



## Can the Use of Antibiotics interfere with the Success of Dental Osseointegrated Implants in Diabetic Patients?

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### ABSTRACT

**Aim:** The present review aims to discuss the last 10 years published data on the topic of the use of osseointegrated implants in diabetic subjects, particularly regarding the influence of antibiotics administration in the perioperative period.

**Background:** In the last decades, oral rehabilitation significantly has evolved particularly with the use of osseointegrated implants. Increased life expectation of population is reflecting in a greater number of diabetic patients who might require dental osseointegrated implants rehabilitation. Diabetes was considered for a long time as a contraindication for oral implant placement. In this context, the use of antibiotics is still a controversial factor when we correlate it to implant success rate.

**Review results:** Although 228 articles were initially selected for evaluation of proposed criteria, only 16 articles were considered valid. Among the 16 selected articles, only six articles represented clinical research that discussed the influence of the antibiotic in the success of osseointegration of dental implants in diabetic subjects. Five were retrospective studies and one a prospective research.

**Conclusion:** Data favors the use of antibiotics without significant side effects but clinical investigations of the need of prophylaxis antibiotic or therapeutic antibiotics are still scarce. The lack of adequate methodology is one of the main problems of the current articles. It is important to emphasize that studies should present detailed methodology in order to allow reproducibility.

**Clinical significance:** Permanent tooth loss is a pathological condition that affects millions of people worldwide. The possibility of successful treatment of edentulous areas through osseointegrated implants in those systemic compromised patients is a matter of scientific discussion. Although antimicrobial agents must be used rationally and carefully to avoid development of bacterial resistance, more studies are needed in order to support evidence regarding the influence of antibiotics in the success of dental implant surgery in diabetic patients.

**Keywords:** Dental implants, Diabetes mellitus, Antibiotics, Complications.

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### INTRODUCTION

The loss of permanent tooth, due to variable conditions, affects millions of people worldwide. Oral rehabilitation in these cases has advanced significantly in recent decades, especially by the use of dental osseointegrated implants, which represent a predictable therapeutic procedure for most patients.<sup>1</sup> The implants simulate the function of tooth roots and are mostly placed under local anesthesia. In a few months, after allowing osseointegration of the implant surface to the adjacent bone, the subsequent prosthetic tooth can be manufactured and mastication can be reestablished.

The success of this therapy is related to the initial stability achieved at the time of implant installation and a subsequent ability to osseointegrate, which allows the implant to be capable of supporting functional masticatory loads in a long term. The osseointegration is established as a direct contact between bone and the titanium implant surface, without interposition of connective tissue. The failure of osseointegration can be classified into early, when it occurs between implant fixing surgery and operation for fitting the abutment or later when it occurs after the installation of abutment or prosthesis.<sup>2</sup>

The etiologic factors of failure in these two periods may be different. During the first months after implant insertion, bone regeneration usually occurs but this can be impaired by a series of local or systemic factors. The failure on bone healing at this time may preclude an intimate contact between the surrounding bone and the implant surface. When the physiological mechanisms that should lead

osseointegration do not happen, a fibrous scar tissue between the surface of the implant and the bone structure occurs.<sup>2</sup>

After bone regeneration, in a later stage the insertion of implants, there may be a recession of the gingival mucosa and excessive exposure of the lateral surface of the implant, causing loss of mobility or even. In other words, osseointegration is not present; late failures are usually associated with peri-implantitis or occlusal overload.

In order to minimize the possibility of factors that may negatively interfere with the osseointegration process, the dentist should include an adequate preoperative evaluation of patients. Individuals eligible to receive treatment through dental implants should undergo thorough medical history and detailed clinical examination. Three main aspects must be considered: systemic and local health status, and osseointegrated implant-supported prosthesis planning. It is known that despite the high success rates of dental implants, systemic diseases, pre-existing or ongoing systemic therapy may complicate or even contraindicate this form of rehabilitation treatment.<sup>1</sup>

Complications and loss of implants are associated with time consuming and financial expending. Moreover, the lack of osseointegration becomes often a complicating factor for further rehabilitative therapy.<sup>3</sup> In this context, the presence of infection, changes in bone metabolism and situations that predispose to bone resorption are negative factors. These facts can be observed frequently in diabetic patients, especially when they are systemically uncontrolled.<sup>4</sup>

With increased life expectancy, a greater number of diabetic patients for oral rehabilitation using dental implants are expected. In Brazil, the number of people with diabetes has increased exponentially. In 2010, Brazil was the 5th place in the world list of countries with the highest number of individuals with diabetes as it was demonstrated by the International Diabetes Federation. This metabolic disorder is characterized by qualitative and/or quantitative discrepancy regarding the role of insulin onto the available glucose in bloodstream. This global impact chronic disease leads to known micro and macrovascular complications that are directly related to high morbidity when the disease is neglected.<sup>5</sup> Considering diabetic patients, dental care literature emphasizes that periodontal disease is the sixth complication of the condition with respect to microvascular problem. Protein metabolism is reduced, nerve regeneration is negatively disturbed and angiogenesis is decreased on affected individuals. Furthermore, tissue repair process can be disturbed by the impairment of vascular and neutrophils function and tissue hypoxia.<sup>6</sup>

The possibility of successful rehabilitation of edentulous areas through the use of dental implants in diabetic patients has recently been subject of scientific discussion considering

that, for a long time, the presence of diabetes was an absolute contraindication for implant placement.<sup>4,5,7</sup> In this context, the relation of the use of antibiotics to the success of dental implants it is still a controversial matter.<sup>2</sup>

Based on the latest 12-year literature, this review aimed to look for evidences that support the necessity of antibiotics in diabetic patients at the preoperative period of osseointegrate dental implants surgery. A critical discussion on the issue is also presented.

