End Stage Renal Disease: Not a Contraindication for Minor Oral Surgery—Protocol for the Management of Oral Surgery patients with ESRD on Hemodialysis

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Abstract

Objective To describe a safe and effective protocol for the management of patients with end stage renal disease (ESRD) undergoing minor oral surgery.

Subjects and Methods A prospective cohort study was conducted on all patients with ESRD who were referred for dental consultation. A definite protocol was designed in consultation with the nephrologist to minimize the risk of bleeding and wound healing complications during and after the minor surgical procedures. 36 patients consented for the protocol to be followed while 4 patients did not comply with the protocol and in 2 cases the protocol could be followed. The intra operative, post operative bleeding, and the wound healing were assessed in these patients.

Results 36 patients had uneventful extractions as the blood pressure was brought down to pre hypertensive stage following the protocol. 4 patients who did not comply with the protocol had episodes of bleeding in the post operative period. There were two special scenarios where additional precautions had to be taken have been discussed. The wound healing was satisfactory in all these patients.

Conclusion The protocol discussed in this article helps us provide safe minor oral surgical treatment in patients with ESRD.

Keywords End stage renal disease · ESRD · Minor oral surgery · Hemodialysis · Bleeding extraction socket

Introduction

The incidence of chronic kidney disease (CKD) is increasing globally, and this increase is reflected in the Indian population as well. A recent study estimated the current incidence in India to be as high as 13–15 % [1]. This is due to the increased incidence of diabetes and hypertension, which, along with glomerulonephritis [2], alone account for 40–60 % of CKD cases [3]. Although only a minority of this population reaches end stage renal disease (ESRD), awareness continues to be poor, which may contribute to an increase in incidence as well as morbidity.

The primary functions of the renal system are maintenance of fluid and electrolyte homeostasis and excretion of metabolic waste. Renal failure, therefore, tends to disturb the body's normal homeostasis. Lack of excretion of the nitrogenous and non nitrogenous metabolites may adversely impact functioning of various organ systems. Apart from this, the compensatory mechanisms that get activated to compensate for the ongoing renal damage further complicate the systemic status [4]. All the aforesaid factors require extreme caution to be taken for patients undergoing minor surgical procedures.

There is inadequate literature pertaining to the standard care to be taken while performing minor oral surgical procedures in these patients and most dental practitioners

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are hesitant to treat such patients for the fear of complications. The purpose of this paper was to describe a definite protocol for the management of patients in ESRD under renal replacement therapy for minor oral surgical procedures. We present a series of cases in which this protocol was followed.

Subjects and Methods

A prospective cohort study was conducted on all the patients with ESRD (creatinine levels 6.5–8.5 mg/dl) who were referred for dental consultation to our unit at a private medical center. 36 patients were referred for therapeutic management and the common reasons for referral were pain and swelling. 6 patients were referred for prophylactic consultation prior to renal transplant (Fig. 1). All of these patients were on hemodialysis under the care of nephrologist. These patients had secondary hypertension and were on anti hypertensives primarily ACE inhibitors and Beta blockers. Patients who were at a high risk of cardiac compromise were on anti-platelet drug like Clopidogrel. These patients needed extraction of multiple teeth secondary to pulpal, periapical and periodontal problems.

A protocol was designed in consultation with the nephrologist to ensure safe surgical procedure in these patients. The protocol to be followed (described in Fig. 2) was explained in detail to all patients and an informed consent was obtained. The procedure was carried out after the blood pressure was brought to pre hypertensive or stage I level [5] and all patients were followed up for 1 h after, 2 days and 7 days after the procedure. Outcomes assessed

included any peri-operative and post-operative complications, and wound healing. Post-operative bleeding, if present, was assessed subjectively by the Visual Analogue Scale (VAS).

Results

A total of 42 patients were referred to the dental unit over a period of 2 years. All the patients were hypertensive (pre hypertensive stage = 7; stage I = 14; stage II = 215 Fig. 3) and an alpha blocker (Prazocin) or an alpha and beta blocker (Carvidalol) were prescribed on day 1 by the physician for patients with stage II hypertension to bring down the blood pressure prior to the procedure. The median INR was in 1.5 in all these patients except for one patient.

36 patients were compliant with the protocol and underwent the procedure without any complications. Of these, one patient tested positive for Hepatitis C with elevated liver function parameters and INR (INR 2.5). He was given 15 mg of Vitamin K injection via intra muscular route for two consecutive days prior to the procedure with clearance from the physician.

