

DENTAL CLEARANCE FOR KIDNEY TRANSPLANT PATIENT

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ABSTRACT

Organ transplant is a rapidly developing medical field. Dentists play an integral part preparing patients before transplantation, as well as treating them after the procedure. Dental clearance is a written approbation provided by dentist stating that a specified patient's oral health has no issues. Generally, clearance is required for patients in need of certain complicated medical procedures such as joint replacement, heart surgery, joint replacement, organ transplantation.

KEY WORLD: Renal transplantation, Dental clearance, Hemodialysis, Oral manifestation, End-stage renal disease

INTRODUCTION

Kidney is a complex organ that effect extensively many physiological mechanisms and process⁽¹⁾. Chronic renal disease is a progressive disease caused by repeated destruction of renal nephrons. This leads to diminish kidney function over a course of several months or years⁽⁶⁾. Renal transplantation has been one of the medical miracles of the 20th century leading to improve the quality of life of thousands of patients suffering from chronic end-stage kidney disease.

CRF (Chronic renal failure) is cause as a result of kidney damage due to the glomerular filtration

rate being less than 60 ml/min for three months or more. Measurement of serum creatinine is the most widely used measure of renal function. This is however a poor predictor of glomerular filtration rate, as it may be easily hampered by endogenous and exogenous substances, renal tubular handling of creatinine, and other factors like age, sex, body weight, muscle mass, diet, drugs⁽²⁾.

The gold standard for determining renal function is by measuring the glomerular filtration rate (GFR). However, there is not constant range as it varies depending on age, gender, and body size. the normal GFR is approximately 120–130 mL/min/1.73 m².

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People with a GFR $<60\text{ mL/min/1.73 m}^2$ for 3 months are indicated as suffering from chronic kidney disease. This is irrespective of any signs of damage to the kidney. The reduced GFR is usually measured by creatinine clearance (CC), which provided an approximation of the true value of GFR ⁽³⁾.

CRF signifies a critical period in the evolution of chronic renal disease as it leads to major complications and comorbidities that begin early in the course of the disease. These can be subclinical initially but tend to eventually have symptomatic repercussion and are irreversible.

End-stage renal disease (ESRD) occurs due to a decline in a person's kidney function. This can be so severe that it could potentially be fatal if not treated with dialysis or transplantation. ESRD is placed under stage 5 of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative classification of chronic kidney disease (CKD). It describes individuals deemed necessary for treatment who have an estimated glomerular filtration rate less than 15 mL per minute per 1.73 m² body surface area, or patients that require emergency dialysis regardless of their GFR. ⁽⁴⁾

Patients with advanced stage kidney disease need considerations with regards to diseases such as hypertension, anemia, infection, medication used, and oral manifestations associated with the disease or with hemodialysis.

Additionally, in this context, infection from any dental source is a potential threat for both organ transplant candidates and recipients. ⁽⁵⁾

Oral manifestation

Chronic kidney disease CKD patients develop significant systemic complication such as cardiovascular diseases, electrolyte imbalance, as well as suppression of immune response and humoral, exacerbation of inflammatory response, and multiples oral manifestation. Several salivary changes occur in renal patients undergoing hemodialysis, such as

changes in flow rate and composition, leading to several oral manifestations. ⁽⁷⁾

The reduction in salivary flow rate observed in this patient is essentially caused by restriction in fluid intake. In addition antihypertensive drugs can cause salivary gland alteration, atrophy, fibrosis. Oral breathing secondary to lung perfusion problems and acute stress levels can also result in the same phenomenon. The decrease of salivary flow is a contributory factor to xerostomia which compromise the salivary defenses first and can facilitate plaque formation, increased calculus formation and dark staining. There were increased levels of salivary pH & urea levels in patients suffering from chronic renal failure as compared to healthy individuals. In fact, salivary pH values in hemodialysis patients were considerably higher. These findings are in conformity with results of the research conducted by Al Nowaiser *et al.*

Salivary urea is broken into ammonium ions and carbon dioxide by urease. These lead to a halitosis in people with kidney diseases.

In addition, hemodialysis patient present reduced calcium levels. The low level of calcium is a result of an increased synthesis and secretion of PTH (parathyroid hormone) or secondary hyperparathyroidism ⁽⁹⁾.

