness and safety have been demonstrated clinically[4,9].

Furthermore, Schwarz *et al*[29] demonstrated in an animal study that Er:YAG lasers also seems to induce new cementum formation. Thus, laser treatment in periodontal pockets may promote more periodontal tissue regeneration than conventional mechanical treatment.

On other hand, the Nd:YAG laser typically emit light with a wavelength of 1064 nm, in the infrared light and is theoretically not absorbed by hard tissues such as cement and dentin. It affects merely soft tissues like gingiva and pocket epithelial lining. Nd:YAG lasers operate in both pulsed and continuous mode and is delivered through a fiber optic tip. The Nd:YAG is commonly used in gingivectomy, gingivoplasty, frenectomies, operculum removal and biopsies procedures[5]. It can be used in a contact or a noncontact mode and is useful for soft tissue surgery. Due to the characteristics of penetration and thermogenesis, the Nd:YAG laser produces a relatively thick coagulation layer on the lased soft tissue surface, and thereby shows strong hemostasis[6]. The Nd:YAG laser is very effective for ablation of potentially hemorrhagic soft tissue. Some studies had shown also a reduction in postoperative pain because of its minimal deep thermal damage[4]. The strong affinity for chromophores in pigmented tissues theoretically makes the Nd:YAG useful in eliminating pigmented bacteria found in periodontal diseases[6], however still no clear in the literature if black pigmented bacteria's as *porphyromonas gingivalis* actually express a pigmented phenotype when colonizing the periodontal pocket or the gingival tissues. Several studies demonstrated the decontamination effect and the inactivation of the endotoxins in the contaminated root surface treated by Nd:YAG lasers[4,9]. However, this laser capacity to replace conventional SRP treatment for chronic periodontitis is still debatable, also the Nd:YAG laser seems to be ineffective for calculus removal when a clinically suitable energy is used[30].

Moreover, in comparison to conventional mechanical instruments, lasers seem to be more effective for complete curettage of soft tissue. In fact, Gold and Vilardi[31] demonstrated the safe application of the Nd:YAG laser for removal of the pocket-lining epithelium in periodontal pockets with no negative effects as necrosis or carbonization of the underlying connective tissue *in vivo*[31]. Yukna *et al*[32] advocated the use of Nd:YAG laser in a laser-assisted new attachment procedure (LANAP) to remove the diseased soft tissue on the inner gingival surface of periodontal pockets. The authors reported that this procedure is associated with cementum-mediated new connective tissue attachment and apparent periodontal regeneration on previously diseased root surfaces in humans. The utilization of this protocol among the dental community seems to be increasing, with several case reports studies clear showing the potential of the technique, however more well controlled and independent studies are need to validate those claims.

The earliest clinical studies regarding the application

of lasers in the nonsurgical pocket treatment of periodontitis began in the early 1990s using an Nd:YAG laser. However, clinical applications of lasers in periodontal pockets began with the development of flexible optical fiber. Many clinical studies reported a strong bactericidal effect of Nd:YAG lasers in periodontal pocket. But the superiority of lasers in root planing compared to conventional therapy is till hard to prove[33]. Neill and Mellonig[34] demonstrated, in their double blinded randomized clinical study, that the use of Nd:YAG as an adjunctive treatment to conventional scaling and root planing led to a significant improvement in gingival index and bleeding on probing. But no differences in attachment level were found. In addition, greater results were found when Nd:YAG laser treatments were followed by mechanical treatments six weeks later compared to the reverse. Moreover, adding local Minocycline to Nd:YAG laser irradiation showed good improvement in pocket depth reduction, attachment gain and reduction of periodontopathic bacteria in comparison witch laser treatment alone[35].

In 2013, Qadri *et al*[30], tried to assess through a short term prospective study the effect of water-cooled pulsed Nd:YAG laser used as an adjunct to SRP compared to treatment with the laser alone. Thirty-nine patients were then equally divided into three groups. The first group received Nd:YAG laser treatments. The second group was treated with SRP alone and the third group Nd:YAG laser application immediately after SRP. Results showed a significant decrease of the probing pocket depth, gingival index and gingival crevicular fluid in group 3 compared to groups 1 and 2, in the one-week and three-month follow up. SRP treatment combined to a single application of water-cooled Nd:YAG seems to be more effective in treating periodontal inflammatory conditions. In fact, SRP mechanically disrupt the subgingival biofilm and remove calculus, whereas Nd:YAG laser therapy significantly reduces periodontopahtogenic bacteria. Furthermore, Tseng and Liew[36] suggested that the use of SRP after Nd:YAG laser treatment may be more efficient in removing root deposition.

