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DENTAL IMPLANTS IN PATIENTS WHO UNDERWENT RADIOTHERAPY IN THE HEAD AND NECK: LITERATURE REVIEW

IMPLANTES DENTÁRIOS EM PACIENTES SUBMETIDOS À RADIOTERAPIA EM REGIÃO DE CABEÇA E PESCOÇO: REVISÃO DE LITERATURA

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ABSTRACT

The patients' rehabilitation who underwent radiotherapeutic treatment in the head and neck is still a challenge to dental implantation. The purpose of the current article is to discuss the installation of dental implants in patients who underwent radiotherapeutic treatment in the head and neck. The study of some literature was held considering revisions and original articles publications from 2002 to 2020. The research included the keywords: implants, osteoradionecrosis, neoplasms in oral cavity, hyperbaric oxygen therapy, laser therapy, ozone therapy e dental implants in irradiated bones. Databases: PubMed, SciELO e Bireme. The criteria for the article's inclusion in the study were: an approach about the oral malignant neoplasm, the sequela treatment which may be formed and the implant installation in bones which underwent irradiation. The analysis was developed considering specific information from each article related to the language, publication year, research type and data results, in which the most of the cases have been positive to implants installation taking into consideration some factors. Taking into account the changes in the treatment concepts at first, then the advance of odontology in using the three-dimensional plans and surgical guides and, the evolution of the improvement in the titanium surface and the accomplishment of the minimum time of 12 months in the end of irradiation, it is possible to obtain a predictability in prosthetic treatment of patients undergoing radiotherapy in the head and neck region.

Keywords: Dental Implants in Irradiated Bones. Implants. Oral Cavity Neoplasia. Osteoradionecrosis.

RESUMO

A reabilitação de pacientes que passaram por tratamento radioterápico em região de cabeça e pescoço ainda é um desafio para a implantodontia. O presente trabalho tem como objetivo discutir a instalação de implantes dentários em pacientes submetidos a tratamento radioterápico na região de cabeça e pescoço. Trata-se de um estudo de revisão de literatura, considerando as publicações de artigos originais e de revisão, do ano de 2002 a 2020. A pesquisa constou das seguintes palavras-chave: *implants*, *osteoradionecrosis*, *neoplasms in oral cavity*, *hyperbaric oxygen therapy*, *laser therapy*, *ozone therapy* e *dental implants in irradiated bones*. Nas bases de dados: PubMed, SciELO e Bireme. Os critérios de inclusão de artigos no estudo foram: abordar sobre neoplasias orais, o tratamento das sequelas que podem ser geradas e a instalação de implantes em ossos que sofreram irradiação. A análise foi realizada considerando informações específicas de cada artigo relacionadas ao idioma, ano de publicação, tipo de pesquisa e o resultado dos dados, que na maioria dos casos mostrou-se positivo à instalação de implantes caso se considerem alguns fatores. Com a mudança nos conceitos de tratamento, o avanço da odontologia ao utilizar o planejamento tridimensional e guias cirúrgicos, a evolução do aprimoramento da superfície do titânio e o cumprimento do tempo mínimo de 12 meses do fim da irradiação, é possível obter-se uma previsibilidade no tratamento protético de pacientes submetidos à radioterapia em região de cabeça e pescoço.

Palavras-chave: Implantes. Implante Dentário em Osso Irradiado. Neoplasia em Cavidade Oral. Osteorradionecrose.

INTRODUCTION

The need to replace tooth loss practically goes hand in hand with human history. There are historical reports of primitive implants in ancient civilizations, such as those that lived in the Neolithic period, and in Egyptian civilization (CRUZ *et al.*, 2009). However, satisfactory results were only obtained from 1965, with the innovative research line of Prof. P. I. Brånemark, who introduced the concepts of osseointegration (OLIVEIRA *et al*., 2013).

Osseointegration is defined as the direct functional and structural connection between the living and organized bone tissue and the surface of an implant under functional load; this technique presents predictable, reproducible and stable results over time (ZAVANELLI *et al.*, 2011).

Nevertheless, the rehabilitation of patients undergoing radiotherapy in the head and neck is still a challenge for implantology (VASCONCELLOS *et al.*, 2004). According to a consensus published in 1988, radiotherapy was considered a contraindication for the installation of implants, because of the adverse reactions generated by irradiation, such as osteoradionecrosis, mainly in dosages above 50 Gy (OLIVEIRA *et al*., 2013).

