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Management of Oral Health in the End Stage of Renal Disease Undergoing Hemodialysis: A Review

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ABSTRACT:

A long-term disorder called chronic renal failure is defined by the slow loss of nephrons and the subsequent deterioration in kidney function. Renal replacement therapy such as peritoneal dialysis, hemodialysis, or transplantation is required by individuals in the final stages of renal disease (ESRD). Individuals with end-stage renal disease (ESRD) or hemodialysis are at risk of developing a variety of comorbidities, including hypertension, anaemia, and increased bleeding risk, susceptibility to infections, drug-related side effects, and oral symptoms related to the disease and treatment. Given their association with infection, inflammation, and malnutrition, oral illnesses emerge as a potentially preventable factor leading to poor health outcomes in people with ESRD. The objective of this article was to examine manifestations related to end-stage renal disease (ESRD) and hemodialysis, while outlining dental operative protocols for individuals awaiting kidney transplantation based on the latest literature.

Introduction

Oral health serves as a potential factor influencing health outcomes in individuals with end-stage renal disease (ESRD). Adults experiencing ESRD exhibit more pronounced oral health issues compared to the general population, including dental disorders. The presence of oral disorders is connected with inflammation and malnutrition, which may accelerate cardiovascular events in ESRD patients. Moreover, within the realm of kidney transplantation, the potential risk of infection originating from dental sources is a concern for both candidates awaiting organ transplant and the recipients. Dental problems are common, but in the transplant population, they are more severe and go untreated.[1] This study investigates the literature concerning overall and specific considerations for dental care in individuals with end-stage renal disease (ESRD) during the pretransplant phase, taking into account systemic issues and treatments that may impact clinical practice.

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Chronic Renal Disease: General Considerations- Chronic renal failure is a long-term condition characterized by the slow loss of nephrons, which leads to a reduction in kidney function over several months or years. With the progression of this process, there is a reduction in the glomerular filtration rate (GFR), accompanied by an increase in serum urea levels.[2] The glomerular filtration rate (GFR) is the speed at which glomeruli generate an ultrafiltrate of plasma per unit of time, serving as the most accurate measure of the number of functioning nephrons or functional renal mass. Typical GFR levels fall within the range of 120 to 130 mL/min/1.73m², with variations based on age, gender, and body size. Individuals maintaining a GFR of 60 mL/min/1.73m² for three months are categorized as having chronic kidney disease, irrespective of the presence or absence of kidney injury. A reduction in glomerular filtration rate (GFR) is frequently assessed through creatinine clearance (CC), offering a reasonable estimate of the GFR quantity.[3] In clinical settings, CC can be indirectly determined by blood creatinine levels (normal range: 0.5-1.4 mg/dl)[4] using various formulas such as the Chronic Kidney Diseases Epidemiologic Collaboration (CKD-EPI) equation or the Modification of Diet in Renal Disease (MDRD) equation. Clinical, instrumental, and laboratory findings can be employed to categorize the progressive decline in renal function. Stage 1: Slightly diminished function involves kidney damage with a normal or relatively high glomerular filtration rate (GFR) (≥90 mL/min/1.73m²). Kidney damage is characterized by pathological abnormalities or markers of damage, including anomalies in blood or urine tests, biopsy results, or imaging studies. Stage 2: Mild reduction in GFR (60–89 mL/min/1.73m²) occurs with accompanying kidney damage. Stage 3: Moderate reduction in GFR (30–59 mL/min/1.73m²). Stage 4: Severe reduction in GFR (15–29 mL/min/1.73m²) signifies preparation for renal replacement therapy. Stage 5: Established kidney failure or end-stage renal disease (ESRD) (GFR <15 mL/min/1.73m²) necessitates permanent renal replacement therapy (RRT). The primary contributors to end-stage renal disease (ESRD) are hypertension and diabetes mellitus, both of which exert detrimental effects on patients' cardiovascular and renal systems both pre- and post-transplantation.[5] Cardiovascular disorders, particularly atherosclerosis, stand as the predominant cause of mortality among kidney transplant recipients. Additionally, ESRD can stem from conditions such as glomerulonephritis, chronic pyelonephritis, urologic disorders, and autoimmune diseases.[6] The leading cause of mortality in individuals with end-stage renal disease (ESRD) is cardiac arrest, followed by infection and malignancy. Treatment for chronic renal insufficiency involves dietary modifications and addressing systemic issues. ESRD, often referred to as the uremic syndrome, necessitates kidney dialysis or transplantation. While dental treatment is generally feasible in stages 1–3, individuals in advanced kidney disease (stages 4-5) require careful consideration, particularly regarding hypertension, anaemia, bleeding risk, susceptibility to infection, medications used, and oral manifestations associated with the disease and hemodialysis treatment.

