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ANAESTHESIA FOR CHRONIC RENAL DISEASE AND RENAL TRANSPLANT: AN UPDATE

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HOW TO CITE THIS ARTICLE:

Vinod Kumar Verma, Arivind Kumar, Gautam Bhardwaj, Shailesh Kumar, Mukesh Kumar, Keshari Kumar Chandan. "Anaesthesia for Chronic Renal Disease and Renal Transplant: an Update". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 19, March 05; Page: 3346-3364, DOI: 10.14260/jemds/2015/482

ABSTRACT: Patients with chronic kidney disease have unique pathophysiology relating to both CKD and its underlying cause and therefore present a challenge to anaesthesiologists & surgeons. The aim of this article is to present the features of chronic kidney disease (CKD) that influence the conduct of anaesthesia and to introduce some of the anaesthetic techniques used for this challenging group of patients.

KEYWORDS: Chronic kidney disease, Anaesthesia, Vascular access surgery, Brachial plexus block, renal transplant.

INTRODUCTION: There have been considerable advances in renal replacement therapy (RRT) and renal transplantation. So a greater number of patients with CKD are presenting for anaesthesia to assist vascular access procedures and renal transplantation. As their survival increases they also present more frequently for surgery unrelated to their renal disease. The aim of this article is to present the features of CKD that influence the conduct of anaesthesia and to describe some of the anaesthetic techniques used for this group of patients.

AETIOLOGY: Chronic renal failure or more appropriately chronic kidney disease (CKD) refers to a decline in the glomerular filtration rate (GFR) caused by a variety of diseases such as diabetes mellitus (40%), hypertension (27%), chronic glomerulonephritis (13%), cystic kidney disease (3.5%), interstitial nephritis (4%) and other diseases such as obstructive uropathy, lupus nephritis and acquired immunodeficiency syndrome.¹ CKD may be categorized as mild (GFR of 60-89 ml/min/1.73 m²), moderate (GFR of 30-59 ml/min/1.73 m²), severe (GFR of 15-29 mL/min/1.73 m²), and end-stage renal disease (ESRD). Haemodialysis or peritoneal dialysis is typically initiated as the GFR falls to less than 15 mL/min/1.73 m². The progression of renal disease from one stage to the next results in deleterious effects on multiple organ systems.² The effects of renal disease are seen in all organ systems and mediated by accumulation of toxic metabolite products and endocrine dysfunction.

PHYSIOLOGICAL EFFECTS: CKD causes multi system dysfunction. This can be mediated by the primary disease process causing renal failure or by the effects of uraemia or both.

CARDIOVASCULAR SYSTEM: Almost 50% of deaths in patients with CKD are due to involvement of the cardiovascular system. Damage starts in early stages and frequently in the form of IHD, dilated cardiomyopathy, CCF, LVH and pulmonary hypertension. Accelerated arteriosclerosis is promoted by diabetes and dyslipidemias, while hypertension and cardiomyopathy are usually due to both volume

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and pressure overload and high levels of renin-angiotensin. Volume overload occurs due to expansion of ECF, high blood flow through AV fistulae and anaemia, while pressure overload is due to hypertension. Administration of erythropoietin for improving haemopoiesis may further raise the blood pressure and increase the requirement of antihypertensive drugs. The goal is to achieve a blood pressure of <130/85 mm Hg. Occasionally, uraemic pericarditis of the hemorrhagic type may be seen which may progress to cardiac tamponade. It is less often seen now a days because dialysis is usually started before it appears.³

RESPIRATORY SYSTEM: Pulmonary congestion due to volume overload results in hypoxemia and hypercapnia. Intraperitoneal fluid used in peritoneal dialysis can cause diaphragmatic splinting with basal atelectasis and shunting. Uraemic lung is a radiological entity characterized by perihilar congestion.

CENTRAL NERVOUS SYSTEM: The manifestations include malaise, fatigue and inability to concentrate, pruritus progressing to myoclonus, seizures, coma and death. Dialysis dysequilibrium syndrome resulting from changes in ECF volume, electrolyte composition and cerebral edema is characterized by dehydration, vomiting and hypotension. Dementia affects those patients who are on long-term dialysis and may be due to aluminium toxicity.

