Review Article

Oral manifestations in renal disease and its related complications

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Abstract

The systemic condition of patients with kidney failure has oral manifestations and specific implications for dental treatment. Dental problems may compromise the patient’s general health and hinder medical efforts to either maintain or replace vital kidney functions. Specifically, the dentist must consider bleeding tendency, risk of infection and medications before treating the patient. Oral and dental health has served as a valuable indicator in measuring the prognosis of chronic kidney disease, while, its role in diagnosing renal pathosis requires to be explored further. Consultation with the nephrologist is essential before any dental treatment is carried out, in order to determine the condition of the patient, define the best moment for dental treatment, introduce the necessary pharmacological adjustments, or to establish other important aspects for preventing complications in the dental clinic. This manuscript reviews the characteristics of the disease, the existing therapeutic options, and the considerations of relevance for the dental professional.

Keywords: Kidneys, Chronic renal disease, Dental Management

Introduction

The kidneys have a number of important functions: (a) Excretion of metabolic waste products. (b) Electrolyte regulation through the control of sodium, potassium and water excretion, and acid-base homeostasis. (c) Endocrine regulatory functions: eicosanoids (prostaglandins, thromboxanes, leukotrienes, prostacyclins, etc.), erythropoietin (EPO), the renin-angiotensin system, and vitamin D metabolism. Renal failure is mostly due to the decrease in glomerular filtration rate (GFR). The consequences are high blood pressure, weight loss, anaemia, neuropathy and osteodystrophy. Chronic renal disease (CRD), a progressive and irreversible decline
in renal function, is the renal disease with the most implications in dentistry. CRF is defined on the basis of a glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m², or by the evidence of renal damage (micro- or macroalbuminuria, persistent hematuria, radiological anomalies) during a period of more than three months. Chronic renal failure (CRF) is characterized by a gradual reduction in the number of functional nephrons.

**Clinical manifestations**
The early signs of chronic renal failure are subtle and may take long time before people tend to notice any symptoms. The symptoms that can easily be detected especially by the patient himself are increased urination, blood in the urine and urine that is cloudy or tea-colored. Other symptoms aren’t obvious, but are a direct result of the kidneys’ inability to eliminate waste and have to be clinically tested.

**Oral manifestations** Up to 90% of patients with renal insufficiency show oral signs and symptoms in soft and hard tissues, some of them being a cause of the disease itself and others deriving from the treatment of the pathology.

**Halitosis** -The diminished function of the kidneys results in an increase in the levels of urea in the blood and also in the saliva, where it will turn into ammonia. For this reason, uremic individuals have a characteristic halitosis (*uremic fetor*). Apart from urea, other factors possibly implied are the increase in the concentration of phosphates and proteins and changes in the pH of saliva.

**Altered taste sensation** - especially, sweet and acid flavours-. These can be due to the high levels of urea, the presence of dimethyl- and trimethyl- amines, or low zinc levels (due to the malabsorption derived from gastrointestinal disorders). Metallic taste due to increased concentration of urea in saliva and its transformation into ammonium.

**Xerostomia (dry mouth)**- as a result of the restriction in fluid intake, the side effects of drugs (mainly antihypertensive agents), possible salivary gland alteration (atrophy of minor salivary gland’s parenchyma), and oral breathing secondary to lung perfusion problems.

**Uremic stomatitis**- an uncommon clinical observation associated to uraemia. As many as four types of uremic stomatitis have been described: erythemo-pultaceous, ulcerative, hemorrhagic and hyperkeratotic. The lesions are very painful and most often appear on the ventral surface of the tongue and on the anterior mucosal surfaces. Clinically, it is characterized by the presence of erythematous lesions which are localized or generalized. These lesions are covered by pseudomembranous exudates that can be removed, leaving an intact or ulcerated mucosa. As there are no histological pathognomonic signs of this manifestation, the definitive diagnosis will be made combining clinical findings and excluding other diseases with the histopathology. It does not require a specific treatment and an involution will usually occur after uraemia is restored (1); but in order to assist lesion healing, 10% hydrogen peroxide gargles (1:1 in water), 4 times a day, can be recommended. These lesions are resistant to treatment for as long as the blood urea levels remain
high\textsuperscript{10}, and heal spontaneously within 2-3 weeks once the background renal disorder has been resolved\textsuperscript{9,10}. Gingival bleeding, petechiae and ecchymosis, also seen resulting from platelet dysfunction and the effects of anticoagulants\textsuperscript{4,7,8}.