Patil *et al.* and Bots *et al.*, have reported that in patients undergoing hemodialysis experience altered sense of taste. This can be due to several reasons including high levels of salivary urea and dimethyl and trimethylamine levels, metabolic disorders, taking medications, reduced number of taste buds, changes in salivary flow rate ⁽⁹⁾.

As direct repercussion of anemia developed in hemodialysis patient is pale mucosa. This results from a loss of red blood cells through dialysis or an increased brittleness of these cells which leads to their early destruction. In some cases, it can also result from malnutrition. Candidiasis and increased

vulnerability to human herpes virus 8 is common among transplant patients. White lesions have been reported in ESRD patients. The increased risk of malignant transformation in ESRD patients is most probably a result of iatrogenic immune suppression. A common documented oral manifestation in patients with renal failure is gingival enlargement which is subordinate to the use of cyclosporine utilized as immunosuppressant in transplant patients, and/or calcium channel blockers (nifedipine, amlodipine, diltiazem, verapamil) used in predialyzed and dialyzed patients for management of hypertension. Deficient oral hygiene aggravates this condition. ⁽⁸⁾

In order to keep the patency of AV fistulae essential for regular vascular access, anticoagulants like heparin are used. The consumption of anticoagulants and platelet dysfunction noticed in hemodialysis patient can lead to ecchymosis, petechiae, and/or gingival bleeding.

Periodontitis has been associated not only with poor oral hygiene and increased calculus formation but also by raised Uremic toxins. The increase of ammonia may irritate the oral mucosa and lead to inflammation.

A decrease in the salivary secretions coating the oral mucosa makes it vulnerable to infections and inflammation, resulting in tissue damage to the tongue and causing mucosal pain.

The presence of periodontal disease in CKF patients is complicated by the fact that periodontal pockets can be habitats of bacteria, representing a dangerous source of inflammation and contributing to increased systemic frameworks, morbidity and mortality of these patients.

Patients, with end stage kidney disease, who are undergoing hemodialysis show evident oral and salivary changes and are thus a greater risk. These patients need special considerations, not only due to the complexity of their disease, but also as a result of its manifestations and sideeffects. It is important

to understand that untreated dental infection, especially in immunosuppressed renal patients, tends to result in morbidity and future transplant rejection. Hence a timely diagnosis and treatment of these oral manifestations will substantially help improve their life satisfaction.

Hence, efforts are paramount to establish an effective treatment or management plan for patients undertaking dialysis treatment. ⁽¹⁰⁾

DENTAL CARE PRIOR TO KIDNEY TRANSPLANTATION

Medical History

An individual who suffers from renal disease may have various other diseases as well. These may either be related directly to the transplantation or coexisting due to the procedure. Therefore, a patient's medical history must be verified attentively, allowing the practitioner to take ample measures prior to the required dental treatment.

Medications

Patients may be prescribed various medications that may either have an impact on dental treatment and/or have oral manifestations such as anticoagulant medicines, beta blockers, calcium channel blockers, diuretics, etc. Dentist should be aware of the various side effects from these of these medicines, varying from xerostomia, postural hypotension to hyperglycemia. Many of the medicines that are used for dental treatment (nonsteroidal anti-inflammatory drugs (NSAIDs), opioid analgesics and some antibiotics, are metabolized by the kidneys). Before prescribing any medication, the dentist should recall the renal function and any need for the nephrologist to adjust either the dosage or the administration rate of that medicine ^(5,11).

Anticoagulant treatment

Patients undergoing dialysis require anticoagulant treatment aimed to facilitate easier

blood flow and to allow maintenance of vascular access (12). Hematological tests such as INR*, PT, PTT and CBC should be conducted prior to any oral treatment that may cause increased risk of bleeding. This should be done in conjunction with the nephrologist, therefore keeping in mind the most effective ways to stop potential hemorrhaging. In this way the nephrologist can also decide whether there is a need to temporarily reduce the patient's anticoagulant treatment (13).

In order to control possible hemorrhage, there are some suggested methods.

- Use of oxidized cellulose
- Collagen fibers
- Suturing
- Mouthwash with tranexamic acid 10-15mg/kg per day in 2-3 doses
- Vitamin K administration

CARE BEFORE THE TRANSPLANTATION

Prior to transplantation, non-invasive examination without probing, reassessment of dental history, and dental radiographs should be carried out to figure out a treatment plan.

The patient should be informed about any potential problems that may arise after the transplantation. In addition, oral hygiene instructions should be explained. These include:

- Brushing,
- Use dental floss,
- Changing eating habits if it is necessary,
- Using fluoride solutions and antiseptics such as chlorhexidine.