HAEMATOLOGICAL: Normochromic, normocytic anaemia occurs due to impaired erythropoiesis secondary to decreased erythropoietin synthesis and release, decreased red cell life span, increased hemolysis and bleeding, repeated loss during hemodialysis, aluminium toxicity, uraemia induced bone marrow suppression and iron, foliate and vitamin B₆ and B₁₂ deficiencies. These patients may have haemoglobin levels of 5 to 7 g/dl (hematocrit of 15-25%). Compensatory mechanisms to overcome the decrease in oxygen carrying capacity include an increase in cardiac output and 2, 3-DPG causing a rightward shift of oxygen dissociation curve and thus improving tissue oxygenation. Use of biosynthetic erythropoietin and darbepoetin is associated with increase in Hb and reduced need for repeated blood transfusions, which decreases the risk of sensitization.⁴ Although the beneficial role of transfusion is controversial in cyclosporine era, there must be no hesitation in replacing volume losses with packed, washed and irradiated red blood cells, keeping in mind that this may lead to an increase in plasma potassium levels.⁵

ELECTROLYTES AND ACID BASE STATUS: Inability to excrete water, electrolytes and free acids results in metabolic acidosis, hyponatremia, hyperchloremia and hyperkalemia. For every 0.1 unit change in pH, potassium increases by 0.6 mEq/L. Severe hyperkalemia increases cardiac and skeletal muscle excitability. The ECG shows peaked T waves, flat P waves, increased PR interval and a wide QRS complex that can progress to sine wave and ventricular fibrillation. Treatment involves use of 10 ml of 10% calcium gluconate I.V slowly, 1 mEq/Kg sodium bicarbonate I.V, β agonists, hyperventilation in mechanically ventilated patients, furosemide and magnesium. However, hemodialysis or peritoneal dialysis is the definite treatment. Hypermagnesemia usually accompanies hyperkalemia (GFR < 10 ml/minute) and can cause neuromuscular weakness, respiratory failure, bradycardia, hypotension and heart block.^{2,6}

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ENDOCRINE SYSTEM: As GFR falls, phosphate excretion falls leading to reduced absorption of calcium from gastrointestinal tract and vitamin D deficiency. Hyperactivity of parathyroid glands attempts to maintain calcium. This secondary hyperparathyroidism however leads to osteomalacia, osteosclerosis and osteitis fibrosa cystica culminating into a clinical entity widely known as uraemic osteodystrophy. The result is bone demineralization making these patients susceptible to spontaneous pathological fractures.⁷

COAGULATION: Accumulation of endogenous toxic products like guanininosuccinate, phenol and phenolic acids leads to platelet dysfunction and decreased levels of platelet. Factor III, PT and aPTT levels remain normal but bleeding time is prolonged. Treatment includes platelet transfusion, cryoprecipitate, desmopressin acetate or conjugated estrogen.⁸

GASTRO-INTESTINAL: Anorexia, nausea, vomiting, gastrointestinal bleeding, diarrhea and hiccups are common. Delayed gastric emptying time, increased acidity and gastric volume necessitate the use of H₂ blockers and proton pump inhibitors.

PROBLEMS OF DIALYSIS: The main sequelae are excessive or persistent heparinization, abnormal fluid shifts, β_2 microglobulinemia, dialysis dysequilibrium syndrome, hepatitis, AIDS, leucopaenia and hypocomplementemia.⁹ Also, poor care of AV fistulae can lead to local gangrene, sepsis and the need for amputation of the limb. Peritoneal dialysis on the other hand can cause peritonitis and sub-acute intestinal obstruction.

IMMUNOLOGICAL: Immunosuppression (physiological, pharmacological)

PHARMACOLOGICAL EFFECTS: Many drugs are eliminated from the body by the kidneys. Water-soluble substances are usually excreted unchanged, whereas lipid-soluble molecules are usually converted to water-soluble metabolites, and then excreted in the urine. CKD causes a reduction of the rate of renal excretion, because of impairment of glomerular filtration and renal tubular function. In turn this can lead to accumulation of the drug and its metabolites. The consequences of this depend on the characteristics of the drugs and the severity of renal failure.

PREMEDICATION DRUGS: Atropine and glycopyrrolate are eliminated 20-50% by kidneys. Because they are administered usually as single doses, accumulation with toxic effects is unlikely to be a significant problem. Metabolism of H₂-histamine receptor antagonists such as ranitidine, famotidine is largely unaltered by end stage renal disease. With metoclopramide (<20% elimination) there is significant reduction in clearance (16.7 L/h compared with 52.5 L/h) and prolongation of the terminal half-life (13.9h compared with 2.8h).¹⁰ With benzodiazepines there is decrease in the plasma protein binding, increased volume of distribution and increased systemic clearance secondary to increased free unbound fraction (1.4% to 7.9%) of diazepam in patients with CKD.¹¹ CKD does not alter the distribution, elimination, or clearance of unbound midazolam. Changes in the pharmacodynamic profile of midazolam in CKD patients, if they exist, are more likely due to inherent alterations in drug sensitivity than to pharmacokinetic changes.¹² After a single oral dose (2.0mg) the biotransformation of lorazepam to its glucuronide conjugate remains unaltered. Urinary excretion of

