

Dental treatment considerations for the organ and bone marrow transplant patient

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Abstract: - Organ and bone marrow transplant represents a chance to life for the patients with end-stage diseases like terminal cardiac, hepatic, renal failure or leukemia, aplastic anemia and immune deficiency syndromes. The success of the transplantation procedure depends on the immune reactivity of the recipient patient, which may trigger the rejection or reject phenomena. The immunosuppressive drugs, administrated in the posttransplant phase have the role of preventing rejection, but they have also side effects, with implications throughout the body, including the oral cavity. The aim of this paper is to make the dentist aware of the particularities and special needs of organ and bone marrow transplant patients, in the context of the general medical aspects, the specific medication and the necessity of an effective dental treatment, which can play an important part in these patients' lives.

Key-Words: - Organ transplant, bone marrow transplant, dental treatment considerations

1. Introduction

Organ transplant represents a new chance to life and for the patients with severe affections, with various serious diseases like terminal renal, hepatic or cardiac failure, organ transplant represents the last chance for survival. Nowadays, transplant operations are successfully performed in specialized clinics all over the world. Depending on the degree of compatibility between the donor and the recipient, there can also be performed heart, lungs, liver, kidney, pancreas, bone marrow, etc. Of course, the ideal combination implies the transplant of an organ from a donor who is genetically identical to the recipient – transplant between identical twins - **iso/syngeneic transplant** or **iso/syngeneic graft**. The following compatibility, with very good chances for survival, is represented by the transplant from a donor who is not genetically identical with the recipient – **allograft** or **allogeneic transplant**, the most used type of transplant. Allograft can be donated by a living-related person (parent, sibling), a living-unrelated person or a person who has died (cadaveric

allograft). Transplantation of an organ from a donor to a recipient of a different species refers to **xenograft** or **xenogeneic transplant**. (baboon or pig to human) [10, 11]. Xenogeneic renal transplant, for instance, represents an alternative treatment for terminal chronic renal disease. Unfortunately, there are ethical and practical considerations that limit this type of transplants, but also an insufficient knowledge regarding the reaction of the xenograft, here referring to the humoral component like the production of anti-donor antibodies which determines the rejection of the graft. The most large organ base for transplant constitutes of the cadaver organs sampling (allograft), using the kidney for that type of transplant is increasing rapidly, considering the limited number of the living donors. From this point of view, in our country, the National Transplant Agency has as objectives the development of a donors program without cardiac activity, as well as the increase of the centers which maintain physiological conditions for the donors in cerebral death [23, 24].

2. Epidemiological aspects

The first successful human organ transplant was performed in 1954 in Boston, by MD Joseph E. Murray, Noble prize laureate. He performed a **renal syngeneic transplant**, using a kidney donated by his monozygotic twin brother. After this, in 1959, Murray performed the first allogeneic renal transplant, applying the total irradiation of the body as immunosuppression and in 1962 he performed the first renal transplant from a cadaver, introducing azathioprine (Imuran) as immunosuppressive drug. Since these first successful transplants, in the United States of America were performed over half million renal transplants [1]. Before these first transplants, the patients with renal diseases, hypertension and azotemia were going under renal dialysis, which wasn't that successful. Nowadays, when comparing to dialysis, the renal transplant offers to children with renal failure bigger chances of surviving on a long term. The usual indications for performing a renal transplant are bilateral chronic renal diseases and end-stage renal diseases. Diseases like: glomerulonephritis, pielonephritis, diabetic nephropaty, nephritic syndrome or congenital renal diseases are the diseases which are most likely to lead to end-stage renal diseases. As the disease evolves to the uremic stage there may appear oral and radiological manifestations such as: uremic fetor, an ammoniacal odor, caused by the high concentration of urea in the saliva and its subsequent breakdown to ammonia, especially in the morning, metallic taste, xerostomia, prolonged gum bleeding, petechiae and ecchymosis, bone demineralization, pulp calcifications, tooth mobility, etc. [25].

The first human **heart transplantation** was performed in 1967, and now it became the standard therapy for patients with heart failure who do not respond to other treatment forms. The usual indications for performing a heart transplant are cardiomyopathy, congestive cardiac insufficiency and severe coronary disease. Furthermore, to patients whose lungs are not working normally anymore (pulmonary emphysema, pulmonary fibrosis, cystic fibrosis), there may be transplanted either a lung, or both lungs. But the heart and the lungs may be transplanted also simultaneously, the first transplant of this kind being made in 1981 [10, 11].