Traumas from laser treatment are not well documented in the literature unlike ultrasonic and manual instrumentations. For this reason, Dilsiz and Sevinc[37] evaluated and compared the immediate effect of trauma after non-surgical periodontal treatment with ultrasonic and Nd:YAG laser. The study included 144 sites selected from 24 chronic periodontitis patients. Plaque index, probing depth and probing attachment level (PAL) were assessed before and 7 d after treatments. The results showed an immediate PAL loss of 0.68 mm after periodontal treatment with ultrasonic treatment, whereas, the Nd:YAG laser treatment caused no PAL loss and seems to reduce significantly the trauma from instrumentation. However, some studies report that the use of dry laser irradiation lead a significant increase in thermal energy delivered, and can cause tissue damage[38]. Water coolant associated to laser seems to reduce these negative thermal effects[39].

Recently data from a multi-center, prospective, longitudinal, clinical trial comparing four different treatments for periodontitis, the LANAP protocol utilizing pulsed-Nd:YAG laser; flap surgery using the Modified Widman technique (MWF); SRP; and coronal debridement. The authors found no statistical treatment differences between SRP, MWF, and LANAP with the exception of less post-treatment patient discomfort with LANAP compared to MWF. In addition there was greater reduction in bleeding in the LANAP™ quadrant than in the other three at both 6 and 12 mo[40].

Finally, Sjöström and Friskopp[41] observed, in their split-mouth study, an increase of 15% in the debridement time needed. The authors claim also a significant decrease in local anesthesia needed, a haemostatic effect, and less postoperative pain and swelling reported by patients.

NEGATIF EFFECT

Variation in experimental design, in laser parameters and a lack of proper controls make studies difficult to compare. In consequence, some authors suggest the use of lasers as a replacement of the conventional mechanical treatments whereas others are much more skeptical. Another problem that arises from this lack of standardized protocols is the possibility of potential negative and yet unknown effects caused by the incorrect use of the laser.

Because of its ablative capacity on mineralized tissues, some *in vitro* studies showed residual rough root surfaces after treatment with the possibility of heat cracking and cratering. Moghare Abed *et al*[42] in 2007, compared the effectiveness of subgingival scaling and root planing with Er:YAG laser and hand instrumentation *in vitro*. Their results indicated a degree of roughness in all of the laser group samples. However, very long pulses (750-1000 μs) of the Er:YAG laser left a smoother surface, in addition to its greater capacity to remove calculus. They then proposed to decrease the energy to less than 22.6 mJ at the finishing stage to obtain a complete smooth surface. The use of water coolant with laser irradiation prevents thermal side effects without compromising its efficiency. Root surfaces irradiated by Er:YAG laser combined with water coolant presented minimal affected layer with no cracks or major changes in root cementum and dentin structure which can be observed after Nd:YAG irradiation[43-45]. Indeed characteristic micro irregularities and structures[44] were reported on the root surface treated by Er:YAG laser. This micro structured surface appears to be incompatible with cell attachment[46]. In contrary, some *in vitro* studies reported that Er:YAG irradiation, at a proper energy level, seems to leave a favorable surface for fibroblast attachment compared to conventional mechanical scaling and root planing[47,48].

In spite of the potential for root surface damage during the process of calculus removal since the Er:

YAG is a hard tissue laser and the operator would not be able to visualize what is being lased, clinical data on attachment level changes when compared to SRP alone are conflicting. Some studies show slight benefit while others find no benefit. Further study is needed to determine if Er:YAG laser-assisted SRP has a real beneficial effect.