ESRD and Dialysis

End-stage renal disease (ESRD) is marked by compromised endocrine and metabolic functions of the kidneys, leading to the retention and accumulation of harmful metabolites. Due to fluid overload and the production of vasoactive hormones through the renin-angiotensin system, blood pressure elevates, heightening the susceptibility to congestive heart failure. As chronic kidney disease advances, the capacity to produce renally hydroxylated 1,25 vitamin D diminishes, leading to insufficient levels of 1,25 vitamin D[7]. Additionally, the synthesis of erythropoietin decreases, potentially causing anaemia. Moreover, the qualitative malfunction of platelets, coupled with anaemia, contributes to a heightened tendency for hemorrhagic events in individuals with uremia. Uremic bleeding is primarily attributed to platelet dysfunction, characterized by reduced platelet aggregation and impaired platelet adhesiveness. This impairment is multifaceted, involving both intrinsic platelet abnormalities and abnormal platelet-endothelial interaction. Uremic toxins and anaemia further contribute to this dysfunction. Correction of platelet dysfunction becomes essential for patients experiencing active bleeding or preparing for a surgical procedure, such as a kidney biopsy. Platelet dysfunction in uremic patients can be managed with desmopressin, an antidiuretic hormone analog with limited vasopressor effect, conjugated estrogen therapy, or cryoprecipitate infusion.[8] These interventions can effectively reduce bleeding time in many uremic patients. In addition, individuals with end-stage renal disease (ESRD)

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experience immunodeficiency characterized by diminished cellular immunity due to malnutrition, heightened vulnerability to bacterial infections, and a compromised ability to produce antibodies.[9] In cases of advanced renal disease, essential interventions like dialysis become imperative. Dialysis, a life-saving operation, has significantly extended life expectancy, especially in younger patients. A dialyzer is a machine that makes hemodialysis possible, which incorporates semipermeable membranes allowing the removal of excess fluid and waste products. Access to the bloodstream is typically achieved through arteriovenous shunts or fistulas. End-stage renal disease (ESRD) causes a persistent buildup of harmful chemicals, necessitating three to four hours of hemodialysis per day, three times per week. It's crucial to note that the efficiency of this process is significantly lower than that of a functioning kidney. Consequently, individuals with ESRD undergoing hemodialysis are consistently in a state of kidney failure and experience hyperuremia.[10] The continuous presence of the uremic syndrome, even in hemodialyzed patients, has been identified as a major factor contributing to the various systemic complications observed in this population. Peritoneal dialysis (PD) offers increased flexibility by placing a catheter through the abdominal wall into the peritoneum, which functions as a membrane capable of filtering catabolic products from the local capillaries.[11] While both hemodialysis and PD address numerous hematologic dysfunctions associated with uremia, it's important to note that these treatments can also exacerbate certain challenges already present in end-stage renal disease (ESRD). To maintain access patency and facilitate the filtration of harmful blood compounds, such as urea through the dialysis membrane, hemodialysis requires the administration of an anticoagulant, either regionally or systemically, typically in the form of heparin. However, the use of heparin in combination with mechanical stress on platelets can reduce the overall platelet count and heighten the risk of hemorrhage. This inclination is further intensified by pre-existing capillary fragility and anaemia. Additionally, patients often experience hypertension due to salt and water retention, as well as the activation of the renin-angiotensin system.[16] Sudden death stands as the predominant cause of mortality in patients undergoing dialysis, while infection is a frequent contributor to morbidity and mortality in individuals receiving hemodialysis therapy.[12] The vascular access increases the risk of endarteritis and endocarditis, with approximately 2.7% of patients experiencing these conditions during hemodialysis and 9% among those with an infection of the vascular access.

