Infections in implantology: From prophylaxis to treatment

Antonio Bowen Antolín, María Tersa Pascua García, Abdul Nasimi

(1) Odontologist. Doctor of Medicine and Surgery. Fellow European Board European Surgery
(2) Degree in Odontology. Degree in Biological Sciences
(3) Degree in Odontotology. Master in Implantology and Oral Rehabilitation

Correspondence:
Dr. Antonio Bowen Antolín
c/ Santa Engracia, 135
28003 Madrid
E-mail: bowen@infomed.es

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ABSTRACT
Since the introduction of osseointegrated implant treatment, odontology, and in particular the area of prosthodontic replacement of lost teeth, has evolved in an unimaginable way, to the extent that the age-old idea of “restitutio ad integrum” has almost become possible.

Implant treatment has a high success rate that has been rated as high as 95 to 99%, according to different casuists, but there is another group of cases in which implants fail, and in fact it is hard to know the causes of such failures.

The microbiological component plays an important role in encouraging and facilitating implant infection during implant placement, and also later when the implant is in function in the mouth, which is a septic medium.

In this paper we will study infections in implantology, classified according to the treatment phase: Infection prior to the implant; Peri-surgical infection; Severe post-surgical infection; Peri-implant disease.

Key words: Infection, antibiotics, dental implants, peri-implantitis.

RESUMEN
Desde la introducción de los tratamientos con implantes osteointegrados, la evolución de la Odontología y en especial la de la parte encargada de la reposición prostodontica de los dientes perdidos ha sufrido una inimaginable evolución, hasta límites tales que el viejo concepto de “restitutio ad integrum” se ha hecho casi posible.

Los tratamientos con implantes tienen un importante porcentaje de éxitos que se ha llegado a cifrar entre un 95 y 99%, según diferentes casuísticas, pero hay otro número de casos en los que el fracaso es una realidad, y es difícil incluso saber cuáles son las causa de ello.

Al realizarse tanto la inserción de los implantes, como el desarrollo de su función ulterior en un medio séptico tal y como es la cavidad bucal, el componente microbiológico juega un importante papel, al favorecer y facilitar las infecciones implantarias.

Estudiaremos en este trabajo las infecciones en Implantología, referidas a cuatro etapas del tratamiento: Infecciones previas del área implantaria; Infecciones periquirúrgicas; Infecciones postquirúrgicas graves; Enfermedad periimplantaria.

Palabras clave: Infecciones, antibióticos, implantes dentales, periimplantitis.
INTRODUCTION
Causes of implant failure
Many causes have been studied on the subject of implant failures. Since Bert’s publication (1) to the present-day it is clear that implant failure can occur at any time during treatment and subsequently when the implant is in function. Implant placement is contraindicated in many cases, and almost all authors (2) agree about these cases, because the failure rate increases sharply, sometimes jeopardizing oral health and even the patient’s general state of health.
Apart from these cases, if there is no contraindication for undergoing the treatment, studies of implant failure reveal two main causes of failure: infection and occlusal overload (3). The first is associated with the phase prior to placing the implant in situ, in direct relation with surgery, and the second is associated with implant function following prosthetic rehabilitation. The latter also involves an infectious component that is encouraged by microfractures in the bone and the appearance of peri-implant pockets, with a clear infectious component.
The study conducted by Tonetti’s group (4) is of particular note amongst the large number in the literature, because it provides a very up-to-date description of predisposing factors in implant failure, and attributes greatest precedence to periodontal disease, smoking, and poor oral hygiene, which are also related to predisposing factors in Periodontal Disease, and determine an aggressive situation from a microbiological point of view, thus favouring infection. When studying the causes of failure, we will follow the classification below, as proposed by Quirynen (5):
Infection prior to the implant
Peri-surgical infection
Severe post-surgical infection
Peri-implant disease