As for the Er:YAG, side negative effects as surface pitting, cracks, carbonization and melting were reported even when the Nd:YAG irradiation was parallel to the root surface[49]. Nevertheless, these alterations seem to be reversible. In fact additional root treatment such as polishing and root planing can restore root surface biocompatibility, essential for fibroblast attachment[50,51]. In addition, because of its capacity to penetrate deeply tissues, the Nd:YAG lasers can induce irreversible intrapulpal thermal damages. However the application of proper protocols seems compensate the potential harmful potential of those lasers and new researches testing different protocols are need to validate the safety and effectiveness of the utilization of Nd:YAG in periodontal treatment.

Thus, many studies tried to determine the Nd:YAG laser place in all therapeutic options in periodontics. When used alone in the nonsurgical treatment of periodontal pockets, the Nd:YAG laser showed less effectiveness for root debridement compared to conventional root planing and scaling. The use of Nd:YAG laser was then suggested as an adjunctive therapy following conventional mechanical therapy in the non surgical treatment of periodontitis.

CLINICAL RECOMMENDATION

While many trials demonstrated that the use of the laser is an effective and safe method of root planing in periodontal non-surgical treatment of chronic periodontitis. It is important to determine the place of lasers in all our treatment options.

It is clear that the use of lasers in periodontics appears to significantly reduce the intensity of pain experienced by the patient during treatment compared to conventional treatment[40,52]. The laser allows the use of less local anesthesia and a better collaboration by the patient[53], thereby facilitating the achievement of the therapeutic goals.

However in view of the results obtained in different clinical and *in vitro* studies found in the literature, it is difficult to conclude of the effectiveness or the superiority of lasers in root planing compared to conventional therapy. Indeed, some authors showed better clinical results when using laser alone[13] while others report no real benefit[21]. Clinical trial with high level of evidence is still needed to determine if the use of laser in the periodontal treatment may one day replace conventional surfacing and root planing.

Furthermore some authors claim the safe handling of this tool, always well tolerated and without damage to the surrounding tissue[39,54]. The use of lasers leaves also a slightly porous surface in favor of fibrin attachment, thus improving the fixation of the blood clot[4]. Other *in vitro* studies, however, mention the presence of a thermal effect on the surrounding tissue in addition to cracks on root surfaces, observed microscopically, weakening then the surrounding tissue[11,52,53].

In addition, some studies were focused on the use of laser as adjuvant to conventional treatment of chronic periodontitis. The clinical trial of Qadri *et al*[39] in 2010 has shown in short and long term, a significant positive effect of lasers coupled to manual and ultrasonic instruments. While other authors, such as Slot *et al*[5], had found no improvement compared to conventional therapy. It is again difficult to demonstrate a real benefit to the use of the laser as an adjunct to manual instruments and ultrasonic.

Finally the use of laser is part of a non-surgical treatment of periodontal disease process, that must respect very specific steps, including the assessment of the patient's medical status, periodontal diagnosis and the development of a treatment plan, patient information and the collection of informed consent, application processing procedures such patient education (oral hygiene, fight against risk factors including tobacco and stress, taking additional charge of systemic diseases such as diabetes) and patient follow-up.

CONCLUSION

Despite of all the potential beneficial effect of lasers in periodontics, the ability to replace or even add on to our conventional periodontal treatment is still doubtful. Further studies are needed to determine laser effectiveness for root scaling and planing, calculus removal, bacterial decontamination and specially, randomized clinical trials performed by independent researches are essential to demonstrated the real role that lasers can play in the management of ours periodontal patients.

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MINIREVIEWS

Retrieving dental instruments through endoscopy: A literature review

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Abstract

Clinical accidents involving dental instruments and materials inside the oral cavity are reported in the medical literature. Specifically, ingestion and aspiration of foreign bodies have greater prevalence in the routine of medicine and dentistry. Despite being less harmful than aspirations, the accidental ingestion of dental instruments does not always culminate in favorable prognoses. Mostly, complex conditions require medical intervention through endoscopy or surgical approaches. The present research aims to review the literature pointing out the specialties of dentistry most involved with accidental ingestion of dental instruments, highlighting the important role of endoscopy for accurately locating and retrieving foreign bodies. Prosthodontics, operative dentistry, orthodontics, and maxillofacial surgery arose as the specialties in which these accidents are more prevalent. Based on that, general dentists and specialists must be aware for the essential care to avoid such clinical accidents, as well as to know the available tools, such as endoscopy, to overcome these situations in the routine of dentistry.