Oral Manifestations

Approximately 90% of people with chronic renal failure are predicted to develop oral symptoms. However, due to developments in hemodialysis technology, many of the oral symptoms associated with renal failure and uremia, as detailed below, are no longer often recognized. Oral manifestations include mucosal and glandular tissues, the gingival and periodontal apparatus, maxillary and mandibular bone, and overall dental health.[13] Pallor of the mucosa, often induced by anaemia (resulting from reduced erythropoietin synthesis), is the most prevalent oral finding in dialyzed patients, particularly in relation to mucosal and glandular involvement. The patients' propensity to bleed is maintained by renal anaemia and alterations in platelet aggregation. Moreover, hemodialysis elevates the risk of oral mucosal bleeding, petechiae, and ecchymoses.[14] Xerostomia, defined as the subjective sensation of a dry mouth, is linked to the total volume status of patients who are restricted from eating excessive fluids, rendering them more prone to retrograde parotitis. About one-third of individuals undergoing hemodialysis experiences a distinctive form of bad breath known as "uremic fetor" and may also encounter a metallic taste, attributed to elevated urea levels in saliva and its subsequent breakdown into ammonia. Moreover, elevated urea levels in saliva and the presence of dimethyl and trimethyl amines can alter the perception of sweet and acid flavours for patients.[15] Those undergoing dialysis may also encounter a burning sensation in their lips and tongue, along with a feeling of an enlarged tongue. Uremia stomatitis, a rare oral complication with an unknown origin. The lesions are made up of erythematous patches coated in pseudomembranous exudates that can be removed to show either an intact or ulcerated mucosa.[16] Typically, these lesions are unpleasant and appear on the ventral tongue and anterior mucosal surfaces. They usually cure on their own when the underlying uremia is treated and the blood urea nitrogen (BUN) level is decreased. Nevertheless, gargling with 10% hydrogen peroxide

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four times a day may be recommended to expedite lesion healing. Angular cheilitis has been documented in over 4% of patients undergoing hemodialysis, and lichenoid disease may emerge in association with antihypertensive medication. According to a study by Naugle et al., it was proposed that all individuals undergoing renal dialysis displayed some form of periodontal disease. Furthermore, diabetic nephropathic patients exhibited deeper periodontal pockets when compared to nondiabetic patients with end-stage renal disease (ESRD).[17] Furthermore, there is a considerably elevated demand for surgical treatment of periodontitis in patients awaiting kidney transplants as opposed to those not undergoing organ transplantation. Periodontitis itself contributes to systemic inflammation and has been linked to adverse outcomes in hemodialysis, including increased mortality. The accelerated progression of periodontal disease, marked by pocket formation, gingival recession, and bone and tooth loss, is attributed not only to inadequate oral hygiene and the burden of inflammatory diseases but also to renal osteodystrophy.[18] Renal osteodystrophy affects the maxillary and mandibular bone tissue due to disturbances in calcium, phosphorus, and vitamin D metabolism, as well as heightened parathyroid activity. This condition influences the parathyroid gland's activity.[19] Renal osteodystrophy can cause tooth mobility, malocclusion, pulp stones, enamel hypoplasia, bone demineralization, reduced cancellous bone trabeculation, decreased cortical bone thickness, radiolucent giant cell lesions, spontaneous or post-dental procedure jaw fractures, and abnormal bone healing after extraction. To prevent hypovitaminosis D and its related effects, calcitriol or its analogs must be administered to compensate for decreased 1,25 vitamin D production, especially in the later stages of chronic renal disease (stages 3). This approach ensures that the classical functions of hormonal 1,25 vitamin D can be addressed. Patients may exhibit dental erosions due to frequent regurgitation induced by the nausea associated with hemodialysis treatments, along with signs such as pulp narrowing and calcification. In children with chronic renal diseases, enamel hypoplasia and delayed eruption can also occur.[20] The prevalence of periodontitis in stage 5D was unchanged by age, but increased in proportion to the number of women and the length of dialysis. The mean plaque index was 1.14 and 1.62 in two groups with CKD stages 1-5, respectively, and 2.19 in kidney transplant patients. The average plaque index in stage 5D was 1.9, which increased with age but was unaffected by gender or length of dialysis treatment. In terms of mucosal disorders, ulcers affected 8.6% of patients in stage 5D and 1.3% of transplant recipients, whereas candidiasis affected 22.2% of people in stages 1-5, 19% of adults in CKD stage 5D, and 13.3% of kidney transplant patients. The prevalence of oral candidiasis in stage 5 rose with age but had no relationship with gender, dialysis duration, or geographic region.[21] Xerostomia was observed by 48.4% of patients in stage 5D, with a mean stimulated predialysis salivary flow rate of 0.86 ml/min and a mean unstimulated salivary flow rate of 0.22 ml/min.