PREVIOUS INFECTION
This refers to two fundamental conditions: an active septic source (regardless of whether or not it is related to root remains), and previous periodontal disease.
Active septic site
The presence of an active septic site has traditionally been considered as a contraindication for implant placement because of the possibility of septic embolism that can cause immediate or late post-surgical infection (osteomyelitis, peri-implant abscess, etc.) and also because of the presence of epithelial remains that may jeopardise osseointegration. Therefore, all authors agree that before performing an implant placement, the affected zone must be carefully debridged and the area must be completely decontaminated (6, 7, 8). In view of the importance of cleaning, aiming for a sterile implant zone, in the last few years laser use has become more common. It has been demonstrated that the use of Er:Yag or Diode lasers can be effective in the decontamination of infected areas (9). Periodontal disease
Implant treatments in patients suffering periodontal disease has been the subject of many studies. From a microbiological point of view, the first studies (10) already reported that implants in patients with periodontal disease in remaining teeth have a more pathogenic microbiota than completely edentulous patients.
A series of important conclusions can be drawn by comparing the microbiology of implants and teeth (11): a) microbiological findings in healthy implants are similar to those of healthy teeth; b) microbiological findings in infected implants are similar to those of teeth with PD; c) subjects at risk of PD are also at risk of peri-implantitis; d) periodontal diseased teeth can contaminate implants in the same mouth.
Studies by Ellegard (12) and Nevins and Langer (13), demonstrated that patients with a history of periodontal disease and advanced bone loss can have successful implant treatment. Likewise, patients with a high risk of periodontal disease can be successfully treated with osseointegrated implants. However, Lang’s group (14) noted that patients who had implants for teeth lost because of periodontitis had lower rates of survival and greater complications than those who had lost teeth from other causes.
Finally, the EAO implantology work group consensus report (15) concluded that patients with PD had an implant success rate of 91–92% and patients without PD had a success rate of 97%. However, the incidence of peri-implantitis and marginal bone loss increases significantly in patients with PD. In any case, it appears that there is a clear relationship between PD history and implant evolution in these patients, in such a way that longitudinal bone loss around implants is related to a history of periodontal support loss. Subjects at risk of periodontitis may have a greater implant failure rate than those who are not (16).
Special considerations regarding implant treatment in periodontal patients:
There are three fundamental factors to consider in implant treatment in patients with periodontal disease:
1. Progressive reabsorption in edentulous maxillas has a direct relation with the implant prognosis and the height of remaining bone.
There are many articles in the literature that describe a clear relation between a long implant length and longevity of implant survival. The 5-year implant failure rate is 10.86% in implants that measure 10 mm or less (17), and at the other end of the scale, there is a 96.4% success rate in implants that measure up to 16 mm (18). There does not appear to be any relation between implant survival and diameter (18).
2. Approach to teeth with a poor prognosis.
One classical study that was conducted in 1978 by Hirschfield and Wasserman (19), reported on 600 patients with periodontal disease who were treated and followed-up over a 5 to 15 year period. It was observed that patients who did not receive regular treatment for their PD lost up to 31% of their teeth, while those who did receive treatment lost 7% of their teeth. The conclusion seems clear: if the future of a tooth is unclear, extraction is the best solution.
3. Need for prior treatment of underlying Periodontal Disease
In 1994, Lang presented a review (20) of the results of implant treatment in patients with PD. From these findings, he made two recommendations: to treat PD before implant placement, and maintain less deep pockets in patients who are implant candidates, increasing surgical periodontal treatment if necessary in order to reduce the pockets. He also advised extreme care in smokers and patients at high risk of PD.

Furthermore, the SEPA Periodontal manual (21), states that teeth with severe periodontal disease should not be used as pillars but should be extracted. It also states that a healthy periodontal condition is required before starting restorative treatment because a mouth in a poor condition will bring complications when restorative treatment is commenced. Therefore, before starting implant treatment, any underlying periodontal disease must be treated.

PERI-SURGICAL INFECTION

Intraoral surgery has traditionally been classified as clean-contaminated surgery or contaminated surgery, depending when the intervention takes place (22). Implant placement surgery is a case of clean-contaminated surgery because the surgical field may be contaminated through many causes and germs can easily penetrate the operating field. However, the excellent vascularisation of the zone and absence of previous infection usually prevent infectious processes from occurring during these interventions.

Brånemark (23) stated that there are many sources of contamination in surgery and almost all are derived from the instrumentation itself (air, aspiration, instruments themselves, etc.) and from the presence of saliva in the surgical field, and its relation with face and lips.

Many different techniques have been used to avoid this situation, such as reducing saliva secretions with atropine (24), double aspiration to avoid salivary contamination of surgery, and the use of chlorhexidine washes that considerably reduce the number of germs present in the mouth (5).