Key words: Endoscopy; Accidents; Dental instruments; Foreign bodies

Core tip: An effort should be made to avoid breaking dental instruments by preventing their over-use and over-stress. Rubber dams should always be used for hygiene control and to prevent patients from swallowing instruments. When the use of a rubber dam is not

possible, dental instruments should be secured with wires to help avoid and accomplish retrieval. All parts of broken instruments must be retrieved immediately following breakage. If ingested broken instrument parts cannot be retrieved, the patient should be referred for a medical opinion.

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INTRODUCTION

The acute perfectionism of dentistry often makes it necessary to use small instruments for dental procedures that require precise intervention, such as crown preparation for fixed prosthodontics, root canal procedures, and the bonding of orthodontic brackets. Consequently, there is always a risk of an instrument accidentally breaking or falling into the throat of patients and becoming ingested as a foreign body[1]. Following an accidental ingestion, the prognoses strongly depend on the morphology and anatomic location of the foreign body[2]. Favorable prognoses mostly require clinical and radiographic follow up of the foreign body inside the digestive tract[2]. Whereas, unfavorable prognoses often involve more invasive approaches, such as endoscopy[3] and surgical retrieval[4]. After an accidental aspiration, the airways are often compromised resulting in unfavorable prognoses. In this context, medical interventions, such as bronchoscopy[5] and surgical access[6] can become necessary. Considering that some fields of dentistry are more susceptible to ingestion accidents, the present research aimed to review the current literature to identify the dental specialties most involved with such accidents, and highlighting the important role of endoscopy for accurately locating and retrieving foreign bodies from the digestive tract.

EPIDEMIOLOGY

Hisanaga *et al*[1], 2014, retrospectively analized 40 cases of accidental ingestion and the aspiration of foreing bodies that occurred during dental treatment over 4 years in hospital dental clinics. The accidental ingestation occurred most frequently as part of prosthodontic and operative dental treatments (50%), followed by orthodontics (15%) and maxillofacial surgery (7.5%). Approximately 97% of these cases (n = 39) involved the accidental ingestion of dental instruments, of which only one instrument required endoscopic retrieval. The remaining ingestion accidents did not require clinical intervention.

A retrospective investigation of ingestion accidents over 10 years within a dental school was also conducted by Tiwana *et al*[7]. Twenty-five cases, out of the twenty-six, involved accidental ingestion. None of the cases required endoscopic or surgical retrieval. Similar to the previous study, prosthodontics and operative dentistry were involved in 50% of the dental instrument ingestation cases. Maxillofacial surgery contributed 19.2% of the ingestion cases, and orthodontics contributed 11.5%, of the ingestion cases.

A study by Obinata *et al*[8], identified 23 accidents over 5 years where patients had ingested dental instruments. Fifty-two percent of the accidents (n = 12) occurred during prosthodontic procedures, while 13% of the accidents occurred during maxillofacial surgery and 8.7% of the accidents occurred during orthodontics. Only, three cases required endoscopic retrieval of the foreign bodies.

A study by Susini *et al*[9], 2007, analyzed the cases of 464 patients who had accidentally ingested or aspirated dental instruments that were reported to insurance companies. The type and number of dental instruments reported within the study indicated that patients having Prosthodontic treatment were most likely to suffer an accidental ingestion, and accounted for 45% of all the cases. The other dental specialties: Operative dentistry (33.6%) and endodontics (18.1%) also had a high incidence of patients suffering an accidental ingestion of dental instruments.

DENTAL INSTRUMENTS AND ENDOSCOPY

In the medical and dental literature, several studies have reported the accidental ingestion of dental instruments used in prosthodontics and operative dentistry, such as metallic cores[10], prosthetic crowns, dental drills[11] and even removable prostheses. Despite being uncommon, the accidental ingestion of entire prostheses were reported during traffic accidents, meals[12] and sleep[13]. Both the ingestion in the daily routine and the ingestion during dental treatment culminate with similar prognosis, making potentially necessary endoscopic retrieval.