The first liver transplant was performed in 1963. At adults, the affections in the case of which it is usually indicated liver transplantation are: primary biliary cirrhosis, chronic hepatitis, sclerosing cholangitis, fulminant hepatic failure and metabolic disorders.

Also, the first **pancreas transplant**, together with a duodenum and kidney transplantation, was performed in 1966 by Kelly and Lillehei at the Minnesota University, to a patient with diabetic nephropathy [10]. The diabetic patients, who will receive a renal transplant, represent good candidates for pancreas transplant. Recently, the transplant of pancreas isolated cells has a considerable success [26].

The improvement of the patients' preparation before the transplant, along with the use of certain well organized immunosuppressive techniques, have increased the success rate of this procedure and prolonged the life of the transplant recipients. According to some statistics published in 2005 in the United States of America, the survival rate at 1 year and at 5 years of the recipients of different transplants is encouraging (Table 1) [10,11].

Organ graft	From deceased donors	From living donors
Kidney	1 year: 94,6% 5 years: 81,1%	1 year: 97,9% 5years: 90,2%
Heart	1 year: 87,5% 5 years: 72,8%	
Liver	1 year: 86,8% 5 years: 73,1%	1 year: 87,7% 5years: 77,4%
Pancreas	1 year: 96,2% 5 years: 90,6%	
Intestine	1 year: 85,7% 5 years: 53,5%	
Lungs	1 year: 83,0% 5 years: 49,3%	

Dates taken over from the Annual Report for year 2005 of the Health and Services Department of the USA.

Table 1 – Survival rate of patients with organ grafts, 1 year and 5 years after the grafting procedure, in the USA

The modern era of the **bone marrow transplant** began together with Jacobsen's (1950) and Lorenz's (1951) experiments, which proved that the mice can be protected by the lethal radiation used to treat leukemia or severe aplastic anemia, by protecting the spleen or by venous perfusion with bone marrow [10]. These represent the choice treatment for patients with aplastic anemia, thalassaemia, falciform anemia and chronic myeloid leukemia, for those in the case of which the conventional therapy for acute leukemia is inefficient and for patients diagnosed with immune deficiency [2, 11].

Regarding the situation in our country, according to the President of Romtransplant, Romania is situated at the end of the list of organ donations in Europe. The results of a survey done by Insomar in 2004 were presented during the International Congress of Romtransplant and showed that 80% of the population of Romania has agreed receiving or donating organs if necessary. The survey was made on a representative sample of 1422 people over 18 years old. The survey also showed that 17% of the Romanian population would refuse to receive an organ from another person and 19% would refuse to donate an organ in order to save another person's life. The most responsive persons, to the idea of transplantation were young people with ages between 25 and 34 years old – 87.4% of the total number of people in favor of donating or receiving an organ [27]. The annual sum up of The National Agency for Transplantation for 2007 registered 34 donors and 440 transplant procedures nationwide, with a mean of 1 donor for 1 million inhabitants, the most transplanted organ being the kidney. In Europe, Spain is at the top of the list of organ donations with 40 donors for 1 million inhabitants, Austria has 20 donors for 1 million inhabitants, Hungary 10 donors/1 million inhabitants, the rest of the countries registering between 12-15 donors/1 million inhabitants. In the USA there are 20 donors/1 million inhabitants [27, 23]. Although the number of donors is small, evident progress regarding the legislation and the financing of transplantation has been made in Romania.