General Considerations for Dental Management

Individuals undergoing conservative medical treatment or peritoneal dialysis for renal disease typically do not necessitate specific measures for dental treatment. The main considerations include avoiding nephrotoxic drugs (such as tetracyclines or aminoglycosides) and monitoring blood pressure during procedures, given the common occurrence of hypertension. Nevertheless, it is highly recommended to maintain open communication with the nephrologist when dealing with hemodialysis patients.[22] This communication is essential to understand the stage of the pathology, the medications prescribed, and other pertinent details. Comorbidities, such as diabetes, can significantly affect the homeostasis of these patients. In diabetic individuals undergoing dialysis, alterations in hypoglycemic medications and dietary adjustments can lead to hypoglycemia due to decreased gluconeogenesis, reduced insulin clearance by the kidney, and increased insulin sensitivity following the initiation of renal replacement treatment. A comprehensive assessment of the diabetic regimen and dietary patterns, along with patient education on self-monitoring of blood glucose, and/or referral to a diabetes specialist, can reduce the likelihood of recurrent hypoglycemia. Additionally, it is crucial to consider drug intolerance and heightened vulnerability to infections in these patients.

a) Risk of Bleeding

Dental procedures with a risk of bleeding should be rescheduled for a nondialysis day when the anticoagulant effect of heparin is absent. In emergency situations, the use of a heparin antagonist (protamine

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sulfate) can help reduce bleeding rates. However, an ongoing tendency for bleeding persists due to anaemia and alterations in platelet aggregation and adhesiveness. According to evidence-based medicine, minor surgical procedures can be safely performed without adjusting for INR2.5. Following the procedure, local hemostatic measures such as compression, cold applications, tranexamic acid, cellulose sponges, and sutures can be employed in case of local hemorrhage, and they are generally effective in achieving hemostasis.[23]

Medications

Due to their hepatic clearance, local anaesthetics can be safely utilized. Paracetamol remains the preferred option for pain relief; however, codeine can be administered without altering the dosages. Other anti-inflammatory medications, including ketoprofen, ibuprofen, or naproxen, may induce hypertension and worsen the bleeding tendency. The use of aspirin is contraindicated as it promotes platelet dysfunction, increases the risk of gastric bleeding, and contributes to the degradation of renal function. In cases of uncertainty, it is advisable to consult with a nephrologist or your personal physician. Individuals who have received prolonged and high-dose corticosteroid treatment, especially in stressful situations, may need steroid supplementation before dental procedures to prevent an adrenal crisis. Additionally, it is recommended that dental sessions be scheduled in the morning, in a calm environment, and that sudden, unexpected movements be minimized during the therapy.[24]