All the patients underwent the procedure the third day from the first consultation as described in the protocol (Fig. 2). On an average of 2–3 teeth were extracted in one single sitting in all these patients for the foresaid reasons.

The patients were reviewed on day 5 and day 7 to assess the healing of the extraction socket which appeared satisfactory. Antibiotics were discontinued from day 5 as the healing was satisfactory and hemodialysis was resumed on the same day.

Fig. 1 Subjects needing therapeutic versus prophylactic procedures

Fig. 2 The protocol

Fig. 3 Presentation of blood pressure in the ESRD population

Four patients refused to comply with the protocol owing to severe dental pain. Therefore extraction in these patients was carried out prior to dialysis with the mean blood pressure of 160/100 in all these patients. All these patients reported bleeding on the day of, and the day after extraction. The patients graded the amount of bleeding on the VAS score in the range of 2–3 and this was managed

conservatively by pressure pack and topical styptic agents.

Two cases were extremely complicated and necessitated modification of the protocol as follows:

Case 1: A 23 year old male patient in ESRD secondary to interstitial nephritis undergoing hemodialysis reported with dentoalveolar abscess in the region of 46, 47. Medical

history revealed the patient was autistic and was hospitalized in the recent past (1 month ago) for bilateral pleural effusion, ascites with ischemic cardiac changes secondary to renal failure. He was on carvedilol to reduce the blood pressure, phenytoin and erythropoietin injections. The patient was not compliant with hemodialysis and the blood pressure recorded at the first dental visit was 170/110. Blood workup revealed a hemoglobin level of 8 g % but normal coagulation profile. Echo cardiogram revealed moderate left ventricular dysfunction with hypokinesia, mitral and tricuspid regurgitation and an ejection fraction of 40 %. The patient was on medical management with inotropic agents to improve the residual cardiac function. Amoxycillin with Clavulanate and metronidazole were prescribed on the first day of dental consultation with Ultracet (tramadol with paracetamol) for pain control.

Owing to the uncooperative nature of the patient, the procedure (extraction and abscess drainage) was performed under short duration of general anesthesia one, considering his medical status under high risk category (ASA IV). Hemodialysis was done 1 day prior to the procedure. The patient's vitals were normal on table except for the blood pressure that was on the higher side of 170/90 mmHg. Conventional inferior alveolar nerve block with plain 2 % lignocaine was administered. After the extraction, there was slightly excess amount of bleeding from the socket with minimal amount of pus. The socket was curetted thoroughly, and gelfoam with an overlay of surgicel was packed into the extraction socket and a pressure pack was placed for 1 h to achieve hemostasis. The extubation was uneventful and the patient was under observation for 24 h and discharged. The patient continued with regular hemodialysis protocol and the antibiotics were discontinued after the 5th post operative day. The patient was reviewed 1 week later and was found to have normal wound healing with no further complications.

Case 2: A 60 year old male patient with ESRD undergoing hemodialysis for a long duration was admitted for continuous spontaneous bleeding from the oral cavity for 2 days. Examination revealed chronic generalized periodontitis with grade III mobile anterior teeth. The patient was on biweekly hemodialysis schedule. He was hypertensive with blood pressure at the time of examination being 200/110 and anaemic with hemoglobin percentage of 6.5 g%. The patient was on clopidogrel which was discontinued by the consulting physician at the time of presentation. The blood pressure was brought down to 170/100 by a nitroglycerine drip; however the bleeding persisted in the form of chronic ooze from the periodontium. Therefore, the mobile teeth were extracted and the extraction sockets were curetted thoroughly. A combination of gelfoam with surgicel and streptokinase was

packed into the extraction socket and sutured. Pressure pack was placed for 1 h and one unit of fresh frozen plasma was infused as the INR was high (INR 2). Bleeding stopped thereafter and the patient was discharged. Review after 3 days revealed normal healing sockets.

Discussion

Kidney is one of the vital organs of the body that plays a key role in maintaining the homeostasis in the body. Apart from the regular excretory function, it aids in maintaining blood pressure and acts as a component of the endocrine system by secreting Erythropoietin, a stimulant of erythropoiesis. It also plays an important role in the calcium metabolism by aiding the synthesis of calcitriol [4]. Renal failure is an important morbid end point of commonly seen diseases including diabetes mellitus and hypertension. These are considered the most common causes of intrinsic RF in the developing countries with other causes of autoimmune and drug induced renal failure.