3. Immunosuppressive therapy

The capacity to accept an organ transplant depends on the existence at the recipient organism of all histocompatibility genes. The success of the transplant depends on the immune reactivity, which may trigger the rejection or reject phenomena. The role of the immunosuppressive drugs is to inhibit the immune reactivity and they are administered, in general, after performing the transplant. The immunosuppressive agents used nowadays for the majority of the cord, liver, kidney and pancreas transplants are: cyclosporine, azathioprin, mycophenolate mofetil, prednisone, tacrolimus, anti-lymphocyte agent, and others. Even since 1980 cyclosporine has been the standard immunosuppressive drug, used in order to prevent the reject of the organ transplants. The best results may be obtained with the help of the triple immunosuppressive therapy – cyclosporine, prednisone and azathioprin or mycophenolate mofetil (MFM). In the case of the bone marrow transplants are used, with good results, as immunosuppressive agents, cyclosporine, prednisone and methotrexate. But the immunosuppressive agents may cause major side effects with important implications over the oral cavity. According to the Wynn and collab [14], the immunosuppressive therapy may determine the following complications in the oro-maxilo-facial sphere: gingival enlargement, gum bleeding, various forms of gingivitis, glossitis, xerostomia, halitosis, abnormal taste, esophagitis, oral ulcerations, fungal and viral infections, stomatitis, anemia, etc. The immunosuppressive therapy has also a permissive effect over the viral proliferation and namely over the development of "de novo" malignancies in the oro-maxilo-facial area, such as: epithelial dysplasia, squamous oral carcinoma, basal cell carcinoma, Kaposi's sarcoma, etc. The incidence of "de novo" malignancies increases proportionally to the time period since the transplant, from a rate of incidence of 10% after 10 years, to 40% after 20 years after the transplant [12, 15]. For instance, azathioprine, an immunosuppressive antimebolite, may produce hepatotoxicity and bone marrow suppression, leading to leucopenia, trombocytopenia and anemia, and in oral cavity may determine a considerable increase of the risk for infections to appear and for the occurrence of "de novo" malignancies. Taking into consideration these reactions, the cyclosporine may successfully replace azathioprine as a key drug in transplants, because it does not produce the suppression of the bone marrow. Although, cyclosporine may cause hepatotoxicity and nephrotoxicity, leading to the

occurrence of hypertension, coagulation disorders and anemia, but it may increase the incidence of gingival hypertrophy/hyperplasia, hirsutism and gynecomastitis, but also of skin cancer. Gingival hypertrophy may have prevalence and a severity proportional to the concomitant use of cyclosporine, especially cyclosporine A with drugs which have the role of reducing hypertension, like the calcium channel blockers (nifedipine, verapamil, diltiazem and others). Clinical manifestations of gum hypertrophy: it initially starts at 1-3 months since the beginning of the treatment, at the interdental papillae and then affects marginal and papillary tissues, while the tissues in edentulous areas seem not to be affected, sometimes the papillary lesions have a cauliflower appearance, of big dimensions, causing mastication, speech, esthetic disorders and changes in the position of the teeth and the occlusion. There was noticed that it especially affects male patients, and the symptoms are more severe at young patients [12]. The use of tacrolimus as a "rescue therapy" in the cases of post-transplant rejection, but also with patients with nephrotoxicity induced by cyclosporine A, represent an efficient alternative due to the absence of several major side effects such as: gingival hypertrophy/hyperplasia or arterial hypertension [16, 17]. Prednisone may determine the occurrence of hypertension, hyperglycemia, osteoporosis, psychoses, but also an increased risk for the appearance of infections and for the delay in the healing process. Usually, the immunosuppressive regime may vary a little from one medical center to another, in what concerns the doses, the moment of administration and the period of time when various immunosuppressive agents are used [3, 4, 5, 11].

4. Pre- and posttransplant medical considerations

4.1 In pretransplant phase

In what concerns the patients who are prepared for the performance of a transplant, there must be attached a special attention to certain medical problems which may occur during the dental treatment, considering the fact that the patient is confronting the terminal phase of sickness of an organ. That is why the preventive and therapeutic dental conduct should be established in collaboration with the surgeon and/or the team who will perform the transplant. The dentist should treat