In oral implantology there are reports of small screws being ingested by patients[14], while in endodontics files and clamps are the most ingested instruments by patients[15-20]. In orthodontics, there are cases where patients had ingested entire and fragmented removable appliances[21,22], as well as activation keys[23,24], orthodontic bands[25] and orthodontic wires[26]. Several other instruments, used in general practice, were also found to be accidentally ingested by patients receiving routine dental treatments. Specifically, these instruments were ingested: (1) due to patients' biting and swallowing reactions in response to a dental instrument, where the instrument ends up being dropped into their mouth or throat and swallowed before the dentist can retrieve it; or (2) due to a professional accident: Where the instrument broke and fell into the patients mouth or throat during clinical procedures. Oncel *et al*[27], 2012,

illustrates the first situation reporting a case of accidental ingestion of intraoral mirror that fractured after a patient suddenly clenched his teeth. The mirror was retrieved through endoscopy after reaching the esophagus. On the other hand, cases reporting the lack of instrumental inspection to ensure there are no broken pieces was investigated by Sankar[28] and by Tsitrou *et al*[29]. Both authors reported cases of endoscopic retrieval of triple syringe tips, measuring 12 cm and 9 cm of length respectively, unscrewed during procedures for dental restoration.

DISCUSSION

Dentists have a critical role in preventing the breakage of instruments by preventing their over-use and over-stress. Rubber dams should always be used for hygiene control and to prevent patients from swallowing instruments. When the use of a rubber dam is not possible, dental instruments should be secured with wires or floss to help avoid and accomplish retrieval[3]. By following these safety measures the ingestion of dental instruments by patients can be prevented. If the safety measures fail, all parts of broken instruments must be retrieved immediately by the dentist following breakage. If any ingested broken instrument parts cannot be retrieved, the patient should be referred for a medical opinion.

Immediately following the instrument ingestion by a patient, the first priority is to attempt to retrieve the instrument to prevent it from blocking the patient's airway. If the instrument cannot be retrieved, it is essential to halt dental treatment, remove rubber dams and devices from the mouth, and to monitor the patient's vital signs, followed by the observation of continuous coughing, voice alterations, discomfort, and other clinical signs and symptoms that may aid the differentiation between accidental ingestion and aspiration[2]. If a patient has trouble breathing or is losing consciousness, the emergency services must be called to attend to the life-threatening condition of the patient. If a patient's condition is not life-threatening they must be referred for a medical exam. If the instrument is not visible a radiographic inspection of thorax and abdomen must be performed[2,20].

If dental instruments reach the digestive tract, they tend to be naturally eliminated without major complications[10,11]. However, instruments with larger dimensions, such as triple syringe tips, prostheses, and dental mirrors may not be eliminated, becoming stuck along the esophagus and stomach, making it necessary to perform an endoscopic intervention[2,16,25]. Endoscopy may also be needed to retrieve instruments with a complex morphology, such as endodontic files and dental drills, which can perforate and adhere to the mucosa of digestive tract[15,19,24]. On the other hand, surgical approaches become indicated when the instruments become stuck in anatomic positions not reachable through endoscopy[13,24]. Consequently, major damages to the mucosa, digestive tract, and systemic health can be avoided. Additional limitations for the use of endoscopy are the time elapsed from the accident and the size of foreign body. Specifically, small foreign bodies ingested a long time ago may reach the intestine and not be visible through endoscopy[14,16].

CONCLUSION

An effort should be made to avoid breaking dental instruments by preventing their over-use and over-stress. Rubber dams should always be used for hygiene control and to prevent patients from swallowing instruments. When the use of a rubber dam is not possible, dental instruments should be secured with wires to help avoid and accomplish retrieval. All parts of broken instruments must be retrieved immediately following breakage. If ingested broken instrument parts cannot be retrieved, the patient should be referred for a medical opinion.

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CASE REPORT

Autotransplantation of a premolar to the maxillary anterior region in young children - how long should the donor root be? A case report

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Author contributions: Both authors contributed to the surgical and dental treatment, writing and revision of the manuscript.