In case of patients suffering from Chronic Renal Failure, dental treatment must be carried out aggressively prior to transplantation as after transplantation patient's immunity is suppressed in order to avoid rejection (3). Dental treatments at this stage include treatment of gingivitis and/

or periodontitis. Carious teeth with favorable prognosis must be sealed. Root canal therapy is carried out, while teeth with uncertain prognosis (deemed to become a source of bacteremia) should be extracted (17).

If the patient is undertaking cyclosporine, any orthodontic brackets present should be removed, while partial dentures must be adjusted. This is because cyclosporine is an immunosuppressant and may lead to gingival enlargement (11). Dental implant placement ideally should be postponed to a later date to when the patient is stable, and the body has fully accepted the donor organ. In case of placement of implants prior to transplantation, adequate period of healing time and time for assessment of osteointegration should be given (18). Care should be taken that the local anesthesia being administered should be without any vasoconstrictor, to avoid complications of hypertension (19). NSAIDs should be avoided, while Paracetamol being the medication of choice (20).

Patients undergoing corticosteroid therapy for an extended period may require an additional dose of corticosteroid to prevent Addisonian crisis. It is suggested that any dental treatment take place in the morning and any abrupt or unexpected movements be avoided during dental therapy (5,12,16). In addition, the dentist needs to be aware that patients undergoing dialysis have a higher risk of being infected with HIV, HBV, HCV and TB, therefore periodic laboratory testing is essential to avoid cross contamination in the dental office (4,13).

CARE AFTER THE TRANSPLANTATION

Before Dental Treatment

It is important to consult with the nephrologist prior to any dental procedure. In order, to determine if there is any adjustment of dosage or regimen of patient's medications as well to discuss the pharmaceutical treatment the patient will receive by the dentist. (11)

Medications

Patients who had receive organs transplant may be taking many medications which can have an impact on dental procedures. In addition, their immune system might detect the transplanted organ as a foreign body which may cause its rejection either immediately or over time. That is why it is primordial to give transplant patients medicines that suppress the immune system for life. ⁽¹⁰⁾

The basis of most immunosuppressive regimens is prednisolone, a corticosteroid.

In fact, Prednisolone suppresses the immune system. However, it is generally insufficient by itself to prevent the rejection of kidney transplant. Therefore, prednisolone is administered in combination with other nonsteroid immunosuppressive medicines, which should allow for a lower dosage of prednisolone.

Nowadays the most used pharmaceutical regimen is a combination of tacrolimus, mycophenolate, and prednisolone. Alternatively, some patients receive cyclosporine, sirolimus or azathioprine ^(3,10).

It is necessary to take anticoagulant/antiplatelet treatment for a lot of transplant patients suffering from hypertension, diabetes or cardiovascular diseases. Due to the dilemma of adapting the level of Coumarin anticoagulants like warfarin, it is recommended to avoid using it. In fact, renal functions are not totally restored even after the kidney transplantation. Thus, hemorrhage may happen. Even though if the patient is receiving coumarin anticoagulants, recent INR should be required prior to any dental procedure that may cause bleeding. Nephrologist should be consulted for the possibility of dose adjustment in case the INR is above 2.5.

However, if the patient is taking antiplatelet treatment with aspirin or clopidogrel, extraction of up to 3 teeth should be safe without the necessity to stop any medication unless the treating doctor recommended it. ^(3,9,21).

Infection risk

After any organ transplant surgery, patients are at greater risk of developing serious infection either viral bacterial or even fungal. Antibiotics Prescription before any dental procedure should always be made in consultation with the patient's doctor ^(3,17,22). No clear guidelines are present with regards to when prophylactic antibiotic therapy should be indicated to transplant patients.

In a questionnaire given to many doctors working in transplant centers within America, majority declared that they recommend the use of prophylactic antibiotic therapy to all the patients subjected to transplantation or who are about to have any dental treatment. Many also stated that they endorse the AHA's standard regimen to prevent endocarditis as a suggested prophylactic therapy ^(3,7,17,22).

THE FIRST 6 MONTHS AFTER THE TRANSPLANTATION

Dental intervention

During the first 6 months, the patient will receive the highest dosage of immunosuppressive medicines as they are at a greater risk of rejection and developing serious complications. It is therefore paramount that only emergency dental intervention be carried out, preferably in a hospital environment. The treatments must be performed after consultation from the patients nephrologist ⁽¹¹⁾.