the patient pre-transplant, taking into account the protocol for treating severe medical complications of that particular organ, protocol for which is responsible the attending surgeon of the patient. Also, there should be a thorough examination of the oro-maxilo-facial area, in order to early diagnosis and treat any affection appeared at this level, especially any infection or oral problem which would need a surgical intervention in the immediate phase post-transplant, when the transplant is very sensitive to infections. The infection in the oral area represents a real reason for concern at these patients, because immediately after the transplant and a few weeks after that, the patient will have a low immunity due to the induction of the immunosuppression by drugs, directed towards the prevention of the graft's rejection. Also, it is preferable to avoid any post-transplant dental treatment, for a variable period of time (usually approx. 6 months), due to certain manifestations such as: fatigue, drugs interaction and side effects of the drugs administered during the post-transplant treatment. There should be taken into account the fact that the patient who will suffer a bone marrow transplant is in general prone to infection, bleeding and delayed healing, due to the leucopenia and thrombocytopenia. Furthermore, the patients who will suffer a hepatic transplant present the risk of massive bleeding during the dental treatment, due to the coagulopathy, and patients who will suffer a renal transplant and periodically have hemodialysis, may need preventive antibiotherapy before the dental treatment, in order to prevent the occurrence of bacterial endocarditis, but also the monitorization of the blood pressure, due to the arterial hypertension, as sign of renal disease. Thus, the dentist shall take into account the fact that, in what concerns certain drugs used before or during the dental treatment and metabolized at a renal and hepatic level, he should modify the doses or even avoid their use. Ibuprofen, as non-steroidal anti-inflammatory, may be used in renal failure, while in the hepatic failure its effects are not known. The administration of antibiotics such as: Tetracycline (Doxycycline) and Cefalexine (Keflex) should be usually avoided or the time period between the doses should be increased [10, 11]. In what concerns certain anesthetics, such as Lidocaine/Xilocaine, Aronoff and collab. assert in one study [18] that this may be usually used, but only if the time period between the doses is increased, or if it's possible, it should be avoided, while Byrne [19] states that it may be used without the change of the doses, both in end-stage renal and hepatic disease. On the other hand, the dental

treatment may be difficult, because patients who will receive an organ or bone marrow transplant may have a poor dental health and hygiene, but also a history of rare visits to the dentist, due to the severe affected general health state. The preventive dental conduct shall focus on providing an optimal oral health to the patient before the surgical intervention, also taking into consideration the dental history, the ability of the patient to make in good conditions the hygienization of the oral cavity in the posttransplant phase and the general medical stability of the patient. In the dental treatment plan shall be taken into account the recommendation to perform several laboratory blood tests, which aim the coagulation of the blood and the organ dysfunction, in order to perform an extraction or other dental procedure which implies bleeding. The general medical state of the patient and the success of the transplant constitute priorities in making a dental treatment plan in the case of a patient who will have a transplant [10, 11].

4.2 In posttransplant phase

For a better management of a patient with organ transplant, the dentist should be aware of the medical aspects characteristic for the stages of the posttransplant period:

1. The immediate posttransplant period
2. The stable posttransplant period
3. The chronic rejection period [1, 2, 6, 11].

Thus, during the immediate posttransplant period, namely the first 3 months as of the transplant, the patient goes under a immunosuppressive therapy, in order to prevent the hyperacute or acute rejection, a reversible phenomena by the adequate modification of the immunosuppressive medication. Although the immunosuppressive agents such as: cyclosporine, prednisone and azathioprine have an important contribution to preventing the rejection and to the increase of the survival rate, they still have major side effects which increase the risk of the occurrence of bacterial infections (with *Porphyromonas gingivalis*, *Prevotella intermedia*, *Treponema denticola*), viral infections (with herpes simple virus, cytomegalovirus, Epstein-Barr virus) or fungal infections (*C. albicans*, *C. dubliniensis* and *C. hyphae*) [12]. Also, there are drugs used by the dentists such as erythromycin, metronidazole, tetracyclines, phenytoin, and others [8, 10, 28], which may interact with the cyclosporine and

others immunosuppressive agents. Taking into consideration all these aspects, before prescribing or administering any drug during the dental treatment, the dentist should consult with the patient's attending physician, in order to confirm the medical state of the patient, the immunosuppression level and the exceed of the critical level in this immediate posttransplant period. For all these reasons, to the patient it will be performed only the emergency dental treatment and only in collaboration with the patient's attending physician, who may decide the pertinence of the use of antibiotic prophylaxis in view of preventing the bacterial endocarditis, according to a specific treatment regimen based on the norms of the American Heart Association (Table 2) [10, 13]:

Patient category	Oral medications	Non-oral medications (for patients unable to take oral medications)
Adults - not allergic to penicillin	Amoxicillin – 2 g, 1 h before procedure	Ampicillin - 2 g IM or IV, 30 min before procedure
Adults- penicillin allergic	Cephalexin – 2 g, 1 h before procedure or Clindamycin – 600 mg, 1 h before procedure (there are some studies which specify that Clindamicyn should not be used in most organ transplant patients because of acute liver toxicity [12])	Cefazolin – 1 g IM or IV, 30 min before procedure or Clindamycin – 600 mg IV, 30 min before procedure
Children – not allergic to penicillin	Amoxicillin – 50 mg/kg, 1 h before procedure (the total pediatric dose, calculated by weight, should not exceed the adult dose)	Ampicillin – 50 mg/kg IM or IV, 30 min before procedure
Children	Cephalexin – 50	Cefazolin – 25