## REVIEW RESULTS

The literature search was conducted in PubMed, LILACS, Medline and Scopus considering the period from 2000 to 2011. Access was made through Dental Documentation Service (ODS) public web portal in the Dental School of the University of Sao Paulo, USP, São Paulo, Brazil ([www.fõ.usp.br/sdo](http://www.fõ.usp.br/sdo)).

Search criteria was limited to scientific articles involving human clinical research, that mentioned the use of antibiotics associated to the installation of dental implants that were published in English, Portuguese and Spanish.

The descriptors established for the internet search were: 'dental implant(s)' and 'diabetes' and/or 'antibiotic(s)' in English or 'antibióticos' and 'diabetes' and 'implantes-dentários' in Portuguese, 'antibióticos' and 'diabetes' and 'implantes dentales' in Spanish.

Articles resulting from the search were then collected and analyzed by at least two of the authors as to its validity within the proposed parameters. Articles that included all of the criteria for inclusion were fully read and its contents were focus of critical discussion among authors. If the full text did not fulfill the proposed topics, the article was excluded.

Two hundred and twenty-eight articles were initially selected for evaluation of proposed criteria. After reading the corresponding abstracts, 112 papers did not involve humans and were not published in English, Portuguese or Spanish. Sixteen articles met those criteria.

Among the 16 selected articles, only six articles represented clinical research that discussed the influence of the antibiotic in the success of osseointegration of dental implants in diabetic subjects. Five were retrospective studies and one a prospective research. All of them were published in English language. The resume of the important aspects described in the articles are presented in Table 1.

## DISCUSSION

The literature presents few scientific bases or relevant results of clinical studies that demonstrate clinical evidence of the influence of antibiotics on the success rate of osseointegrated dental implants in diabetic patients.

**Table 1: Clinical studies related to the success of dental implants associated with the use of antibiotics**

Author/year of publication	Diabetes type	Type of study	Sample size (n)	Type of glycemic control	Type of dental implant	Amount of implants	Antibiotics used	Outcomes
Abdulwassie, Dhanrajani, 2002	Not specified	Retrospective	25	Preoperative glucose-level testing (no further details)	Brånemark implants (Nobel Biocare) except for two (one Calcitek Sulzer, and other FRIALIT)	113 implants	Amoxicillin 500 mg 8/8 hours, initiating one day prior to surgery and continued for 10 days	Success rate of 95.57% during uncovering phase
Farzad et al, 2002	Type 1 and type 2	Retrospective	25 types-1 (n = 9) and type 2 (n = 16)	Report of glycemic control	Brånemark implants	136 installed implants; five of them lost upon uncovering; three of them lost one year later	One hour before and one week post-operatively (no specification of which antibiotic)	Overall success rate of 96.3% during healing period. During prosthetic rehabilitation, 94.1% of success
Peled et al, 2003	Type 2	Retrospective	41 patients (26 men and 15 women)	Fast plasma glucose test or postprandial glucose	Medical implant system (MIS)	141 implants in the anterior mandible	18 patients received two grams amoxicillin (daily dose) one day before until 5 days after surgery; 16 penicillin-allergic patients received clindamycin 600 mg daily	Success rate was 97.3% and 94.4% 1 and 5 years following implantation
Alsaadi et al, 2008	Type 1 and type 2	Prospective	283 patients (no specification for diabetic subjects)	Not specified	MkIII TiUnite	720 implants, being one in a diabetic type-1 patient and 25 in type-2 patients	The article did not consider diabetes as an indication for antibiotics	98.1% success rate
Anner et al, 2010	Not specified	Retrospective	475 patients being 49 with diabetes	Not specified	Not specified	1,626 implants	Not specified	Success rate of 95.3% for dental implants after a mean period of 24 months
Turkyilmaz, 2010	Type 2	Retrospective	10 patients	Glycosylated hemoglobin	Astra OsseOspeed	23 implants	Amoxicillin and potassium clavulanate 500 mg, 12/12 hours for 5 days	100% success rate

An analysis of 3,030 patients demonstrated that in normoreactive patients, the use of preoperative antibiotic prophylaxis significantly increased the success rate of osseointegrated dental implants.<sup>8</sup> The success rate for patients who received antibiotic was 95.4% against 90% from those who did not receive antibiotics. The authors suggested that this results from a less contaminated surgical field during dental implant placement, leading to a better immediate postoperative osseointegration condition. Another study evaluating preoperative use of antibiotics in type-2 diabetic patients with adequate glucose control demonstrated an increase of 10.5% of dental implants survival.<sup>9</sup>

