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Review Article

Oral manifestations, dental considerations and treatment protocols for chronic renal disease or end-stage renal disease

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Abstract

90% of patients suffering from Chronic Renal Disease (CRD) or Chronic Kidney Disease (CKD) show various oral manifestations of the disease. As such, these oral manifestations should be considered as an alarm clock or an early indicator for undiagnosed renal failure. Over the last couple of decades, more and more researchers have noticed the importance of maintaining good oral hygiene in patients with renal disease, especially ESRD patients and transplant candidates. Now, dental protocols have been initiated by them to highlight the psychological aspect of the patient and the importance of maintaining good control of plaque and daily oral hygiene. In this article, we discuss renal disease, its oral manifestations, dental considerations and treatment protocols.

Keywords: Renal system, Chronic renal disease, End-Stage renal disease, Dental Considerations, Treatment protocols.

Introduction

Renal system, also known as Urinary system, or urinary tract, consists of the kidneys, ureters, bladder, and urethra. Its main functions are:

1. Regulate blood volume and composition (e.g. sodium, potassium and calcium)
2. Regulate blood pressure.
3. Regulate pH homeostasis of the blood.
4. Contributes to the production of red blood cells by the kidney.
5. Helps synthesize calcitrol the (active form of Vitamin D).
6. Stores waste product (mainly urea and uric acid) before it and other products are removed from the body.

Urologic disease can involve congenital or acquired dysfunction of the urinary system.[1]

Chronic kidney disease (CKD) is a type of kidney disease in which a person gradually losses kidney function over a period of months to years. Symptoms may include leg swelling, feeling tired, vomiting, loss of appetite, and confusion. There may be complications like an increased risk of heart disease, high blood pressure, bone disease, and anemia.[2]

The most common signs and symptoms of chronic kidney disease include: anemia, blood in urine, dark urine, decreased mental alertness, decreased urine output, edema - swollen feet, hands, and ankles (face if edema is severe), fatigue (tiredness), hypertension (high blood pressure), insomnia, itchy skin, can become persistent, loss of appetite, male inability to get or maintain an erection (erectile dysfunction), more frequent urination, especially at night, muscle cramps, muscle twitches, nausea, pain on the side or mid to lower back, panting (shortness of breath), protein in urine, sudden change in bodyweight, andunexplained headaches.[3]

Diseases and conditions that cause chronic kidney disease include:

1. Type 1 or type 2 diabetes
2. High blood pressure
3. Glomerulonephritis, an inflammation of the kidney's filtering units (glomeruli)
4. Interstitial nephritis, an inflammation of the kidney's tubules and surrounding structures
5. Polycystic kidney disease

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6. Prolonged obstruction of the urinary tract, from conditions such as enlarged prostate, kidney stones and some cancers
7. Vesicoureteral reflux, a condition that causes urine to back up into your kidneys
8. Recurrent kidney infection, also called pyelonephritis
9. Heart and blood vessel (cardiovascular) disease
10. Smoking
11. Obesity
12. Being African-American, Native American or Asian-American
13. Family history of kidney disease
14. Abnormal kidney structure
15. Older age[4]

Oral manifestations of CRD

Oral cavity commonly shows changes like periodontitis and other manifestations of poor oral health in CKD which may contribute to increased morbidity and mortality because of systemic consequences such as inflammation, infections, protein-energy wasting, and atherosclerotic complications. There is increased incidence of decayed, missing, and filled teeth, loss of attachment, and periapical and mucosal lesions in uremic patients than the general population because of advanced age, common comorbidities such as diabetes, concurrent medications, and a state of immune dysfunction that may increase the risk for systemic consequences of periodontitis and other oral and dental pathologic conditions.[5]

Major signs of CKD are uremic odor, dry mouth, taste change, petechia and/or ecchymosis and increase of tongue coating. There is decrease in flow rates of unstimulated whole and stimulated parotid saliva while the pH and buffer capacity of unstimulated whole saliva are increased.[6]

CRD patients often show ammonia-like smell, dysgeusia, stomatitis, gingivitis, decreased salivary flow, xerostomia, and parotitis due to reduced erythropoietin which results in anemia ecchymosis, petechiae, and hemorrhages in the oral cavity, causing pain and inflammation of the tongue and oral mucosa. It can also result in altered taste sensations, as well as bacterial and candidiasis infections. Dry mouth, caused by restricted fluid intake (necessary to accommodate the reduced excretory capacity of the kidney), adverse effects of drug therapy, and the low salivary flow rate, odorous breath (uremic breath) and sensations of metallic tastes in the mouth (uremic fetor) are also commonly observed.