– penicillin allergic	mg/kg, 1 h before procedure or Clindamycin – 20 mg/kg, 1 h before procedure	mg/kg IM or IV, 30 min before procedure or Clindamicyn – 20 mg/kg IV, 30 min before procedure
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Table 2 – Standard regimens for antibiotic prophylaxis to prevent bacterial endocarditis during dental treatment

On the basis of the AHA norms, Dajani and collab [20] have outlined the oral procedures which requires prophylactic antibiotherapy (Table 3):

Oral procedures that requires prophylactic antibiotherapy	Oral procedures that, usually, do not requires prophylactic antibiotherapy
Dental extractions	Prosthetic procedures with/without retraction cord, including the restoration of the teeth affected by dental caries
Periodontal procedures including the surgical ones, scaling and root planning	Insertion of certain removable prosthetic or orthodontic appliances
Dental implants placement and teeth re-implantation.	Impression taking
Endodontic instrumentation (beyond the apex) or surgery	Endodontic procedures, including post placement and buildup
Intraligamentary injections	Local anesthetic injections (non-intraligamentary)
Prophylactic cleaning of teeth, where bleeding is anticipated	Local fluoridation
Other procedures in which major bleeding is anticipated	Exfoliation of primary teeth

Table 3 – Oral procedures that requires prophylactic anti-biotherapy

The following posttransplant stage is the one when the graft is stable and functional, namely at 3 months after the transplant. During this period, the main concern constitutes of the over-immunosuppression, which increases the risk for the infections or infra-immunosuppression to occur, which increases the risk for the graft acute rejection occurrence.

The period of the chronic rejection starts slowly, insidious, by associated signs and symptoms, usually with organ failure and it's irreversible. This may lead to the necessity of retransplantation or even to death, in the case of the cardiac or hepatic transplants, while the renal transplants may need dialysis or even retransplantation [1, 2, 6].

5. Dental management – prophylactic and therapeutic conduct

5.1 In pretransplant phase

In a first phase, the patients who are being prepared for an organ transplantation should go under an attentive un-invasive oral examination, after previously studying the medical and dental history. In the case of the patients with a good oral hygiene, a special emphasis shall be laid on the education for oro-dental health, referring to the instruction, motivation of the patient and the control of his capacity to comprehend, to digest and fulfill in an efficient way the techniques of removing the microbial dental plaque. The education for the oro-dental health shall be supplemented by the education for a correct and balanced alimentation [9, 29]. Before the transplant operation, all the active dental caries should be treated and non-vital teeth should be endodontically treated or extracted at these patients. In case of patients with a poor oral hygiene and who are not motivated to improve their oral health level, there should be taken into account the extraction of teeth that cannot be treated due to the evolution of the dental caries and of teeth affected by advanced periodontal disease and there will be performed dentures. During the pretransplant period, before performing any invasive dental procedures, the dentist shall consult the patient's attending physician in order to establish the severity level of the organ dysfunction, the necessity to introduce

prophylactic antibiotherapy, but also to take into account other treatment options [1, 2, 3, 6].

Dental management of the patient before an organ transplantation may be summarized as follows [7, 10, 12, 31]:

- Initial consultation of the patient's attending physician, in order to discuss the current medical state of the patient and of the laboratory blood tests, but also for the opportunity to introduce the antibiotic prophylaxis or certain drugs, as well as their doses;
- Conduct a complete series of radiographs for the dentate patients and a panoramic dental x-ray for the edentulous patients [21, 30];
- Attentive oro-maxilo-facial examination, considering the potential development of the malignancies at this level;
- Remove of the microbial dental plaque by plaque control techniques and a careful instruction in view of the oral self-care, both by the individualization of the dental brushing technique, but also by using certain means additional to the oral brushing. There will be taken into consideration the use of electric toothbrushes and oral irrigators. The parents of the pediatric patients will be instructed to perform/supervise their child oral hygiene [29];
- Prescribe fluoridated toothpastes and perform topical fluoridation with custom fluoride trays, in case of multiple dental caries;
- Instruct in view of changing the diet, if necessary;
- Perform mechanical debridement and root planning, taking into consideration the introduction of the antibiotic prophylaxis;
- Use chlorhexidine 0.12% mouthwash, which may be beneficial as antimicrobial and anti-fungal, by rinsing before any dental procedures;

- Try to maintain the teeth by endodontic treatment (preferred over extraction);
- Perform extraction of the nonrestorable teeth, using suturing techniques and haemostatic agents in order to ensure the haemostasis;
- Use pain management with Acetaminophen (Paracetamol, Tylenol) in adjusted doses. The administration of Aspirin shall be avoided, because it increases the bleeding potential.