During this stage, treatments in the dental office need to be. Emphasis on oral hygiene maintenance is essential and must be followed. The use of a soft toothbrush with fluoridated toothpaste and an antiseptic mouthwash is recommended. Smoking and alcohol consumption should be ceased, and a daily soft diet needs to be implemented. Dentures and orthodontic appliances are removed if traumatizing soft tissues. ^(5,17,18,23).

AFTER 6 MONTHS OF TRANSPLANTATION

No signs of rejection - Dental Treatment

Only selective dental treatment can be performed. These include treatment like scaling, endodontic treatments and fixed prosthodontic work. It should be commented that any periodontal intervention should be carried out in multiple sessions. Also, in each session only a small number of teeth should be scaled. Prior to invasive dental treatments like implants or extraction, a hematological test such as INR, PT, APTT or CBC should be carried out. All measures to prevent hemorrhage should be taken and it is essential to consult with the nephrologist for the need of chemoprophylaxis administration. Patients' nephrologist should adjust the dosage of anticoagulants in order to avoid uncontrolled bleeding. He/she may also need to add or adjust the prescription of corticosteroids prescribed to the patient thus avoiding the possibility of Addisonian crisis. The dentist for their part needs to make sure that the treatment sessions are short and take place in the morning ^(12, 20, 24).

During dental treatment sessions, the patient needs to be evaluated for the presence of soft tissue lesions or malignancies which might result from the ongoing immunosuppressive therapy. Complications, such as candidiasis and secondary recurrent oral herpes may result due to this immunosuppressive pharmaceutical therapy ^(3, 20, 25).

Malignancies occur earlier in such cases. Kidney transplant recipients have shown a higher sensitivity towards epithelial dysplasia which may be due to iatrogenic immunosuppression. Therefore, it is essential that if the dentist observes any suspicious lesion or mucosal changes, he/she must inform the treating nephrologist immediately ^(3, 7, 17, 26).

Transplant rejection by the body - Dental Treatment

Rejection of the transplant may take place within either the first few months or over a period of 5 years. In such cases the dental treatment should

be postponed to a later date and only emergency treatment should be undertaken, that too within a hospital environment. Dental intervention at this stage requires frequent liaisons with the treating nephrologist, as it is they who will determine the patient's prophylactic regimen to prevent bacteremia. The pain medication and other medication adjustments should also be governed by the nephrologist ^(23, 24).

DISCUSSION

Before starting any dental treatment, several factors should be examined: first, antibiotic Prophylaxis may be indicated to avoid any systemic infection prior to invasive dental procedures. Assessment of any postoperative bleeding with the appropriate laboratory tests is primordial to take necessary precautions to limit bleeding. Patients prepared for organ transplantation usually take multiple medications as anticoagulants, beta blockers, calcium channel blockers, diuretics, and others.

Due to this we should consider the side effects caused by these medications; xerostomia and gingival hyperplasia to orthostatic hypotension and hyperglycemia, and their interactions with drugs we might prescribe. Patients with end-stage organ failure may have other major medical conditions that we should take in considerations.

Identification and elimination of active and any potential foci of infection within the oral cavity should be done systematically prior to kidney transplant surgery ⁽¹⁰⁾. However, complete sanitation of oral cavity prior to transplantation is not always achievable. The major elements that modify oral treatment plan are the urgency of transplantation, patient's general health and remission status, peripheral blood counts, nature and complexity of oral disease, patient's financial resources, motivation, and difficult access to dental services ⁽⁷⁾. The first 6 months after transplantation are very critical. In fact, during this period high dose of immunosuppressive medicines are administered to the patient

because of the higher risk of rejection. Only emergency palliative and preventive procedures can be performed. The patient will need to undergo these treatments in a hospital environment and following a nephrologist consultation. Dental hygiene must be maintained using an extra soft toothbrush & fluoridated toothpaste with an antiseptic mouthwash, such as chlorhexidine).

CONCLUSION

In order to find infectious foci and to establish adequate treatment plan, it is important to perform meticulous clinical examination including extraoral and intraoral, and radiographic examinations. These examinations are all part of the protocol for pre-organ-transplant dental evaluation and clearance. Patients should have constant dental follow up in the first 6 months in order to eradicate any oral-source infections which can represent a potential threat to transplant candidates (8).

Conflicts of interest

The authors deny any conflicts of interest related to this study.

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