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lorazepam-glucuronide considerably decreases in chronic renal failure associated with accumulation of high concentrations of this conjugate in plasma during days after a single oral dose.¹³

INDUCTION AGENTS: Low serum albumin levels leads to an increase in free fraction of the drug in plasma while uraemia associated altered blood brain barrier can increase the levels of unbound drug crossing it into CNS receptors. Hence, the dose of induction agents may need to be adjusted according to the volume status, acidic pH and consequent increased sensitivity of the nervous system to these drugs. In chronic renal failure patients, the underlying rate and extent of thiopental distribution and elimination are much the same as in normal patients.¹⁴ However, a higher dose of propofol is required to reach the clinical end point of hypnosis and bispectral index of 50. The hyperdynamic circulation and high plasma volume resulting from anaemia can counteract the effects of low serum albumin explaining the higher dose requirement with propofol.¹⁵ Ketamine pharmacokinetics are not significantly changed by renal disease, but its hypertensive effects make it undesirable in patients with underlying hypertension. Etomidate is well tolerated and preserves hemodynamic stability. The associated adrenocortical suppression is short-lived and is of little relevance in transplant patients concurrently receiving hydrocortisone for immunosuppression.

OPIOIDS: Morphine is metabolized in liver to morphine-6-glucuronide (M6G), morphine-3-glucuronide (M3G) and normorphine, all of which are excreted by the kidneys. M6G accumulates in renal failure and mediates CNS and respiratory depression. Meperidine is metabolized in liver to normeperidine, also excreted by kidneys. Accumulation of these metabolic products leads to excitatory CNS effects such as convulsions. Fentanyl is metabolized by the liver with only 7% excreted unchanged in urine, thus making it suitable and safe for short-term use during surgery. However, if used for long duration, the pharmacodynamic effects should be monitored in view of parent compound accumulation. The clearance and half-life of sufentanil are not significantly altered in patients with reduced renal function. Remifentanyl is mainly metabolized by blood and tissue esterases while its principle metabolite is eliminated by kidneys. Reduced elimination of this metabolite is not of clinical significance because of its low potency - 1/4000 of its parent compound.¹⁶

MUSCLE RELAXANTS: Succinylcholine can be used in patients with renal failure provided potassium concentration is less than 5.5 mEq/l and repeated doses are to be avoided. Plasma cholinesterase has been reported to be below normal in more than 20% of end stage renal disease patients whether they are receiving any form of dialysis or not.¹⁷ Prolonged duration of action of non-depolarizing agents is primarily due to delayed clearance.

VOLATILE ANAESTHETICS: Sevoflurane and enflurane undergo biodegradation to inorganic fluoride. A serum fluoride concentration of 50 micromoles/L is the peak value that is nephrotoxic. There is evidence of transient impairment of renal concentrating ability and renal tubular injury in patients receiving sevoflurane and enflurane.¹⁸ FDA recommends the use of sevoflurane with fresh gas flow rate of at least 1 L/min for exposures up to 1 hr and at least 2 L/min for exposures greater than 1 hr. Fluoride levels after isoflurane and halothane increase by 3-5 micro-moles/L and 1-2 micro-moles/L, respectively. Hence, the risk of nephrotoxicity is remote. Desflurane is resistant to

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biodegradation and so even a prolonged exposure to desflurane (7.0 MAC hrs) has been associated with normal renal function.

ANTICHOLINESTERASE DRUGS: Renal excretion accounts for approximately 50% of the clearance of neostigmine and approximately 75% of elimination of edrophonium and pyridostigmine. Renal failure allows some protection against residual NM blockade because renal elimination half time of anticholinesterase drugs is prolonged.⁵

Principles of anaesthesia for patients with CKD.

PREOPERATIVE PREPARATION: The aim of preoperative preparation of patients with CKD is to identify and optimise any pre-existing pathophysiology in order to minimise the risk of anaesthesia and surgery. This requires a multidisciplinary approach involving anaesthetists, surgeons and nephrologists. Because CKD affects all organ systems, it is important to identify and optimise existing organ pathology. A systemic approach is therefore useful.

CARDIOVASCULAR SYSTEM: Ischemic heart disease - CKD is strongly associated with an accelerated form of ischemic heart disease, which should be identified and optimised to reduce perioperative cardiac morbidity and mortality. Other forms of vascular disease (e.g. cerebrovascular disease and hypertension) and resulting end organ dysfunction (e.g. CKD, cardiac failure) are associated with adverse perioperative cardiac events.¹⁹ Therefore, in patients with CKD a positive.