5.2. In posttransplant phase

Considering the increased potential of the post-surgery complications and of the hyperacute or acute graft rejection, during the immediate posttransplant period (the first 3 months) there shall be NO routine dental treatment. The only dental treatment allowed is the noninvasive emergency procedures, but only after taking counsel together with the attending surgeon. During the stabile posttransplant period, usually between 3-6 months after the surgery, when the graft is in healing process and the reactions of acute rejection are under attentive control, the patient is considered to be in a stable phase, allowing to continue the election dental treatment.

Dental management of the stable patient in posttransplant phase may be synthesized as follows [1, 2, 7, 8, 10, 12, 22]:

- Daily control of the microbial dental plaque, on basis of an oral hygiene program established since pretransplant phase, using extra soft toothbrushes for sensitive teeth, mild toothpaste without whitening or tartar control agents to avoid irritation of a dry mouth, mouthwashes containing chlorhexidine 0.12% or without alcohol;
- Attentive examination for an early discovery of dental infection, since immunosuppressive medication can hide signs of such a problem. Thus, the infections may be often in an advanced phase when detected and should be treated accordingly;

- Check patient's blood pressure before the beginning of the dental treatment and if it exceeds accepted levels call immediately patient physician;
- Management of patient's excessive bleeding potential, using blood screening tests and establishing special precautions, depending on the particularities of the case;
- Conduct quadrant scaling and of root planning in gingival inflammations, with the eventuality of introducing antibiotic prophylaxis, due to antibiotic potential of nephro- and hepatotoxicity;
- Avoid certain drugs that are toxic to liver or kidney – non-steroidal anti-inflammatory drugs, local (amides) or general anesthetics (halothane), sedatives (barbiturates, long-acting benzodiazepines), etc;
- At patients with xerostomia use synthetic saliva substitutes, sugar-free chewing gum to stimulate salivary flow and prescribe 1,1% neutral sodium fluoride toothpastes, 0.63% stannous fluoride rinse or 0.4% stannous fluoride gels to minimize the potential of occurrence of root caries [21];
- At patients with oral candidiasis use local antifungal medications: clotrimazole troche 10mg (1 troche slowly dissolved in the oral cavity, 5 times/day, 14 consecutive days) and nystatin oral suspension 5 ml (1 teaspoon maintained in the oral cavity for 2 minutes and then swallowed) [21];
- Counseling the patient for a meticulous oral self-care and emphasizing the importance of maintaining oral health, both before and after the transplantation;
- Initiate an active recall program every 3-6 months, depending on the particularities of the case.

6. Conclusions

6.1 Organ and bone marrow transplant addresses to the marked patients, with end-stage diseases such as: cardiac, hepatic or renal failure, aplastic anemia,

chronic myelogenous leukemia, thalassaemia, falciform anemia or major genetic immunodeficiency.

6.2 The success of an organ or bone marrow transplant depends on the immune reactivity of the recipient organism, which may trigger the rejection phenomena. The immunosuppressive drugs, administrated in the posttransplant phase have the role of inhibiting the immune reactivity, but they have also side effects, with implications at the level of oral cavity, which should be known also by the dentist.

6.3 Both in the pretransplant and posttransplant phase, the dentist should take into account the general medical state of the patient which shall go under any dental treatment. The general medical state of patient and the success of transplantation are priorities in drafting a dental treatment plan, in the case of any patient which shall have a solid organ or bone marrow transplant.

6.4 The efficient dental treatment may have an important role in the favorable posttransplant evolution, especially by preventing the occurrence of severe infections.

6.5 For an optimal dental management of both the patients who are in pretransplant phase and in posttransplant phase it is necessary to permanently collaborate with the patient's attending physician.

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