Renal osteodystrophy is common in CRD patients, resulting from disorders in calcium, phosphorus, or vitamin D metabolism and increased parathyroid activity, which manifests as demineralization, decreased trabeculation, and a "ground-glass" appearance of the bone with decreased cortical bone thickness, loss of lamina dura, radiolucent giant cell lesions, maxillary brown tumors, enlargement of the skeletal base, and metastatic soft-tissue calcification. Patients have an increased risk of jaw fracture due to trauma or oral surgery. Socket sclerosis is commonly seen in patients with CRF, with the incidence of pulp calcification high in both renal transplant and hemodialysis patients.

CRF patients show elevated serum fluoride concentration, causing fluorosis, which might result in enamel hypoplasia, especially in children where incidence rates of enamel hypoplasia range from 31% to 83%. The risk of caries formation is increased by poor oral hygiene and a carbohydrate-rich diet (necessary to reduce the renal workload), in addition to disease-related debilitation, hypoplastic enamel, low salivary flow rate, and long-term medication use.[7]

Gingival inflammation might occur due to plaque accumulation and poor oral hygiene and gingival enlargement secondary to drug therapy or transplantation. Gingival enlargement is aesthetically bad and might distort occlusion, which has adverse psychological impacts on the patient, interferes with the normal oral function, speech, and oral hygiene, and results in delayed or ectopic eruption.

CRD patients also show stomatitis, occurring due to a loss of tissue resistance. Uremic stomatitis has two forms: the erythematous form, characterized by red burning mucosa covered with a gray exudate and pseudomembrane; and the ulcerative form, characterized by frank ulceration with redness and a pultaceous covering. These lesions are commonly painful and most often appear on the ventral tongue and anterior mucosal surfaces. They heal

spontaneously once the underlying uremia and elevated BUN levels are resolved.

White patches of the skin, called "uremic frost," is occasionally seen intraorally. Uremic frost results from the formation of urea crystal on the epithelial surfaces after perspiration and saliva evaporation, which is different from candidiasis that occurs as patients lose the ability to fight infection, like transplant patients.[8]

Dental considerations and management of the patient with chronic renal disease

CRD patients often have bleeding tendency, hypertension, anemia, drug intolerance, increased susceptibility to infections and the presence of several manifestations associated with either the disease or its treatment. Patients have increased susceptibility to infective endocarditis, valvulopathies, particularly cardiac valvular calcification, and vascular access infections due to hemodialysis.

Many antibiotics are actively removed by the kidney, so their dosage and frequency has to be adjusted. Penicillin, clindamycin and cephalosporins are preferred. For non- narcotic analgesics, paracetamol is preferred and the remaining NSAIDs are avoided, as they produce hypertension. Benzodiazepines can be prescribed without dose adjustment. Narcotic analgesics do not need a dose adjustment either.

For severe gingival enlargement, a surgical treatment should be performed (gingivectomy). The clinical decision of performing the surgery is based generally in the presence of functional discomfort and esthetic alteration.

General considerations for dental management

For conservative medical treatment or periodontitis, patients do not generally require special measures regarding dental treatment, apart from avoiding nephrotoxic drugs (such as tetracyclines or aminoglycosides) and monitoring blood pressure during the procedures due to the frequent hypertension.

In diabetic dialysis patients, hypoglycemic agents and nutritional alterations can trigger hypoglycemia due to diminished gluconeogenesis, reduced insulin clearance by the kidney, and improved insulin sensitivity following initiation of renal replacement therapy. Detailed evaluation of antidiabetic regimen and nutritional patterns, patient education on self-monitoring of blood glucose, and/or referral to a diabetes specialist should be done.

Risk of Bleeding: Dental treatment with risk of bleeding should be postponed to non-dialysis day since the anticoagulant effect of heparin is absent, the bloodstream is free from toxic metabolites, and the patient is not debilitated by the treatment.