History should be actively sought and investigated appropriately. According to published guidelines, all patients with co-morbidity associated with cardiovascular disease, including CKD, should get a baseline electrocardiogram (ECG) done regardless of the severity of surgery²⁰ Cardiopulmonary exercise testing is a novel method of dynamic cardiorespiratory assessment. It appears to be able to predict patients at high risk of perioperative cardiovascular mortality more accurately than other methods,²¹ and may become a powerful tool in preoperative assessment. In patients with significant cardiovascular morbidity consideration should be given preoperatively on optimisation of long-term medical therapy, further investigation of cardiorespiratory function and preoperative optimisation in an intensive care environment.

Vascular access- Patients with CKD may have difficult IV access. Access should be considered and planned preoperatively. Current or potential future fistula sites should be avoided, including all forearm and antecubital veins, if possible. Central venous cannulation may also be difficult if haemodialysis catheters have previously been cited in the central veins, and the use of ultrasound guidance is recommended.²²

RENAL SYSTEM: Patients with CKD are often well informed of their condition and under the long-term care of nephrologist. A detailed background renal history enables perioperative renal support to be planned.

CONSIDERATIONS IN THE RENAL HISTORY:

- Usual fluid intake (may be restricted, and therefore caution with perioperative intravenous fluids is required).
- Usual daily urine output.

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- Regime of renal replacement therapy (e.g. frequency of dialysis).
- Renal function (baseline and current).
- Serum urea and creatinine concentration.
- Glomerular filtration rate.
- Serum electrolyte concentration- Sodium, Potassium.
- Timing of preoperative dialysis.

Haemodialysis and peritoneal dialysis are renal replacement therapies used to remove metabolic waste materials and fluid from the circulation. In addition, these processes also attempt to normalise fluid volume and electrolyte concentrations. Anaesthesia and surgery should take place in a near normal physiological environment and it therefore seems logical that dialysis should take place just before surgery. However, the dialysis process may itself cause physiological disturbance.

Effects of recent dialysis include:

- Fluid depletion and redistribution to extravascular spaces resulting in depletion of intravascular volume
- Electrolyte disturbance, especially hypokalaemia
- Residual anticoagulation from heparinisation of the haemodialysis circuit.

Dialysis is therefore usually scheduled about 12–24 hours prior to surgery. The ionic content of the dialysate may be altered to influence the amount and composition of fluid removed and so collaboration with nephrologist preoperatively is very important. A post-dialysis measurement of serum electrolytes is required before surgery as dialysis induced electrolyte disturbance can predispose to intraoperative cardiac dysrhythmias.

Correction of serum potassium abnormalities.

CKD patients may present preoperatively with hyper or hypokalaemia. The former is due to impaired renal potassium elimination and the latter usually due to excessive removal by recent dialysis. This patient subgroup is normally tolerant of large variations of serum potassium concentration, so discussion with nephrologist is advisable prior to correction. Emergency treatment of hyperkalaemia is indicated if there are ECG manifestations such as bradycardia, PR prolongation, QRS widening, peaked T waves, AV block.

TREATMENT INCLUDES:

- Continuous cardiac monitoring and large bore IV access.
- Basic and advanced life support measures as required.
- Cardiac membrane stabilisation using calcium chloride or calcium gluconate.
- Promote intracellular shift of serum potassium using an infusion of insulin and dextrose whilst monitoring plasma glucose concentrations.
- Excretion of excess potassium (method depends on intrinsic renal function): options include diuretic therapy to promote renal excretion, oral/rectal cation exchange resins and renal replacement therapy using dialysis or haemofiltration. Emergency correction of hypokalaemia is required only if associated with cardiac arrhythmias or ECG changes. These changes are variable and include flattened or inverted T waves, prominent U waves that appear as QT prolongation, ST depression and both atrial and ventricular tachyarrhythmias.
- Involvement of a nephrologist is strongly advised prior to starting potassium replacement.