However, from the elucidation of new studies in line with the addition of a joint therapy, the osseointegration process seems to increase significantly, causing the success rate to be above 90% (ZAVANELLI *et al.*, 2011).

This study aimed to discuss the installation of dental implants in patients undergoing radiotherapy treatment in the head and neck region.

METHODOLOGY

This was a literature review study, considering the publications of original and review articles, from 2002 to 2020. The research included the following keywords: implants, osteoradionecrosis, neoplasms in oral cavity, hyperbaric oxygen therapy, laser therapy, ozone therapy and dental implants in irradiated bones, in the databases: PubMed, SciELO and Bireme. Inclusion criteria for articles in the study: addressing oral neoplasms, the treatment of sequelae that can be generated and the installation of implants in bones undergoing irradiation. Dissertations, theses, abstracts, incomplete or unavailable journals and those published before 2002 were excluded from the selection.

The analysis and selection of the material considered the specific information of each article: related to the language (articles in Portuguese, English and Spanish), publication year (studies conducted between 2002 and 2020), type of research (randomized studies, systematic reviews, literature reviews and experimental research), and data results (studies with significant numbers of participants and executed in well-known centers/institutions). In most cases, this result was positive for the installation of implants if some factors are considered, such as the interval between the end of the radiotherapy treatment and the installation of the implant, the location of the implant installation and the habits and periodontal health of the patients.

DEVELOPMENT

Oral Cavity Neoplasms

According to the estimate of the Ministry of Health (INCA, 2019), for each year of the 2020-2022 triennium, 11,180 new cases of cancer in the oral cavity will be registered in men, and 4,010 in women; this type being the fifth most frequent in the Southeast, Central West and Northeast regions. In addition, neoplasms in the oral cavity are the fifth most common cancer in men and the thirteenth most frequent in women, among all types of cancers, and the cancer that most affects the head and neck region worldwide is squamous cell carcinoma (DI CARLO *et al.*, 2019).

The main risk factors are alcoholism, smoking and HPV infections. When smoking and alcoholism are combined, there is a synergism and the risk increases even more (INCA, 2015). In general, treatment is performed through surgery, radiotherapy and/or chemotherapy (BRENER *et al*., 2007).

There are two forms of radiotherapy application: teletherapy and brachytherapy. The choice of one of these depends on the type of cancer and the depth in which it is found (FREITAS *et al.*, 2011).

In teletherapy, the radiation source is emitted by the equipment at a variable distance, from 80 to 100 cm, from the patient's skin and is directed to the tumor. In brachytherapy, the radioactive isotope emitting gamma rays is placed in direct contact with the tumor, and is often intracavitary or interstitial. It presents an advantage in relation to the other form, since the tumor can be irradiated with high doses, without affecting the surrounding organs and structures (FREITAS *et al*., 2011).

Osteoradionecrosis

Osteoradionecrosis (ORN) is one of the most serious sequelae of radiotherapy and occurs in 7% cases. It is characterized as an ischemic necrosis of the bone, caused by the reduction of the vascularization potential of the tissue by radiation. In bone, there is an imbalance between osteoblastic and osteoclastic activities. Osteoblasts are more radiosensitive than osteoclasts, thus, there is an increase in their cell lysis, due to irradiation and, consequently, the bone matrix formation stops, so that mineralization does not occur. The dose and field where the irradiation was performed is one of the most relevant risk factors for ORN. In addition, its progression usually leads to pathological fracture of the affected bone (VASCONCELLOS *et al.*, 2004; GRIMALDI *et al.*, 2005; MONTEIRO *et al*., 2005; RAGGIO *et al.*, 2018).

According to Ragghianti *et al.* (2002), two peaks of higher ORN incidence have been identified: the first peak occurs during the first year after treatment, and the second peak between the second and fifth year after the end of radiotherapy.

Its signs and symptoms can manifest in several ways, such as: trismus, pain at the site, halitosis, bone exposure, secretion drainage and intra or extraoral fistulas, however, half of the cases are asymptomatic and are diagnosed by the presence of an area with exposure of necrotic bone (MONTEIRO *et al.*, 2005; ALDUNATE *et al.*, 2010). According to Aldunate *et al*. (2010), imaging tests are important and should always be performed, as they enable the identification of bone lesions suggestive of necrosis. Radiological changes are of late onset, as they require bone demineralization of 12% to 30% in order to be visualized, making the cone beam computed tomography the exam of choice, as it provides more reliable data on the extent of involvement. bone and collaborates for surgical planning.