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Abstract

Autotransplantation of premolars to anterior region after incisor loss due to trauma is accepted as the best restoration procedure with very long follow-ups. There are two main protocols: Premolars with only two thirds of the root or premolars with complete root development. Premolars with two thirds of the root completed remain vital and show complete pulp obliteration while premolars with closed apex require root canal treatment. The problem arises when the child is very young and the root of the donor premolar is developed for only one third. This case report describes the outcome of an autotransplantation of a lower first premolar with only a third of developed root to the anterior region. The donor tooth was extracted with his follicle and placed instead of tooth No. 21. For the first month esthetics was restored with a glass-fibers ribbon attached to tooth No. 11 and composite material. After a month, the crown erupted and was reshaped to mimic an incisor with composite. Orthodontic movement was performed after 5 mo, in order to alleviate the gingival contour. The final restoration was performed after 15 mo. Follow up showed full root development with normal mobility, continuous periodontal ligament and complete pulp obliteration. A multidisciplinary approach and meticulous preparation are necessary for a positive result in autotransplantation of premolars with only a third of root development to the anterior region and this case report show that this method can be performed in very young children.

Key words: Autotransplantation; Dental trauma; Donor tooth root length

Core tip: Autotransplantation of a premolar to the anterior region has a success rate of more than 90% if the donor tooth has a developing root and pulp healing occurs. The only negative outcome is total obliteration of the pulp. This case report describe an autotransplantation of a lower first premolar with only a third of root length to the incisor area after a dental trauma that caused root resorption of a permanent upper left incisor, in a 8-year-old boy. Follow up of 15 mo showed full root growth and periodontal healing with normal mobility and obliteration of the pulp. The crown was restored using composite material to resemble the adjacent incisor. This case report shows that even with very short donor root length, autotransplantation to the anterior region can be performed in young children.

Zilberman U, Zagury A. Autotransplantation of a premolar to the maxillary anterior region in young children - how long should the donor root be? A case report. *World J Stomatol* 2015; 4(4): 141-145 Available from: URL: http://www.wjgnet.com/2218-6263/full/v4/i4/141.htm DOI: http://dx.doi.org/10.5321/wjs.v4.i4.141

INTRODUCTION

The method of autotransplantation of premolars to maxillary anterior region in order to replace severely traumatized permanent incisors is known for more than 40 years[1,2]. There are two main protocols regarding the stage of root development of the donor premolars - full root development[3] or half to two thirds root length[1,4]. The survival rate of premolars with complete root formation was 100% after 5 years and 72.7% after 10 years[3] and the survival rate of premolars with half to two-thirds root formation was 100% after 6-78 mo follow-up[5]. and the success rate was 91.3%. Pulp healing of the autotransplanted premolar is related to root development. For premolars with half to two thirds root length pulp healing was observed in 96% of the premolars after 6 mo follow-up[5] while for premolars with complete root length pulp healing was observed in only 15%[5], implicating that root canal treatment is necessary after autotransplantation in premolars with full root length and closed apex. The major sign for pulp healing was obliteration of the pulp and normal periodontal ligament[5]. The problem is that the minimal age for autotransplantation should be between 9-10 years, when the donor premolar has half-two thirds of root length, while for root length of less than half absence of further root development was observed[6]. But sometimes the autotransplantation have to be performed earlier. This case report describe a successful autotransplantation of a lower first premolar with only a third of root length for an upper left incisor in an 8-year-old boy with a follow-up of 15 mo.