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PREOPERATIVE OPTIMIZATION: Some patients are at a greater risk of perioperative morbidity and mortality than others. It is difficult to predict the patient and surgical factors that increase risk. Renal insufficiency alone is a risk factor for perioperative adverse cardiac events according to widely accepted guidelines.¹⁹ All patients, regardless of risk, benefit from thorough preoperative preparation and optimisation of co-morbidities. There may be some additional benefit of a period of preoperative physiological optimisation in the intensive care unit (ICU) for those patients with the highest perioperative risk, including patients with severe cardiovascular disease undergoing major surgery.²³ However there is no specific evidence of such aggressive preoperative optimisation strategies being beneficial in patients with CKD. Many trials have attempted to improve preoperative tissue oxygen delivery to high-risk patients by increasing oxygen uptake using goal-directed therapy with fluid and inotropic drugs. Some have shown a significant reduction in 30-day postoperative mortality.^{24,25}

ANAESTHETIC TECHNIQUES SUITABLE FOR PATIENTS WITH CKD: These patients may undergo elective or emergency surgery, related or unrelated to their underlying renal dysfunction. Anaesthetic techniques for these situations are outlined in the following paragraphs, illustrated by a detailed discussion of anaesthesia for vascular access surgery. This is followed by the principles of anaesthesia for other elective and emergency surgery and for renal transplantation.

VASCULAR ACCESS SURGERY: Patients with ESRD undergoing renal replacement therapy with intermittent haemodialysis will often require anaesthesia and surgery to form an arteriovenous fistula or graft.

THE AIMS OF ANAESTHESIA FOR VASCULAR ACCESS SURGERY ARE TO:

- Ensure intraoperative patient comfort.
- Optimize surgical conditions.
- Minimise risk of anaesthetic complications, e.g. perioperative cardiac events.
- Optimise postoperative state – avoidance of prolonged sedation, minimal requirement for postoperative analgesia.

ANAESTHETIC TECHNIQUES INCLUDE:

- Local anaesthetic (LA) infiltration (with or without sedation).
- Regional anaesthesia (RA) using brachial plexus local anaesthetic block (with or without sedation).
- General anaesthesia (GA).
- There are advantages and disadvantages of each technique. The choice of technique is based on individual patient assessment, the preferences of the patient and local practice (Box 4.)

LOCAL ANAESTHETIC INFILTRATION: LA infiltration of the surgical field by the surgeon is the most physiologically stable type of all the anaesthetic techniques, and is therefore used in patients with severe co-morbidity. Its main disadvantage is that it is the least well tolerated by patients of all the anaesthetic options. Also, in contrast to regional and general anaesthesia, LA infiltration does not improve the flow characteristics of the brachial artery.²⁶

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Box 1. Comparison of anaesthetic techniques for CKD patients

	Technical difficulty	Patient tolerability	Post-operative analgesia	Physiological disturbance	General Complications
LA	Simple	Often poor	Variable	Insignificant	Systemic LA toxicity Inadvertent vascular injection
RA	May be complex	Variable	Good	Mild	as written in box 3
RA and sedation	As for RA	Good	Good	Moderate	As for RA Side effects of sedation drugs Unexpected loss of airway
GA	Variable	Good	Variable	May be severe	Airway protection and maintenance Cardiovascular instability Unpredictable drug effects Perioperative blood Glucose control in diabetic patients

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REGIONAL ANAESTHESIA: Regional anaesthesia of the upper limb requires LA block of the brachial plexus. This offers many advantages over other techniques, including intraoperative haemodynamic stability and good postoperative analgesia. There is also evidence that it improves vascular flow via regional sympathectomy²⁷ although evidence of improved graft survival is lacking. Successful blockade adequate for sole anaesthesia may be technically difficult and time consuming and may require supplementation with LA by the surgeon. Several approaches to the brachial plexus have been described (Box 5), each with its own set of indications and complications. General complications are outlined in Box 6, the incidences of which vary according to the specific approach used.

Box 2. A summary of different approaches to the brachial plexus. Advantages of each are outlined with their important problems (percentage incidences)

	Advantages	Specific problems
<u>Axillary</u>	Technically simple Few serious complications	Slow onset (15–25 minutes) ²⁸ <u>Missed radial and musculocutaneous nerve</u> (50%) ²⁹
<u>Supraclavicular/Infraclavicular</u>	Effective anaesthesia Low incidence of 'missed nerves' Fast onset	Technically difficult. Pneumothorax (supraclavicular, 0.2–4%) ³⁰ <u>Subclavian artery injury</u> (2%) ³¹
<u>Interscalene</u>	Effective anaesthesia Lower risk of pneumothorax than supra/infra-clavicular block	Inadequate block of ulnar nerve (50%) ³² Inadvertent LA injection to vertebral artery, epidural, subdural or subarachnoid spaces (case reports only) Pneumothorax (0.2%) ³¹ Phrenic nerve block (100%) ³³

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Box 3 General complications of brachial plexus block

Inadequate anaesthesia/analgesia

Needle malposition distant from brachial plexus, 'Missed' nerves

Local anaesthetic toxicity

Idiosyncratic (anaphylactic reactions), Dose related toxicity

Injury to nearby structures

Neuronal

Mechanical (needle trauma)

Chemical (secondary to infiltrated drug e.g. LA)

Vascular

Arterial

Venous

Lung pleura

Pneumothorax

Unintended destination of LA

Intravascular injection, subarachnoid or epidural injection, blockade of phrenic nerve, cervical sympathetic chain or recurrent laryngeal nerve (RLN)

REGIONAL ANAESTHESIA AND SEDATION: An alternative is a combined approach using RA and sedation. This improves patient tolerability of RA whilst maintaining its advantages over LA infiltration and GA (minimal physiological disturbance, improvement in regional vascular flow and good postoperative analgesia).