**Gingival inflammation** - There is some controversy in the literature in relation to gingival inflammation in patients with CRF, since some studies report low incidences of gingivitis -explained in terms of immune suppression and uraemia, which would inhibit gingival inflammatory response to plaque accumulation – while other studies report the opposite\textsuperscript{13}.

Gingival hyperplasia secondary to drug treatment, which is one of the most widely, documented oral manifestations in patients with renal failure. Such hyperplasia can be induced by cyclosporine, and/or calcium channel blockers (nifedipine, amlodipine, diltiazem, verapamil, etc.). The condition in turn is aggravated by the deficient oral hygiene. A number of studies suggest that replacing cyclosporine with tacrolimus may reduce the severity of gingival hyperplasia, and in any case thorough oral hygiene is required \textsuperscript{13,14,15}. The problem also can increase in incidence and severity when combining cyclosporine and nifedipine this suggesting an additive effect. Hyperplasia mainly affects the labial surface of the interdental papilla, though greater extensions can be affected - including the gingival margins and lingual and palatal surfaces. Periodontal problems with important attachment loss, recesses and deep pockets \textsuperscript{13,16}.

**Enamel hypoplasia** – Related to alteration in calcium and phosphorus metabolism. Erosions on the surface of the teeth because of acidic regurgitation and vomiting induced by uraemia. Pulp obliteration due to calcium and phosphorus metabolism. Delayed eruption, changes in maxillary bone and these changes comprise bone demineralization with trabeculation, cortical loss, giant cell radiotransparencies or metastatic calcifications of the soft tissues. Increased risk of fracture when suffering from chronic renal disease while doing other treatments such as extractions, tooth mobility etc.

**Caries**- Diminished prevalence of caries due to urea which inhibits bacterial growth and neutralizes bacterial plaque acids. Sometimes an antibacterial effect has been attributed to the increase of the pH (due to urea hydrolization by saliva), which suggests a protective function against caries. However, non-carious tooth tissue loss is more prevalent in individuals with chronic renal disease than in the general population. This may be due to nausea, oesophageal regurgitation, or induced vomiting in bulimia nervosa (in patients who dislike the restrictive diet, which is suggested as a part of the treatment)\textsuperscript{5}. The majority of studies agree that there is a greater incidence of periodontal disease, bone loss, recessions and deep periodontal pockets\textsuperscript{17} with increase in formation of tartar due to increased level of urea in saliva. **Infections** - Oral hygiene of patients receiving haemodialysis is usually poor, so deposits of calculus and plaque may be increased. Treatment received by patients with renal disease also produces oral clinical manifestations. In particular, lichenoid disease may arise, associated with antihypertensive medication (diuretics, beta-blockers).\textsuperscript{5,16} Kidney- transplanted patients are given a lifelong immunosuppressive therapy, and therefore more susceptible to infections and to the development of
malignant neoplasms. Where fungal infections are concerned, there are mainly lesions related to *Candida albicans*. Various forms of candidiasis have been reported in allograft recipients: pseudomembranous (1.9%), erythematous (3.8%), chronic atrophic – also called prosthetic stomatitis (3.8%). It should be highlighted that these figures may underestimate the increased susceptibility of immunosuppressed allograft recipients to fungal infection, since systemic anti-fungal agents are commonly prescribed prophylactically. The herpes group of viruses, in particular cytomegalovirus (CMV) and herpes virus simplex (HSV), are frequently associated with immunosuppressed organ transplant recipients. Mucosal ulceration is often associated with CMV, having a predilection for the lateral borders of the tongue. Due to this immunosuppression, a reactivation of HSV, characterized by the onset of recurrent, severe and long-standing infections. In the case of recurrent infections of HSV in these patients, doses of 400 mg of acyclovir can be administered orally, 3 times a day during 10 days or more (usually, more than 2 weeks).