Based on clinical studies related to diabetes type-2, one can conclude that antibiotics can favorably interfere for osseointegration process in dental implants either for systemically healthy or diabetic patients.<sup>5,10-14</sup> It was observed that most authors indicate the use of antibiotics for implant surgery in diabetic subjects relying on their increased infection susceptibility. Either the pre-emptive or the therapeutic use of antibiotic would be advisable to counteract possible complications related to diabetes, especially infection.<sup>14</sup> Therefore, some authors suggested the use of antibiotics for seven or ten days, beginning one day or one hour prior to surgery; however, details of the prescription were not specified.<sup>5,10</sup>

In well-controlled diabetics, type-2 patients dental implant survival demonstrated a success rate of 97.3% in 1 year and 94.4% in 5 years of follow-up, when 2 g amoxicillin or 600 mg clindamycin were daily used.<sup>13</sup>

Data from the present research shows that diabetic patients frequently present wound healing delay, increased alveolar bone loss, more severe periodontal disease and increased inflammatory tissue compromise; negative factors that can be associated with dental implants. Diabetic type-2 subjects have 2.9 to 3.4 time greater risk to develop periodontal disease than nondiabetic subjects. This predisposition to periodontal disease can be justified between others to an impairment of host defense mechanism, and this feature can be extrapolated to peri-implant disease.

In implant surgeries, anaerobic Gram-positive cocci and anaerobic Gram-negative spirochetes are the pathogens that apparently cause more negative interference in tissue repair. Thus, the antibiotic of choice to prevent complications should be bactericide and present low toxicity, such as amoxicillin. In cases of penicillin allergy, the use of clindamycin, metronidazole or a first generation cephalosporin is recommended. When surgery is expected to last to much long or many surgical sites are involved, considering patients with impaired immune response, as occurs in diabetes, preoperative antibiotics are advised.

Administration of antibiotics at least one hour prior to surgery might be effective to promote sufficient tissue concentration of this drug in order to avoid infection.

It is well-known that maintaining the surgical field as disinfected as possible is one of the main surgical principles. This can be accomplished in a number of ways: employing antiseptic mouthwashes, surgical wounds irrigation or rinsing. Chlorhexidine digluconate is currently one of the most recommended antiseptic for those procedures. It has been demonstrated that the use of 0.12% chlorhexidine mouthwash during immediately preoperative moment can reduce the rate of implant loss from 13.5 to 4.4% in type-2 diabetic subjects.<sup>7</sup>

Conscious anamnesis and careful physical examination for all patients to be submitted to dental implant surgery is paramount. For diabetic subjects, literature is unanimous in emphasizing the need for glucose control monitoring prior to surgery, either by plasma glucose tests, capillary test and glycosylated hemoglobin.<sup>13,14</sup>

The presence of microvascular disturbance is also highlighted in the literature. Blood supply deficiency will probably contribute to a higher infection rate. However, these alterations do not apply to all diabetic subjects but to those that lack appropriate glycemic control. Systemically, balanced patients present health conditions similar to those without diabetes.<sup>6,7</sup> Hence, lack of glucose control is closely associated to a greater risk of periodontal disease.<sup>4,6</sup>

There is no evidence that indicates diabetic subjects with adequate glucose level control and routine medical follow-up present increased risk of failure for dental implants.<sup>12</sup> In spite some dental complications related to diabetes have been published in recent literature, it is a general agreement that diabetes is not an absolute contraindication for dental implants surgery. Recent data demonstrate rates varying from 92 and 100% of success for those patients with adequate glucose control.<sup>5,7</sup> A relative contraindication seems to exist to diabetic type-1 patients which is more related to a more difficult and unstable glycemic control than to the disease itself.<sup>11</sup>

## CONCLUSION

As a result of the present literature review, data favor the use of antibiotics without significant side effects.<sup>2</sup> Clinical investigations of the need of prophylaxis antibiotic or therapeutic antibiotics are still scarce.<sup>8</sup> Lack of research on this field might occur by methodological difficulties, such as the number of the sample, a long follow-up and ethical implications. The only prospective study was not specific for diabetic patient.<sup>11</sup> Three of the clinical studies had specific diabetic groups but all of them had negative points, such as small sample or lack of a specific antibiotic regimen.<sup>5,13,14</sup>

These obstacles can be overcome by properly designed randomized double-blind studies using the 'split-mouth' technique, standardizing the type of implant, the type of antibiotics, the dose, the dosage and follow-up period.

The lack of adequate methodology is one of the main problems of the current articles. It is important to emphasize that studies should present detailed methodology in order to allow reproducibility.

### CLINICAL SIGNIFICANCE

Permanent tooth loss is a pathological condition that affects millions of people worldwide. The possibility of successful treatment of edentulous areas through osseointegrated implants in those systemic compromised patients is a matter of scientific discussion. Although antimicrobial agents must be used rationally and carefully to avoid development of bacterial resistance, more studies are needed in order to support evidence regarding the influence of antibiotics in the success of dental implant surgery in diabetic patients.

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