GENERAL ANAESTHESIA: Patients with CKD have multiple risk factors for GA, as described previously in this article. However there is no evidence that GA presents a higher risk than other techniques. In general, there is a lack of research comparing outcomes from different anaesthetic methods. In one retrospective study there was no increase in mortality, cardiac morbidity or fistula failure in patients undergoing procedures under general anaesthesia compared to LA infiltration or RA brachial plexus block³⁴ although the comparison was underpowered. Patients often have an expectation of general anaesthesia when presenting for surgery. With careful planning they can be offered GA with minimal increased risk.

OTHER ELECTIVE PROCEDURES: As the long-term management of CKD improves and life-expectancy increases, patients are more frequently presenting for elective surgery unrelated to their renal disease. Perioperative care follows the principles already described in this article and a recently published article in this series.³⁵

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SUMMARY OF PERIOPERATIVE CONSIDERATIONS:

- Anaesthetic options – general, regional or local anaesthesia.
- Airway management.
- Vascular access.
- Fluid and electrolyte management.
- Blood transfusion.
- Immune function and antibiotic prophylaxis.
- Steroid supplementation.

Unplanned urgent and emergency surgery: Patients may present for unplanned surgery relating or coincidental to their renal disease. Examples of renal disease related surgical problems include

- Haemodialysis vascular access problems – blocked fistula
- Peritonitis secondary to infected peritoneal dialysis catheter.

Unplanned surgery has many anaesthetic implications, both generic and specific to patients with CKD.

GENERAL CONSIDERATIONS:

- Presenting condition causing physiological disturbance (e.g. abdominal sepsis, bleeding, GI Obstruction).
- Co-morbidities not optimised and affected by presenting condition (e.g. cardiovascular disease, diabetes).
- A full stomach in a patient requiring emergency surgery introduces the risk of regurgitation and aspiration under general anaesthesia. This may require a rapid sequence intubation technique.
- Postoperative care environment (e.g. intensive care unit).
- Psychological stress.

SPECIFIC IMPLICATIONS FOR CKD:

- Fluid and electrolyte disturbance – many influences including presenting condition, chronic renal function, dialysis regime.
- Immune suppression increases risk of postoperative sepsis.
- A preoperative assessment with baseline investigations is always necessary, except in a dire emergency. A multi-disciplinary approach should be used, including surgeons, anaesthetists, renal physicians, intensive care physicians and microbiologists as appropriate. Anaesthetic technique varies according to the individual situation, but attention to detail is of paramount importance.

POSTOPERATIVE MANAGEMENT:

ENVIRONMENT: Most patients with CKD can return to a surgical hospital ward postoperatively. Admission to high dependency or intensive care facilities may be suitable for patients with significant co-morbidity and after major surgical procedures. The decision to admit a patient to such an environment requires input from critical care physicians. An important factor in the decision is often the limited resources available for these facilities, a problem that varies between countries. In the UK, guidelines for appropriate admissions have been published by the Department of Health.³⁶

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PRINCIPLES INCLUDE:

HIGH DEPENDENCY CARE:

- Postoperative patients who need detailed monitoring for longer than can be accommodated in a recovery unit.
- Unstable patients requiring greater observation than can be provided on a general ward.
- Patients requiring single organ support, excluding advanced respiratory support.
- Patients no longer needing Intensive Care but who are not yet well enough to be returned to a general ward.

INTENSIVE CARE:

- Patients with respiratory failure requiring advanced respiratory support.
- Patients requiring support of two or more organ system.
- Patients with chronic co-morbidity of one or more organ systems that require support for an acute reversible failure of another system.

ANALGESIA: Alternatives can be categorised into local, regional and systemic analgesia. They may be combined to improve analgesic quality and reduce adverse effects. Advantages and disadvantages of each are described.

INTRAOPERATIVE LA INFILTRATION: Advantages: This is the simplest form of postoperative analgesia, often used in conjunction with other techniques. No postoperative management is required, with a reduced requirement for systemic analgesia.