It has also been suggested that germs from the nose may also be significant in surgical field contamination (25) and therefore surgical isolation and a clean field play a vital role in preventing infection during implant placement.

Clinical manifestations of the infections caused by peri-operative contamination are usually in the form of peri-implant abscesses, characterised by peri-apical radiolucency on X-ray, often leading to fistulas (5, 26).

SEVERE POSTOPERATIVE INFECTION

Infectious complications of implant surgery can be significant. The virulence of the germs involved can cause all sorts of infections that can even become life threatening.

In practice, a full range of oral and maxillofacial infectious processes can be found, and treatment of such infection includes explantation of the implant and appropriate surgical treatment, as well as full antibiotic cover.

One infectious process of particular importance is infection derived from bone graft surgery associated with implant placement. This occurs either simultaneously or prior to the intervention and its importance lies in the fact that in addition to the infectious process, there may be repercussions at other levels (immunological reactions, reactions to a foreign body, etc.).

The Gottlow Nyman principles, established over 20 years ago, should always be followed in bone regeneration (27):

1. When preparing the area to be regenerated: maintain good graft vascularisation, in order to attain sufficient nutrition that will prevent early necrosis, at the same time as facilitating the regenerative and wound-healing process.

2. Prevent surrounding tissues from collapsing in order to maintain space for regeneration. This can be achieved by different means: self-maintenance using graft morphology, use of a titanium mesh, block grafts...

3. Ensure that the flap completely covers the graft, using sliding plasty or periosteal discharges. In the event of dehiscence, use topical antiseptics to avoid colonisation of the exposed zone.

2 Tissue exclusion

Dahlin's principles on guided tissue regeneration (28) are of full application because it is essential to use membranes or other barrier methods to prevent soft tissue infiltration of the graft. This is because soft tissues grow much more quickly and this would lead to repair rather than regeneration, and proposed objectives would not be attained.

3. The technique used to incorporate regeneration materials is very well known and has been discussed by many authors (29, 30), but we believe that it is important to mention several basic principles: a) immobility of graft material; b) continuous maintenance of the sterile chain; c) ensure vascularisation; d) safety and biocompatibility of graft material.

Likewise, a series of basic post-operative principles should be followed to ensure that the graft progresses well (31): a) antibiotic therapy; b) use of chlorhexidine mouthwash; c) local application of cold pads; d) use of steroid anti-inflammatory therapy if necessary; d) application of chlorhexidine gel after the first week; e) impeccable oral hygiene; f) no smoking; g) avoid loading the regenerated zone.

Graft infection is manifested by pain and inflammation and is usually accompanied by fistulas. This normally leads to expulsion of the material. Treatment consists of removing the graft material and careful debridement of the zone to ensure good vascularisation and an area free of any remainders of the graft material. Systemic antibiotics are always given.

PERI-IMPLANT INFECTION

It is essential to study and understand the gum-implant interface in order to understand peri-implant physiopathology, because the soft tissues that surround implants have a very similar structure and composition to periodontal tissue.

Supracrestal soft tissue that surrounds implants is called peri-implant mucosa and it forms a structure called peri-implant sulcus around the implant, similar to the gingival sulcus. This tissue is covered with surcus epithelium and adherence epithelium on its internal surface, and oral
epithelium on its external surface that may be keratinised epithelium or simple alveolar mucosa. Amongst the cells nearest the root of the adherence epithelium and alveolar bone is the connective tissue zone that also comes into direct contact with the implant surface. This is called lamina propria.

This anatomy determines a series of characteristics such as peri-implant probing, because the probe penetrates further in tissues surrounding the implants than in the periodontal surcus, also causing compression and lateral movement of peri-implant mucosa (32). This means that bleeding during probing is not a good indicator of peri-implant mucosa inflammation when pressure greater than 0.2 N/cm is used because it causes sideways dislocation of the mucosa (33, 34).

The microbiology of peri-implant infection.

Mouth microbiology determines peri-implant microbiology: colonisation of implants is similar to the periodontal surcus following dental eruption (35) and therefore if there is no pathological alteration, bacterial flora is similar to that of healthy periodontium (36, 37). When the implant is in function, in the event of pathological or para-axial loading leading to occlusal overloading or osseointegration loss due microfractured bone, this can cause apical migration of the epithelium that favours infection in the zone (38-41).