Antibiotic Prophylaxis and Therapy

Recent investigations have highlighted the absence of scientific evidence to administer antibiotic prophylaxis for avoiding infective endocarditis (IE) in ESRD patients. ESRD or hemodialyses are not criteria for IE prophylaxis. According to the American Heart Association guidelines, antibiotic administration remains indicated for patients suffering from concomitant cardiac comorbidities such as those with prosthetic cardiac valve, previous IE, unrepaired cyanotic congenital heart disease (CHD), completely repaired congenital heart defect with prosthetic material or device during the first six months after the procedure, and repaired CHD with residual defects at the site or adjacent to the site of a Nonetheless, people with end-stage renal disease (ESRD) are more susceptible to infective endocarditis (IE), especially if the condition is inadequately treated. Moreover, those undergoing hemodialysis may be prone to infections of the vascular access, such as endarteritis, which can potentially serve as a source of bacteraemia. Therefore, there might be potential benefits for these individuals in receiving antibiotic prophylaxis, particularly within the first six months after the creation of the vascular access.

Psychological Aspect

In the management of end-stage renal disease (ESRD) or hemodialyzed patients, it is crucial to consider the psychosocial aspect. Hemodialysis has been associated with a diminished quality of life and an increased prevalence of depression, leading to a higher likelihood of non-compliance compared to the general population. However, there is ongoing debate regarding whether systemic alterations and overall morbidity are causally linked to worsened dental and periodontal status, or if the impact on quality of life is a result of hemodialysis itself in combination with psychological factors.[25]

Operative Protocols

In the past two decades, the scientific community has witnessed a growing recognition of the significance of oral health in patients with end-stage renal disease (ESRD) and those awaiting transplantation. Various dental regimens advocated by different authors have increasingly emphasized not only the importance of maintaining adequate plaque control and regular oral cleanliness but also the psychological well-being of the patients. Given the significantly heightened incidence and severity of periodontitis in the hemodialysis population, minimizing the spread of oral bacteria becomes crucial through the elimination of oral foci and the reduction of mucosal and gingival inflammation. Achieving effective control of oral hygiene and addressing dental foci are fundamental steps, particularly for individuals deemed medically suitable for a pre-emptive kidney transplant from a living donor before the need for dialysis arises. Additionally, effective dental treatment with the maintenance of good oral hygiene is crucial in the post-transplant phase, particularly in preventing severe infections and thereby enhancing the survival of the transplanted organ.[26] Moreover, ensuring proper plaque removal and addressing gingivitis and periodontitis can help prevent

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or minimize gingival hypertrophy associated with the use of immunosuppressive drugs such as cyclosporine. The dental examination involves a non-invasive comprehensive assessment of dental, periodontal, and mucosal tissues. Special attention should be paid to the patient's positioning, avoiding compression of the arm with the vascular access for hemodialysis. All potential foci, including periodontal and endodontic lesions, residual roots, partially erupted and malpositioned third molars, as well as peri-implantitis, along with oral pathologies such as caries and mucosal lesions, should be addressed. Radiographs, including orthopantomography and intraoral x-rays, contribute to the comprehensive diagnostic process in both dentate and edentulous patients. Carious lesions must be identified, and when necessary, pulp vitality should be tested. In cases of pulp necrosis and/or apical lesions, the treatment plan may include endodontic treatment, apicectomy, or extraction.[27] Typically, extractions are advised when conservative, endodontic, and periodontal treatments cannot ensure the complete resolution of the pathology. Extraction of partially erupted and malpositioned third molars is recommended to prevent pericoronal infection, particularly in the early post-transplant period. In instances of peri-implantitis, the appropriate course of action involves the surgical removal of the implant.

Conclusion

Chronic Kidney Disease (CKD) is a significant global public health concern, with its terminal stage (ESRD) necessitating either renal replacement therapy or a kidney transplant. As the population of kidney transplant recipients grows, so does the demand for their dental care. Effective coordination with a nephrologist is imperative for dental interventions, as they can impact the patient's overall health both during and after treatment. Individuals with renal dysfunction require comprehensive treatment and stringent follow-up until transplantation. Early detection of oral diseases and the implementation of preventive interventions can minimize the need for extensive dental care. Active patient engagement is essential for motivating individuals to prioritize and maintain their dental health.

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