CASE REPORT

OB, a 7-year-old boy arrived to the pediatric dental unit at Barzilai medical center two days after a head trauma at school. The avulsed upper left central incisor was kept in dry condition and was re-implanted 3 h after the trauma at a different hospital. The tooth was splinted to the adjacent teeth with composite (Figure 1). Two weeks after the trauma, the splint was removed and the pulp canal was filled with calcium hydroxide paste. At follow-up visit after 3 mo the root was resorbed and mobility of 2 mm was observed. A split with glass-fibers ribbon was performed (Figures 2 and 3). After 12 mo and four more traumas to the tooth, the option of autotransplantation was described to the child and the parents. Under general anesthesia, tooth No. 21 was extracted (Figure 4), and germ of tooth No. 34 was exposed from the buccal aspect, without damaging tooth No. 74 (Figure 5). The premolar was extracted with the full follicle and reimplanted rotated and infra-occluded at the site of tooth No. 21, and kept in place with cross-over sutures (Figures 6 and 7). For esthetic reasons tooth No. 21 was restored using fiber-glass ribbon attached to tooth No. 11 and composite material (Figure 8). Ten days after the auto-transplantation, the sutures were removed. A month after the surgery the composite and the glass-fiber ribbon were removed and the crown of tooth No. 21 was reconstructed on top of the erupted premolar and splinted to tooth No. 11 with glass-fibers ribbon (Figure 9). Two months after surgery root development was observed. Five months after surgery, forced eruption of the autotransplanted tooth was performed in order to bring the gingival margin at the same height as tooth No. 11. The brackets were removed 4 mo later (Figure 10). At the last follow-up visit, 15 mo after the surgery, the root was completed, the mobility was similar to tooth No. 11, and the pulp was obliterated completely. A new composite restoration was performed for better esthetic (Figures 11 and 12).

DISCUSSION

Autotransplantation of premolars to the anterior region subsequent to trauma have several advantages in comparison to other modalities, especially for young children. A tooth transplant keeps the alveolar margin at optimal height and facilitates continuous growth of the maxillary complex. It also keeps the bucco-palatal dimension of the alveolar bone in the very esthetic region. The transplanted tooth allows also orthodontic movements, necessary for gingival margin reconstruction. For premolars with half to three forth root formation, pulp and periodontal healing was reported in 80% of the cases after 14 years[7]. Complete pulp obliteration, followed by continuous root formation was

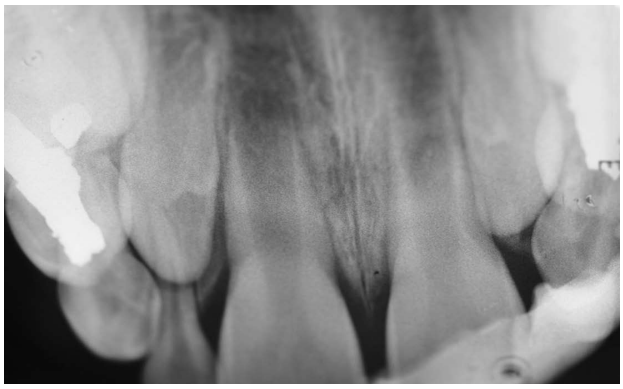

Figure 1 Two days after the avulsion and re-implantation of tooth number 21. A composite splint is in place (November 2012).

Figure 2 Three months after trauma. Note complete root resorption of tooth number 21 (December 2012).

Figure 3 Splint with glass-fibers ribbon as temporary treatment till the surgery.

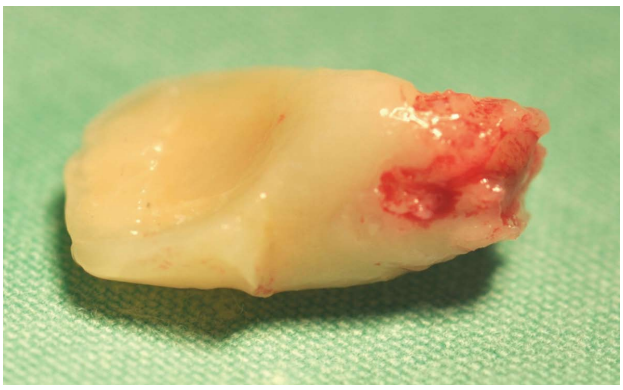

Figure 4 Tooth number 21 after extraction. Note the resorption lacunae.

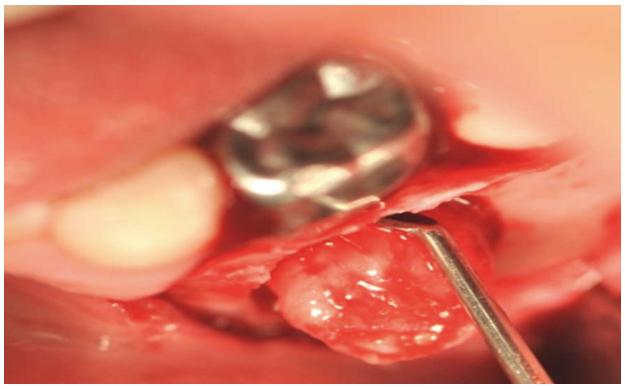

Figure 5 Exposure of the donor germ, tooth number 34 from the buccal, while tooth number 74 covered by a stainless steel crown remained stable and functioning in the mouth.