Periodontal and peri-implant diseases are multifactor pathologies that have major bacterial aetiology (42). Strains associated with the onset and development of periodontal disease have also been identified in peri-implant tissue suffering peri-implantitis (43, 44). The main pathogens involved in peri-implantitis are gram-negative anaerobic bacteria, with an increased percentage of motile rods, fusiform and spirochete bacilli (45-47). The most frequent ones are Prevotella intermedia, Fusobacterium nucleatum, Porphyromonas gingivalis, Capnocytophaga and Campylobacter rectus.

It is uncommon to find Actinobacillus actinomycetemcomitans in peri-implantitis, and it appears to be more associated with Periodontal Disease. The presence of Porphyromonas gingivalis appears to indicate previous peri-implantitis or peri-implant mucositis (48). The presence of Porphyromonas gingivalis, Actinobacillus Actinomycetemcomitans or Prevotella Intermedia in the peri-implant pocket indicates a higher risk of insertion loss during later phases (49, 50), and therefore patients who are partially edentulous are at a higher risk of infection than completely edentulous patients (5).

Clinical presentation of peri-implant diseases

A) Peri-implant mucositis

This is a reversible inflammatory reaction in the soft tissues that surround an implant in function. Clinically it is characterised by:

- Presence of bacterial plaque and calculus.
- Oedema, redness and mucosal hyperplasia.
- Bleeding affecting mucosal sealing on probing.
- Exudate or pus formation on occasions (gingival microabsscess).
- Radiological absence of bone reabsorption.

B) Peri-implant osteitis (Peri-implantitis)

This is an irreversible inflammatory reaction in the soft and hard tissues that surround an implant in function, because natural bone loss occurs if no treatment is given. It has more floral clinical symptoms because in the initial phase it may present the same signs as peri-implant mucositis, but these are later accompanied by the symptoms of bone loss itself. The most common signs are:

- Presence of bacterial plaque and calculus.
- Oedema and redness of peripheral tissues.
- Mucosal hyperplasia in zones with a lack of keratinised gingiva.
- Increased probe depth. The level of probe reaches the apex.
- Bleeding and slight pus formation after probing and/or palpation.
- Vertical bone destruction in relation to peri-implant pocket.
- Radiological presence of bone reabsorption.
- Implant mobility.
- Pain is not very common, but is sometimes present.

A continuously moving implant and peri-implant radiolucency indicate that the disease is reaching its final outcome, characterised by total loss of the bone-implant interface. Radiological examination is very important because although X-rays only show bone on mesial and distal implant surfaces, the bone defects have a circular or funnel-shaped form and therefore are larger than those observed on an X-ray. (51) Therefore two types of defects can be observed that will provide guidance to the aetiology, clinical development and prognosis of the case.

- Horizontal defects: These develop slowly. They tend to have a more favourable prognosis because they are often associated with soft tissue recession. The angle that forms with the implant surface is greater than 60 degrees.
- Vertical defects: These develop more quickly. They cause pockets with epithelial growth inside, and purulent infections when probe depth is greater than 5 mm. The angle that forms with the implant surface is less than 60 degrees.


Peri-implantitis class 1: minimum horizontal bone destruction with slight peri-implant bone loss
Peri-implantitis class 2: moderate bone destruction with solitary vertical loss
Peri-implantitis class 3: moderate or intense horizontal bone destruction with extensive circumferential bone lysis
Peri-implantitis class 4: intense horizontal bone destruction with extensive circumferential bone lysis and loss of lingual or vestibular bone wall