DISADVANTAGES: Alone LA infiltration is often inadequate with a finite duration of action. Inadvertent intravascular injection and LA toxicity is possible but unlikely. There is a risk of surgical wound haematoma.

Regional analgesia (e.g. epidural analgesia, brachial plexus block):

ADVANTAGES: RA provides both intra- and postoperative analgesia with reduced requirement for systemic analgesic drugs. Epidural analgesia potentially reduces the incidence of postoperative respiratory complications³⁷ and venous thromboembolic events, especially in orthopaedic surgery.³⁸ Importantly, however, there are as yet no studies investigating the benefits of epidural analgesia in patients with CKD.

Disadvantages: Some disadvantages have been discussed in a previous section of this article. Ongoing nursing and anaesthetic input is required into the postoperative period to prevent potential complications such as analgesic failure or hypotension.

SYSTEMIC ANALGESIA: There is a wide range of systemic analgesia available, each with a profile of indications, contra-indications and side effects. A detailed discussion of each class of drug is outside the realm of this article, but the principles of systemic analgesia are outlined.

The World Health Organisation analgesic Ladder: The World Health Organisation analgesic Ladder³⁹ was initially developed for use in cancer pain, but has been adopted as a guide for the provision of postoperative systemic analgesia

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WHO analgesic Ladder

There are three steps on the ladder. The patient is moved up a step if pain is poorly controlled.

Step 1 – non-opioid (paracetamol, NSAID) +/- adjuvants

step 2 – weak opioids (e.g. tramadol/codeine)+ non-opioid +/- adjuvants

step 3 – strong opioids (e.g. morphine))+ non-opioid +/- adjuvants

The use of NSAIDS including COX II selective analgesics is avoided in patients with CKD since they have well documented renal side effects with subsequent loss of glomerular function.^{40,41}

ROUTE OF ADMINISTRATION: There are different options for the administration of postoperative systemic analgesia. Traditional nurse-administered oral or intramuscular analgesia is most frequently employed. This is simple and allows regular assessment of pain control by nursing staff. However the onset of analgesia is slow after each dose, there are potential delays in administration and the regime lacks patient autonomy. More recently patient controlled administration of intravenous opioid analgesia (PCA) has been used safely and successfully in the early postoperative period. This encourages patients to titrate analgesia to their perceived pain. It provides fast onset pain relief and is empowering to patients. There are several disadvantages, however. It requires intravenous access and the availability of experienced staff. There is potential for opioid overdose with equipment malfunction.

OPIOIDS: The choice of opioid is an important consideration in CKD patients. The action of opioids is curtailed by redistribution away from the central and peripheral opioid receptors to fat stores and then by hepatic and renal elimination. If renal elimination is impaired then the beneficial and unwanted effects of opioids can be accentuated and prolonged. Accumulation of morphine and its metabolites may be a particular problem and a cause of delayed respiratory depression postoperatively. Fentanyl, a faster acting synthetic opioid is preferred for IV PCA opioid administration in CKD. It has a preferable pharmacokinetic profile with fast onset and offset times and it has less propensity for the accumulation of active metabolites that cause side effects. An area of current interest is in the use of buprenorphine either as a patch or sublingually. This opioid is almost exclusively metabolised by hepatic pathways and theoretically should not accumulate in CKD ⁴²

Therefore there is clearly a wide choice of techniques available for postoperative analgesia.

Choice of technique depends on a variety of patient, surgical and institutional factors:

PATIENT FACTORS:

- Patient preference.
- Physical and mental capabilities (e.g. Patient Controlled Analgesia).
- Co-morbidities (e.g. bleeding diathesis and epidural analgesia).

SURGICAL FACTORS:

- Surgical procedure and anatomical site.
- Institutional factors.

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- Anaesthetic experience and out-of-hours support.
- Postoperative nursing experience.

RENAL TRANSPLANTATION: Renal transplant is one of the most efficient treatments for End Stage Renal Failure (ESRF) in terms of cost, survival benefit and quality of life. There is a 40–60% reduced mortality in those transplanted compared to those remaining on dialysis.⁴³ The first renal transplant occurred between identical twins in the mid-1950s. The first description of anaesthesia for transplant was in the 1960s between living donor identical twins using a spinal anaesthetic technique.⁴⁴ With the introduction of effective renal dialysis between 1960s and 1970s there has been a large increase in the number of patients with end stage renal failure surviving to be considered for renal transplantation. Now a days, demand for renal transplant has grown by around one third although supply of donor organs has remained approximately the same. For this reason the number of living donors has gradually risen to address this increased demand, requiring these otherwise healthy individuals to undergo major surgery. There may yet be future consequences of organ donation to these individuals in terms of reduced renal reserve, but this will not be apparent at time of renal donation.