**Malignization** - effects of iatrogenic immune suppression that leads to tumours.

**Treatment:**

a) **Conservative management.** Such treatment aims to prevent or correct the metabolic alterations and preserve the remaining renal functional capacity. The measures include a high carbohydrate and low protein diet (though consensus is lacking on this point), body weight control, treatment with antihypertensive drugs, lipid lowering agents, vitamin D supplements, and correction of the anaemia with erythropoietin.\(^\text{18,19}\)

b) **Renal replacement therapy** is considered when conservative management fails to be effective against the progression of renal deterioration, and comprises dialysis and renal transplantation.

c) **Prevention of infections.** Infections are one of the most important causes of morbidity and mortality in chronic renal failure. Vaccination is therefore potentially very useful in patients of this kind, though such treatment is underused, since no clear guidelines have been established, and vaccination response with the normal doses and regimens may be limited.\(^\text{20}\)

**Prognosis:** The life expectancy of patients on dialysis remains sombre (approximately one-third that of the general population). The prognosis of individuals with diabetes mellitus and/or hypertension is poorer than that of patients with glomerulonephritis. The most common causes of death among patients with ESRF are cardiovascular problems (about 50% of global mortality) followed by infections and malignization.\(^\text{21}\)

**Dental management of renal failure patients**

Patients with renal failure require special considerations in relation to dental treatment, not only because of the conditions inherent to the disease and its multiple oral manifestations, but also because of the side effects and characteristics of the treatments they receive.
Consultation with the nephrologist provides information on the state of the disease, the type of treatment, the best timing of dental management, or the medical complications that may arise. Any modification of the usual medication used by the patients or of other aspects of their treatment must first be consulted with the nephrologist.

Close cooperation between medical and dental professionals is desirable in order to improve the oral and general health of the patient, based on the creation of a dental care program in the context of a multidiscipline approach to the disease. Prior to any invasive dental treatment, a complete blood count is to be obtained, together with coagulation tests, in view of the possible haematological alterations.

It is essential to eliminate any infection in the oral cavity as soon as possible, with the consideration of antibiotic prophylaxis when bleeding and/or a risk of septicaemia is expected. Blood pressure is to be monitored before and during treatment, with the administration of sedation to lessen anxiety.

**Drug complications:** The metabolism and elimination of certain drugs are altered in situations of renal failure. In such cases dose adjustment or modification of the dosing frequency is needed. The prescription of aminoglycoside antibiotics and tetracyclines is to be avoided, because of their nephrotoxicity. Penicillins, clindamycin and cephalosporins can be administered at the usual doses, and are the antibiotics of choice – though the dosing interval should be prolonged. As regards analgesics, paracetamol is the non-narcotic analgesic of choice in application to episodic pain. Aspirin possesses antiplatelet activity, and as such should be avoided in uremic patients. As regards the rest of nonsteroidal anti-inflammatory drugs (indomethacin, ibuprofen, naproxen and sodium diclofenac), dose reduction or even avoidance is indicated in the more advanced stages of renal failure, since they inhibit prostaglandins and generate a hypertensive effect. Benzodiazepines can be prescribed without the need of dose adjustments, though excessive sedation may occur. The narcotic analgesics (codeine, morphine, fentanyl) are metabolized by the liver, and so usually do not require dose adjustment.
Conclusion
The most important renal pathology in dentistry is CRD. Up to 90% of patients with CRD show oral signs and symptoms, such as bleeding tendency, greater susceptibility to infections and gingival overgrowth produced by cyclosporine. Recognition of the oral manifestations of this disease is important, since they may be indicators of the presence or extent of a specific disease and may therefore be useful to the clinician in diagnosing the disorder, determining treatment requirements, or assessing the prognosis of the disease in question. Dentists will probably see more dialysis patients in the future, given the 10% to 15% annual growth in the incidence of endstage renal disease. All parties must be knowledgeable about the treatment priorities, operative concerns and precautions to be taken in this special population.

References