- Treatment

A) Treatment of implant mucositis

Treatment is principally focused on controlling bacterial plaque, although other surgical treatments may be performed to eliminate the hyperplasia of surrounding soft tissue as well as to graft keratinised gingiva, if necessary.
Thus, treatment consists of several phases:
1. Professional peri-implant hygiene
   • Mechanical elimination of bacterial plaque (Vector-Durr) (54).
   • Irrigation of the surcus-pocket with 0.12% chlorhexidine (55).
   • Removal and disinfection of the prosthesis and pillars.
   • Modification of unhygienic prosthesis designs.
   • Sometimes a partial-thickness flap is performed to irrigate with sterile physiological saline, followed by the application of a tetracycline cream.
   • LASER treatment with 1.5-2W diodes in refractory cases (56, 57).
2. Personal peri-implant hygiene
   • Chemical plaque control with 0.12% chlorhexidine 12 hourly.
3. Local and systemic antibiotics
4. Regular professional control
B) Treatment of peri-implantitis
The fundamental requirement in successful peri-implantitis treatment, with or without the use of bone regeneration protocols, is to decontaminate the implant surface, removing bacteria and toxins.
Peri-implantitis treatment must be based on the stabilisation of progressive bone loss, and in special cases, to retrieve lost bone with regenerative treatment.
The treatment can be divided into two phases:
   Phase 1: Initial conservation treatment
   A. Manual-mechanical methods to control bacterial plaque (similar to mucositis)
   B. Chemical methods
      B.1. Local
         • 0.12% chlorhexidine.
         • Citric acid
         • Local application of tetracycline (58)
   B.2. Systemic
      • Antibiotic therapy
C. Diode laser: 1 W for 20 seconds (59)
Phase 2: Regenerative treatment
Treatment of soft tissues.
A crestal incision is scalloped around the implant neck to eliminate the internal epithelium and granulation tissue from the pocket. A mucoperiostic flap is lifted to expose the implant, and bone tissue and granulation tissue is eliminated from the bone defect with a metal curette without touching the implant. A cold sterile physiological saline solution is irrigated throughout the procedure to prevent bone dehydration.
Treatment of the implant surface.
First, the implant surface is decontaminated with successive topical applications of citric acid, tetracycline, chlorhexidine and sterile physiological saline.
In the thread zone of the implant that will be exposed, an implantoplasty is performed to attain a smooth, polished surface that will facilitate maintaining healthy peri-implant tissue.
Finally, the surgical field is then irrigated with 0.2% chlorhexidine and sterile physiological saline.
Therapeutic guidelines, according to the degree of peri-implantitis
Peri-implantitis class 1
Surgical reduction of pocket depth, thinning of mucosal flaps and apical repositioning of flaps at a bone edge level, using the corresponding suture technique.
The implant surface is clean and decontaminated. Implantoplasty is only performed if threads are exposed.
Peri-implantitis class 2
Similar to class 1, but repositioning is performed more apically, leaving more implant surface exposed, thus requiring an implantoplasty.
If local vertical reabsorption has three or more walls, this bone defect is restored using classical GTR techniques. In cases where the defect involves one or two walls, osteoplasty or bone levelling is performed to favour soft tissue repositioning, to fulfil self-cleaning criteria.
Peri-implantitis class 3 and 4
In peri-implantitis class 3 and 4, the presence of vertical defects almost always permits the use of GTR techniques. The following combinations can be employed, the exact choice depends on intra-operative findings.
   • Osteoplasty + implantoplasty + apical repositioning of the flap.
   • Closed GTR + graft + coronal repositioning of the flap.
   • Semiopen or transgingival GTR + implantoplasty + apical repositioning of the flap.
Antibiotic therapy in peri-implant diseases
One classical question that many authors have asked is whether the use of antibiotics is indicated in peri-implant disease. Back in 1985, Bascones (60) suggested that appropriate antibiotic therapy in PD has many benefits: it reduces the need for surgery, improves the patient’s clinical situation, and increases the success rate of graft and reinsertion techniques.
Since the early 90’s, experimental studies have reported on peri-implantitis lesions in animals that are resolved with antibiotic therapy (61, 62); finally, in a study by Gutiérrez Pérez et al. in 2003 (42) it was concluded that “treatment strategies in PD and peri-implant disease should be focused on the rational use of potent antimicrobial therapy”. García Calderón’s study (46) demonstrated the importance of giving systemic antibiotic therapy if the peri-implant pocket is greater than 5 mm, because local antiseptics cannot reach the bottom of the pocket. Therefore, the only possible answer to the question “Should antibiotics be used in peri-implant infections?” is “yes”.
Choice of antibiotic
The association amoxicillin-clavulanic acid is the treatment of choice in peri-implant disease because of the sensitivity of the germs involved and the low rate of resistant strains. Clindamycin and metronidazole are also indicated, but they are less effective against residual streptococcus and Actinomyces, and since they grow after R and A techniques are used, these antibiotics should be considered as second line treatment. High-dose amoxicillin-clavulanic acid should be used due to the increased resistance of germs (42).
ANTIBIOTIC THERAPY AND ANTIBIOTIC PROPHYLAXIS IN IMPLANTOLOGY

One of the most controversial issues in implantology is whether to use antibiotics preventively when performing an implant placement surgical procedure. Antibiotic prophylaxis is understood as pre- or peri-operative administration of an antibiotic agent to prevent a local and/or systemic infectious complication and its corresponding clinical consequences. The aim is therefore to prevent the onset of infection in the surgical wound by achieving an antibiotic concentration in the blood that will prevent bacterial proliferation and dissemination (62).