Renal failure may be acute or chronic based on the duration. RF is considered chronic when it progresses beyond duration of 2–3 weeks. Prolonged duration of renal insult (>2–3 weeks) leads to irreversible damage to the renal parenchyma leading to chronic renal failure [5].

The most common causes of acute RF are due to renal hypoperfusion secondary to hypovolemia and compromised cardiac status. Nephrotoxic drugs are the second common cause of acute intrinsic RF. Frequently used nephrotoxic drugs include anti microbials like aminoglycosides, anti virals such as acyclovir, anti fungal agents (except liposomal complex of Amphotericin B), NSAIDs and immune suppressants. Intravenous contrast agents are the other most commonly used agents that can cause damage to the renal parenchyma. Use of nephrotoxic drugs for duration of 7–10 days should be avoided in patients to avoid renal parenchymal injury. These drugs cause nephronal injury by either altering the permeability of the plasma membrane or by interfering with the cellular energy derived from the mitochondria [6]. It is essential to evaluate blood urea, serum creatinine levels after 3–4 days of usage of nephrotoxic drugs. The use of these drugs in Acute RF secondary to hypovolemia may have a synergistic effect on renal destruction [4]. Reversal of the cause of acute RF may allow the rest of the renal parenchymal mass to undergo regeneration, which will restore the renal function, clinically presenting as high GFR and urinary output secondary to the excretion of the retained salts, metabolites [4, 7].

CRF may be treated conservatively or by renal replacement therapy. Renal replacement therapy is reserved for ESRD patients where residual renal function is

inadequate. This can be in the form of dialysis, or renal transplant. The current case series only included patients who were undergoing hemodialysis on a regular basis.

Patients in CRF/ESRD present with multitude of systemic problems that pose significant problems for performing minor oral surgeries. Each of these has been systematically addressed in the protocol developed.

Role of Vital Signs

Recording the vital signs at the initial visit will establish whether or not the patient is hypertensive, and the degree of hypertension. The main cause of hypertension in CRF patients is deterioration of ultrafiltration at the nephron level, which in turn leads to sodium retention and expansion of the extracellular fluid volume. Proteinuria, activation of the Renin Angiotensin pathway, sympathetic overactivity [8] and decrease in the release of intra vascular nitric oxide [9] have also been reported to act synergistically in these patients to cause hypertension.

Role of Blood Workup

Complete blood workup carried out at the first visit, includes several tests, which may in turn influence the treatment. Haemoglobin is checked to determine the degree of anemia. Reduced levels of erythropoietin (produced by the kidney) leads to anemia that can cause relative hemodilution and unwanted bleeding.

Retention of nitrogenous waste in CRF patients may affect the white blood cells and complement system and may lead to leukocyte dysfunction. This may predispose the patient to infections from the surgical site and subsequent sepsis. It is therefore essential to check the total and differential counts, and perform extractions under an antibiotic cover. In our protocol, antibiotics were

routinely started 2 days prior to the procedure, on day 1. The antimicrobial agents that can be safely administered in patients with renal failure are discussed in Table 1 [10].

Several factors may lead to increased bleeding tendencies in ESRD patients, which necessitates tests such as bleeding time, clotting time, prothrombin time, activated partial thromboplastin time and INR. Renal failure leads to an accumulation of multiple nitrogenous and non nitrogenous wastes like guanidinosuccinic acid. Guanidinosuccinic acid is known antagonist of ATP–ADP metabolism and thus prevents the platelet aggregation [4]. Patients with compromised cardiac status may also be on antiplatelet drug clopidogrel. These may need to be stopped with the approval of the physician. In our protocol, these drugs were stopped on day 1, 2 days prior to the planned procedure.

Blood urea and creatinine are assessed to properly define the extent of CRF. Random blood sugar is also checked, keeping in mind that diabetes is one of the leading causes for CRF as this may also compromise wound healing. Patients on long term hemodialysis are extremely vulnerable for blood borne diseases, and hence HIV and Hepatitis status needs to be assessed. Universal precautions must be taken, if positive, and Vitamin K injections are given to Hepatitis patients to make up for the decreased secretion of clotting factors by the liver.

Role of Echocardiogram

The combination of anemia, hypertension and increased fluid retention in these patients contributes to increased cardiac workload. This in turn leads to left ventricular hypertrophy and cardiac failure. This establishes a vicious cycle which may further deteriorate renal function, the so called cardio-renal-anemia syndrome [11, 12]. Echocardiogram is therefore essential to determine the cardiac status. One of the patient's in this series who had decreased cardiac function required inotropic agents to improve cardiac output (Special Case 1).