The administration of a heparin antagonist (protamine sulphate) can reduce the rate of bleeding in case of urgency. However, bleeding tendency remains due to anemia and alteration in platelet aggregation and adhesiveness. A hematologic study before planning any invasive treatment should be done to give information about coagulation times, platelets count, hematocrit, and hemoglobin. In renal patients taking warfarin, International Normalized Ratio (INR) should be measured. Local hemostatic measures (compression, cold applications, tranexamic acid, cellulose sponges, and sutures) can be used in case of local hemorrhage and are generally sufficient to obtain hemostasis.

Medications: Local anesthetics have a hepatic elimination so they can be safely used. Paracetamol is the best choice for pain management, and also codeine can be used without modification of the dosages. Other NSAIDs could cause hypertension and worsen the bleeding tendency, while aspirin is contraindicated because it increases platelet dysfunction, the risk of gastric hemorrhage, and contributes to the deterioration of renal function. Patients who have been treated with high doses of corticosteroids for a long time and or in stressful situations may require steroid supplementation prior to dental treatment to avoid an episode of adrenal crisis. Dental sessions should take place in the morning, in a quiet environment and that abrupt and unexpected movements be avoided during therapy.

Antibiotic Prophylaxis and Therapy: Patients affected by ESRD are more susceptible to infective endocarditis. Furthermore, patients in hemodialysis can develop infections of the vascular access (endarteritis) that can become itself the source of bacteremia, and thus, benefit from antibiotic

prophylaxis, especially in the 6 months after the creation of the vascular access. In the cases of an acute or re-exacerbated dental infection (periapical periodontitis; periapical, or periodontal abscess), a complete cycle of antibiotic therapy should be administered using non-nephrotoxic antibiotics. Penicillin and its derivatives, clindamycin and cephalosporins are safer antibiotics for these patients. Aminoglycosides, tetracyclines, and polypeptide antibiotics should be avoided because of their nephrotoxicity.

Psychological Aspect: A poor quality of life with depression have been associated with patients undergoing hemodialysis, and a reduction of compliance with health protocols should be expected in a higher percentage of patients compared with general population. Patients on hemodialysis have poor oral health status, OHRQoL (oral health-related quality of life), and GHRQoL (general health-related quality of life) compared to healthy subjects. Conversely, some researchers think that the patient's perception does not reflect the oral deficiencies and that education and motivation of these patients represent a focus in oral health maintenance.

Special considerations for dental treatment in CRD Patients

Patient with renal disease in conservative medical treatment: Nephrologist should be consulted to be aware of the stage of the pathology suffered and the treatment prescribed. Before any invasive dental procedure, possible hematologic problem in the patient should be studied and infective foci should be removed. Due to the frequent hypertension, blood pressure should be monitored. When prescribing drugs, those that are nephrotoxic must be avoided.

Patient with renal disease in peritoneal dialysis: In cases of peritoneal dialysis, a catheter is placed in the abdominal wall and inserted in the peritoneum achieves access to the body, in order to remove nitrogen and other metabolic toxic products; through this, a hypertonic glucosated solution is introduced. Peritoneal membrane of the patient filters blood waste products by means of an osmotic mechanism, so they would be transferred to the electrolytic solution and then evacuated to the exterior. This form of dyalisis can be performed at home, but must be done every day. These patients do not require special measures with regard to dental treatment.

Patient with renal disease in hemodialysis: In hemodialysis, the filtering process is carried out by a machine (dialyzer), outside the patient's body. Permanent access is obtained by surgically connecting an artery to a vein, using a blood vessel (arteriovenous fistula) or a synthetic bridge (arteriovenous graft). A special solution (dyalisate) corrects the chemical disturbances and impurities of the blood, which is then introduced into the body. During the process of hemodialysis, the patient's blood is anticoagulated with heparin to facilitate blood transit. For this reason, dental treatments with a risk of bleeding must not be performed the day of hemodialysis. If an emergency dental treatment must be performed, protamine sulphate (heparin antagonist) can be administered to block the anticoagulant effect. There is a risk of infection because of the vascular access, and of transmission of HBV, HCV and HIV.