There are two fundamental factors that must be considered in odonto-stomatology and oral surgery:

A) The invasive nature of the procedure: traditionally, two types of procedures have been described:
   - Invasive oral-dental procedures
   - Non-invasive oral-dental procedures

Invasive procedures are defined as procedures in which ruptured biological membranes might encourage bacterial dissemination throughout the body. High-risk invasive procedures are as follows (62):

- Intraligamentous anesthesia
- Extractions
- Dental re-implants
- Biopsies
- Incisions for drainage
- Bone grafts
- Root curettage and polishing
- Periodontal surgery
- Implant placement surgery
- Mucogingival surgery
- Endodontic surgery and apicectomy
- Shaping procedures including bleeding
- Pre-prosthetic surgery
- Orthognatic surgery
- Reduction of maxillary fractures
- Salivary gland surgery
- Maxilofacial oncology surgery

B) Patient risk profile: this second parameter classifies patients into three groups:
   - Healthy patients
   - Patients with a risk factor of local or systemic infection
   - Patients with a risk factor of local infection following bacteremia

In the case of the first group there is nothing of note. However the following types of diseases would be included in the risk profile:

1. **Inflammatory joint diseases**: Rheumatoid arthritis, systemic lupus erythematosus.
2. **Immunosuppression** due to disease, drugs, transplants and radiotherapy
3. **Diabetes mellitus type I**
4. **Infectious endocarditis** protocols: previous endocarditis, prosthetic valves, congenital heart disease, surgical derivatives, acquired valve disease, hypertrophic cardiomyopathy, mitral valve prolapse, sustained murmurs and Marfan syndrome
5. Osteoarticular prosthetic protocols: Within 2 years of implant, and having suffered previous infection in the prosthesis.
6. **Malnutrition**
7. **Haemophilia**
8. **Grafts** (local factor)
9. Other uncontrolled associated pathologies (RENAL or hepatic impairment), and splenectomy patients.

Therefore, antibiotic prophylaxis is recommended in at risk patients who are undergoing high-risk invasive procedures (62).

The use of antibiotic prophylaxis is not so clear in implantology. In Exposito’s study (64), it was demonstrated that the rate of infectious complications was higher in the case of osteotomy and long surgical procedures. The infecting inoculum increases in proportion to the length of time of the surgical procedure.

Therefore the probability of infection around dental implants fundamentally depends on how traumatic and how long the surgery is. It is believed that uncommon early implant loss is due to contamination during implant placement (65, 66).

There is little work in the literature that refers to the application of pre-operative antibiotics, and results are varied. Binhamed (67) found that greater efficacy was not observed with the use of a 7-day post-operative antibiotic course against a single intra-operative dose. Similarly, Gynther (68) did not find significant differences in success rate or in complications between two patient groups using penicillin V against placebo pre-operatively. However, Laskin’s study (69) demonstrated a lower failure rate in patients given pre-operative antibiotics.

Finally, the 2003 Cochrane review (70), concluded that there is no evidence either to be able to recommend or to advise against the use of antibiotics to prevent dental implant complications and failure, due to the absence of randomised, controlled clinical trials.

In view of all this, should antibiotic prophylaxis be used in implantology? In our opinion, there are two situations in which it should be used, always under the same guidelines that apply in odontology in general: 1) whenever a patient has a major systemic risk factor; 2) if surgery is expected to be long and/or traumatic.

With regard to other cases, there are no clear criteria to recommend or advise against prophylaxis.

Antibiotic regimens for the treatment of implantology infections.

According to the criteria established by Gutiérrez Pérez et al. (42), and in the Consensus Document for the treatment and prophylaxis of infections in odonto-stomatology and oral surgery (62), the following antibiotic regimens should be used:

**First choice:**
- Amoxicillin-clavulanic acid

**Alternatives:**
1. - Clindamycin
2. - Spiramycin and Metronidazole
3. - Clarithromycin

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REFERENCES