Figure 6 Donor tooth extracted with its entire follicle, before transplantation.

positively related to autotransplant viability. Clinical variables for transplanted premolars were found to be similar to the natural incisors when the mean age of surgery was 11 years[8]. A slight increased mobility was observed but the crown-root ratio and the distance between the CEJ and alveolar bone crest was similar to the adjacent incisor after a mean follow-up period of 4 years[8]. The size of the apical foramen, as long as the apex is not closed, seems not to be a very important factor for successful revascularization and ingrowth of new tissue after transplantation in dogs[9]. Resorption of the root was higher in reimplanted teeth with more than three-quarters or apex-closed stages. The authors described that teeth with root length of less than one-half had a higher probability of having arrested root growth, but no description was given to the type of the donor tooth, and the higher failure rate was observed during the first year after transplantation. Other esthetic and restorative options for missing permanent upper centrals at young age include removable flipper with acrylic tooth or orthodontic device with bands on the molars and acrylic tooth on orthodontic wire, till

Figure 7 Donor tooth transplanted to the anterior region instead of tooth number 21.

Figure 8 Final X-ray after autotransplantation and fiber-glass and composite bridge.

Figure 9 Crown restoration of the donor tooth after a month and splint to tooth number 11.

Figure 10 End of the orthodontic stage.

Figure 11 Follow up 15 mo after autotransplantation. Note root development, pulp obliteration and continuous periodontal ligament.

Figure 12 Clinical views of the 15 mo and last composite restoration.

after the puberty growth is completed and an intra-osseous implant can be placed. The main problems with the removable or orthodontic appliances are the accumulation of plaque, the compliance of the child and his family and the possibility of losing the removable appliance or dislodgement of the orthodontic bands. Moreover, the alveolar bone will be resorbed till the insertion of the implant causing a marked discrepancy in gingival contour between the implant and the adjacent incisor. Auto-transplantation results in favorable growth of the alveolar bone and reconstruction of the gingival contour. Successful tooth transplantation offers almost ideal esthetics, arch form and dentofacial development. A transplanted tooth diminishes the extent of resorption of newly formed alveolar bone and provides functional stimulation. Periodontal healing is usually completed after 8 wk and is affected mainly by infection at the host site due to improper postoperative control of supragingival plaque.

The case report showed that for young patients, premolars with only one third of root length can be considered suitable for autotransplantation in the anterior

region after loss of incisors due to trauma. Fifteen months follow-up showed complete root length formation, obliteration of the pulp, favorable crown/root ratio and mobility similar to the adjacent incisor. Orthodontic movement was performed in order to reconstruct a similar gingival margin and the reconstruction of the crown was performed using composite material. The final clinical result was highly accepted by both the patient and the parents. More follow-up is needed, but this case shows that autotransplantation of premolars to the anterior area can be performed even in young children.

COMMENTS

Case characteristics

An 8-year-old boy with no significant medical history, with an upper left central incisor with total root resorption after avulsion and unsuccessful re-implantation.

Clinical diagnosis

Esthetic replacement of the lost upper permanent incisor is needed.

Treatment

Removable orthodontic appliance with an acrylic tooth, fixed orthodontic appliance with an acrylic tooth, autotransplantation of a premolar, till implant insertion and crown restoration can be performed. Autotransplantation of a lower first premolar with only a third of root length was performed.

Related reports

Success of autotransplantation of premolars to upper anterior region was related to the length of the donor tooth root. Better success rate were observed with root length of half-two thirds.

Experiences and lessons

Autotransplantation of a premolar to replace a lost upper permanent incisor can be performed very early when the root length is only a third. This method results in a very esthetic and long lasting restoration that can be performed in very young children after dental trauma.

Peer-review

Excellent written, the weaknesses are that the method is common knowledge with very high successful rate but this case report remind the audience of this possibility to restore missing permanent incisor after dental trauma.

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