Prevention is the most important factor to prevent the development of ORN, and the execution plan should be carried out with the objective of eliminating outbreaks of infection and traumatic elements, reducing microbial activity, in addition to covering oral hygiene instructions and nutritional recommendations (RAGGHIANTI *et al*., 2002).

According to Monteiro (2005), the treatment can be carried out in a more conservative way, with the irrigation of the affected area (with saline solutions, chlorhexidine, hydrogen peroxide or povidone iodine), curettage of the lesion, elimination of small sequestrum, with or without the use of hyperbaric oxygenation (HO), or more invasively, when using resources such as osteotomies and resections of the affected tissue.

The use of HO is still widely discussed, however, several authors, Moura *et al*. (2003), Grimaldi *et al*. (2005), Monteiro *et al*. (2005) e Morais *et al*. (2008) recommend its use as adjunctive therapy.

Other auxiliary therapies can also be used, such as ozone therapy and laser therapy. Ozone therapy has been gaining more and more space in dentistry, being an excellent bactericide, fungicide and virucide; in addition to promoting tissue oxygenation and stimulating the immune

response. The use of low-intensity lasers has analgesic effects and also reduces the effects of radiation therapy on irradiated bone (EL-MAGHRABY *et al*., 2013; BATINJAN *et al*., 2014).

Dental Implants in Irradiated Patients

The treatment of patients affected by oral neoplasms should not be directed only to cure the malignancy, but should be associated with the maintenance of the stomatognathic system in its entirety. Prosthetic rehabilitation significantly improves the patient's quality of life, as it restores phonation, stable occlusion and self-esteem (BARROWMAN *et al*., 2011).

The success of the procedure is directly influenced by factors such as the irradiation dose, the location, the shape of the implant to be installed, periodontal health and habits of the patients, the need for bone grafts, the time between the end of the radiotherapy treatment and implant installation (CHAMBRONE *et al*., 2013; SCHIEGNITZ *et al*., 2014; POMPA *et al*., 2015; CHRCANOVIC *et al*., 2016; WU *et al*., 2016; DI CARLO *et al.*, 2019).

The irradiation dose is the determining factor for the prognosis of the case. Studies show that doses below 20 Gy can cause damage to salivary glands; doses below 50 Gy can cause necrosis in soft tissues, while doses above 50 Gy increase the risk of osteoradionecrosis and decrease the healing capacity (POMPA *et al*., 2015).

Several authors like Schiegnitz *et al*. (2014), Pompa *et al*. (2015), Chrcanovic *et al*. (2016) e Wu *et al*. (2016) point to the mandible as the most favorable site for implant installation when compared to the maxilla. The risk of failure of the implant in the maxilla can be greater than 400% (CHAMBRONE *et al*., 2013).

The shape of the implant chosen also influences the result. The chemical treatment of titanium and the topography of these are significant for the osseointegration process. The infinity of modifications that exist in the surface treatment alters its chemical and physical properties, thereby increasing the success rate when compared to smooth implants (CHAMBRONE *et al*., 2013; CHRCANOVIC *et al*., 2016; WU *et al*., 2016).

The unsatisfactory oral hygiene of patients acts adversely towards osseointegration, given that, with radiotherapy, salivary glands are extensively affected, so that there is a reduction in salivary flow, thus, changes in the microflora of the oral cavity occur, which favors a rapid accumulation of biofilm and infections, which can be aggravated by the use of alcoholic beverages, cigarettes and steroidal medications (BARROWMAN *et al*., 2011; CHRCANOVIC *et al*., 2016).

The need for bone grafts in irradiated bone is a negative prognosis; if necessary, the autogenous graft, harvested from an area that has not suffered the effects of irradiation (such as the iliac crest, fibula and rib), is the best option (BARROWMAN *et al*., 2011; POMPA *et al*., 2015; CHRCANOVIC *et al*., 2016).

The periodontium around the implant is extremely important for its survival. Evaluations of soft tissue grafts are rare, however, grafting with upper thigh tissues has shown promise (SCHIEGNITZ *et al*., 2014).