Role of OPG

Kidneys play a central role in the hydroxylation of 1–25 calcitriol (Vitamin D₃), an active form of Vitamin D that regulates the calcium–phosphorus metabolism. Renal failure leads to lack of Vitamin D₃ as a result of which the absorption of calcium from the hind gut is inhibited. At the same time there is high renal loss of calcium due to the lack reabsorption of calcium from the distal convoluted tubule in the kidneys. Low serum calcium leads to secondary hyperparathyroidism that stimulates active bone resorption (Renal osteodystrophy/Von Recklinghausen's disease of

Table 1 Antibiotics in renal failure

<i>Reduce dose even in mild failure</i>	
Aminoglycosides	Amphotericin B
Cephalosporins	Ethambutol
Vancomycin	Flucytosine
<i>Reduce dose only in moderate–severe failure</i>	
Metronidazole	Carbenicillin
Cotrimoxazole	Fluoroquinolones
Aztreonam	Clarithromycin
Meropenem	Imipenem
<i>Drugs to be avoided</i>	
Cephalothin	Talampicillin
Nalidixic acid	Tetracyclines
Nitrofurantoin	(Except doxycycline)

bone) [13]. The bone mineral density is reduced with hypocalcaemia and hyperphosphatemia. These osteoporotic bones are prone for pathologic fractures [14]. Ostitis fibrosa cystic of the jaws, commonly known as Browns tumor presents a multilocular radiolucency which needs to be identified. Therefore, we decided to take an orthopantomograph for all patients to avoid the possibility of pathologic fractures.

Role and Timing of Hemodialysis

Hemodialysis should be ideally performed 1 day prior to the minor surgical procedure. This reduces the intra vascular volume and thus the blood pressure prior to surgery [4]. Moreover, low molecular weight heparin that is administered during hemodialysis has a half life of four to 5 h, and will not contribute to bleeding on the day of the procedure. In this series, only patients who deviated from the protocol and had hemodialysis the day after the procedure had bleeding post operatively.

The advantage of performing hemodialysis 2 days after extraction is that the drug metabolites are removed from circulation and administration of LMWH at this point does not cause problems of bleeding at the extraction socket. At the same time, hemodialysis aids in controlling the blood pressure preventing bleeding from the extraction site.

Precautions During the Surgical Procedure

Plain lignocaine (without adrenaline) was used keeping in mind the hypertensive nature of these patients. To avoid the possibility of bleeding from the healing granulation tissue, thorough curettage post extraction is extremely important. Topical hemostatic agents may be used to achieve hemostasis. In this protocol, we packed the socket with gelfoam (gelatin sponge–thrombin powder), overlaid with surgicel (oxidized cellulose) and sutured the socket. The use of systemic antifibrinolytic agents tranexamic acid, if necessary, must be at reduced doses. [15–17] Protamine sulphate may be used to reverse the effects of low molecular weight heparin that is used for dialysis if the bleeding post extraction is uncontrollable. The usage of blood and blood products should be avoided as it can sensitize the patient prior to receiving renal transplant.

All the patients were reviewed after 1 week to assess the adequacy of healing which was found to be satisfactory with no complications. Our protocol therefore helped us minimize the intra and post operative complication rate and achieve satisfactory results with minimal morbidity.

The other wing of treatment of ESRD includes post renal transplant patients. This group of patients would require a totally different protocol because, while the

kidney function returns to normal in successful cases, they would be on immune-suppressants that can blunt the inflammatory response which can lead to serious infectious complications and wound healing issues. Apart from this, the transplanted kidney also needs healing time and all nephrotoxic drugs especially NSAIDS must be avoided during this phase. Our experience with renal transplants is limited and this group falls beyond the scope of this study. Separate studies for patients with renal transplant are needed in order to establish guidelines for the management of these patients.

There is a paucity in the current literature with regards to the guidelines for the management of patients with ESRD on hemodialysis. Our protocol is a first of its kind that provides definite guidelines for the management of these patients undergoing minor oral surgical procedures. However, large volume multicentre studies are essential to validate this protocol.

Compliance with Ethical Standards

Conflict of interest None.

Ethical Approval Ethical guidelines as per National Research Committee and Helsinki declaration 1964 followed and informed consent of the patient obtained.

Informed Consent Informed consent of the patients obtained.

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