Renal transplant patient: These patients are immunosuppressed by medication. Maintenance of a proper oral health is especially important asoral infections in transplant patients can contribute to its morbidity or even rejection. They are usually receiving a treatment of corticosteroids, calcineurin inhibitors and inhibitors of lymphocyte proliferation. Long-standing treatment with high doses of corticosteroids produces an adrenal function suppression, which predisposes the patient to suffer an acute complication, adrenal crisis, when exposed to stressful situations (disease, infection, surgery). Furthermore, this chronic excess of corticosteroids can cause Cushing's syndrome. To minimize the risk of suffering an adrenal crisis in patients taking high doses of corticosteroids who are undergoing a surgical procedure, they should take a double dose of corticosteroids the day of the surgery. This supplement will not be necessary if the patient is being treated with low doses (less than 7.5 mg of prednisolone) or if the patient is undergoing a conservative treatmen. However, the risk of developing an adrenal crisis after oral surgery procedures under local anesthesia is very low and the majority of dental treatments can be

carried out without prescribing a supplement of corticosteroids.[9]

Operative Protocols for dentists for CRD patients

Because of the increased incidence and severity of periodontitis in the hemodialysis population, the dentist should remember that the lack of oral hygiene may put the patient at higher risk of local or disseminated infection because of the persisting daily episodes of bacteremia from the oral cavity. The spread of oral bacteria can be reduced by the elimination of oral foci and by reducing the grade of mucosal and gingival inflammation. A good oral hygiene and the absence of dental foci represent a fundamental step to receive a preemptive kidney transplant. Also, an efficient dental treatment with maintenance of good oral hygiene should be maintained in the post-transplant phase. Furthermore, adequate plaque removal and the treatment of gingivitis and periodontitis can avoid or minimize gingival hypertrophy due to assumption of immunosuppressive drugs.

The dental practitioner should know the correct practical approach and the operative sequences to follow when treating renal patients. From the first appointment, it is fundamental to have the patient recognize the importance of oral health maintenance.

An accurate medical history should be collected with particular reference to ESRD-related illnesses, medications and their dosage, blood parameters, timing, and type of dialysis performed. The dental exam is a noninvasive complete assessment of dental, periodontal, and mucosal tissue. Compression of the arm with the vascular access for hemodialysis, should be avoided. All possible foci and oral pathologies have to be intercepted. Radiographs should be taken. A periodontal chart should be performed if periodontitis is suspected.

The treatment plan for periodontal disease must include the assessment of the patient's oral hygiene. Therapy of gingivitis and periodontitis should consist primarily in accurate motivation and instruction for home oral hygiene, adapted and personalized to the necessities of the patient. Mechanical removal of supra- and subgingival calculus should be performed with ultrasound devices and curettes.

Carious lesions must be recognized and when necessary pulp vitality should be tested. In the presence of pulp necrosis and/or apical lesions, endodontic treatment, apicoectomy, or extraction should be performed. In cases of peri-implantitis, surgical removal of the implant should be performed. The surgery should be as atraumatic as possible to avoid maxillo-mandibular fractures due to renal osteodystrophy.

In the presence of suspected mucosal lesions that do not resolve in 7–10 days, a biopsy must be performed. Before any procedure that could lead to bleeding, a 15 ml rinse of chlorhexidine 0.12% for 60 seconds is recommended to reduce the amount of oral bacteria that could reach the bloodstream.

Adaptation of removable prostheses should be done to determine the necessity of adjustment or substitution, and the patient should be instructed regarding the cleaning and maintenance of the device.

Orthodontic appliances can be maintained if they do not interfere with oral hygiene. The removal of orthodontic brackets is indicated just before transplantation because the immunosuppressive therapy administered in the post-transplant period can induce gingival overgrowth that seems to be much more accentuated in the presence of fixed appliance.

After the first cycle of dental therapy, all patients should have a strict follow-up program to maintain the results obtained and to maintain a high level of compliance. The frequency of follow-up depends on the needs and motivation of the patient as they could be psychologically affected and poorly compliant with respect to dental appointments. For this reason, the education on the importance of oral health is crucial to maintain the best motivation of the patient. At each appointment, a review of medical history is indicated and a complete noninvasive examination of the oral cavity should be repeated. Radiographs must be performed if the presence of new foci is suspected.

It is important that this protocol is followed until the patient undergoes renal transplantation. In fact, the adherence to periodic follow-up reduces the risk of oral infection just before the transplant and avoids the possibility of losing the compatible organ because of an acute infection from a dental source.[10]

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