The time between the end of the radiotherapy treatment and the installation of the implant must be observed with caution. Most studies on this aspect suggest that there are no statistical differences for the installation of the implant between the 6th and 12th month of the post-radiotherapy period; however, installation before the 6th month is not indicated, since the failure rate in the period of 0-6 months increases by 34% (CLAUDY *et al*., 2015; POMPA *et al*., 2015; DI CARLO *et al.*, 2019).

Rehabilitation after any neoplasm treatment, whether by surgical, radiotherapy, chemotherapy, or even a combination of these methods, can be challenging. However, the installation of prostheses on implants has been shown to considerably improve the quality of life of patients, which reinforces the importance of adequate dental rehabilitation, with a minimal negative impact on these individuals, using appropriate techniques, or a specific combination of these, to reduce the general recovery time (ALBERGA *et al.*, 2020; PATEL, 2020).

The high failure rates, found by Chambrone *et al.* (2013), of implants installed in the maxilla, can be justified by Pompa *et al.* (2015), Schiegnitz *et al.* (2015) and Wu *et al.* (2016), since, most of the studied implants were installed in the mandible; by the bone difference between the two bones. This because the mandible has a higher bone density, providing better primary stability; and the incidence of radiation in the mandible is lower, since, in most radiotherapy treatments, the region of the mandibular symphysis is not affected, which allows greater predictability of the treatment.

Another point refers to oral hygiene, which should be rigorously evaluated. Instructions for brushing and flossing should be given to the patient; factors such as old age, other diseases and motor disabilities can lead to poor oral hygiene; it should also be considered that irradiated patients are more susceptible to peri-implantitis. Therefore, to motivate them to perform a good brushing followed by the use of dental floss, as well as to plan a prosthesis that is easy to be sanitized, that does not have an occlusal overload on the implant, associated with reduced alcohol intake and smoking cessation, long-term success rates increase (BARROWMAN *et al*., 2011; CHAMBRONE *et al*., 2013; CHRCANOVIC *et al*., 2016).

Failure rates increase in the installation of the implant during the period of 0-6 months after the end of radiotherapy, because according to Claudy *et al.* (2015), neovascularization and new bone formation are not yet complete; furthermore, studies have shown that tumor recurrence is more frequent between the 8th and 12th months after surgery. Thus, the dentist must wait at least 12 months for implant installation (CHRCANOVIC *et al*., 2016).

HO is recommended by several authors as a joint therapy, which report good results with the technique (GRIMALDI *et al*., 2005; MONTEIRO *et al*., 2005; MORAIS *et al*., 2008; ALDUNATE *et al*., 2010). However, its use has been widely discussed and its results quite controversial. Furthermore, more recent studies suggest that the treatment entails a high cost to the patient, provides discomfort, is not widely available and is not indicated for claustrophobics. Thus, there are no statistically significant differences in efficacy that justify its use (BARROWMAN *et al*., 2011; CHAMBRONE *et al*., 2013; SCHIEGNITZ *et al*., 2014; CLAUDY *et al*., 2015; CHRCANOVIC *et al*., 2016; RICE *et al*., 2016; WU *et al*., 2016).

Based on this fact, ozone therapy has stood out as an alternative for the treatment of ORN, achieving satisfactory results and long-term injury control (FERREIRA *et al*., 2013; BATINJAN *et al*., 2014; VESCOVI *et al*., 2014).

CO_2 laser has been widely used in several studies. Laser therapy, in addition to being able to accelerate osseointegration and soft tissue healing, is an excellent ally against peri-implantitis, in a way that reduces bacterial microflora, thereby reducing the aggression of pathological agents on the periodontium (HESSLING *et al*., 2015; NOBA *et al*., 2018). Ribeiro *et al*. (2018) reported immediate results after the initial sessions.

CONCLUSION

It is a fact that irradiation negatively affects the success rate of dental implants. However, the change in the concepts of cancer treatment, combined with the advancement of dentistry in using three-dimensional planning and surgical guides, the evolution of the improvement of the titanium surface and the compliance with the minimum time of 12 months from the end of irradiation, it is possible to predict the prosthetic treatment, as well as a survival of implants, of an average of 90%, in patients undergoing radiotherapy in the head and neck. In this way, it is possible to promote an increase in self-esteem and an improvement in the functionality of the stomatognathic system.

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