SELECTION OF POTENTIAL RECIPIENTS: All ESRF patients should be considered for transplant unless there are specific contraindications: predicted patient survival of <5 years, predicted graft loss of >50% at one year, patients who are unable to comply with the required immunosuppression regimen, and those who cannot tolerate immunosuppression. All patients are extensively evaluated by nephrologist and transplant surgeons prior to entering the transplant programme, with specialist opinions sought from other disciplines as appropriate.

ANAESTHETIC MANAGEMENT: Renal transplant surgery may be performed under regional or general anaesthesia. The former was used exclusively in the early history of renal transplant surgery⁴³ but general anaesthesia (GA) with neuromuscular blockade and controlled ventilation is now the method of choice. GA provides the most stable haemodynamics and good muscle relaxation for surgical access.

PREMEDICATION: Gastric paresis, gastritis and reflux disease are common in this patient group necessitating antacids, H₂ blockers or proton pump inhibitors. Many patients are also extremely anxious during this emotive period and anxiolytics are appropriate in this circumstance.

INTRAOPERATIVE MONITORING: This should consist of standard minimum monitoring in addition to core temperature and central venous pressure (CVP). CVP is measured via a central venous catheter sited after induction of anaesthesia, usually in the right internal jugular vein. Direct arterial pressure monitoring may be useful for some patients but is not mandatory and care should be taken when choosing an insertion site so as not to compromise future fistula formation. If the patient is likely to require new haemodialysis postoperatively then access should be sited at induction. As with all invasive procedures, strict asepsis should be used as this patient group is at higher risk of infective complications due to the post-operative immunosuppression.

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INTRAOPERATIVE GRAFT OPTIMISATION: Future graft function is directly related to several factors including: warm ischaemic time (harvest time and transplant); cold ischaemic time (e.g. storage >24 hours); transplanted graft perfusion and pre-donation graft state. In order to maximise graft function the intraoperative aims should be a warm, well-perfused patient with a systolic arterial pressure >130mm Hg. Traditionally aggressive volume loading has been recommended using volumes up to 30 ml/kg of warmed crystalloid solution, aiming for a CVP >15mm Hg; however patients with pre-existing cardiac disease or impaired cardiac function are at risk of volume overload, leading to pulmonary oedema necessitating a period of postoperative ventilation. More recently it has been suggested that 15 ml/kg, aiming for a CVP 7– 9 mmHg at the point of reperfusion may be associated with equally good graft recovery, whilst reducing the risks associated with volume overload ⁴⁵ Adjuvant drugs are also commonly employed in an attempt to improve graft recovery and function. Evidence for the effectiveness of these agents however is often sparse or contradictory and not supported by the Cochrane review on perioperative renal protection ⁴⁶, although these studies did not deal with the transplanted kidney. Transplant units have their own protocols for these adjuvant drugs, but those commonly used are mannitol, furosemide and dopamine. Mannitol in a dose of 0.25– 0.5 g/kg leads to an osmotic diuresis and intravascular volume expansion. It also has free radical scavenging properties which have been suggested as offering some protection against ischaemic injury. It may also promote renal artery dilatation and thus improve blood flow through the transplanted organ⁴⁷ Furosemide in low to high dose (40–250 mg) has also been used and may result in massive diuresis in well-functioning grafts, which may make fluid management difficult. The use of furosemide may be beneficial in promoting urine flow and avoiding oliguria but the benefits in terms of improved graft function remain unclear. High dose boluses should be used with caution, as they are associated with ototoxicity.

Dopamine use in low 'renal' dose infusions (2–3 mcg/kg/min) is contentious as only a few small studies have shown an improvement in urine output or creatinine clearance, compared to several large studies showing no such improvements ⁴⁸. A recent study involving living donor nephrectomy also found no beneficial effect to either donor or recipient from low dose dopamine infusion.⁴⁹

POSTOPERATIVE CARE: Most renal transplant patients have their anaesthesia reversed and are extubated at the end of surgery. Postoperative patients are usually nursed in a high dependency setting on a renal ward. Only 1% requires admission to an Intensive Care Unit (ICU), usually as a consequence of fluid overload or sepsis. Postoperative management goals are to maintain a well perfused patient with a sufficient blood pressure to allow good graft function. New oliguria (<50 ml/hr) in a well filled cardiovascularly stable patient should trigger surgical discussion and assessment of graft blood supply with Doppler ultrasound or surgical reexploration.

PAIN: Postoperative pain is usually mild to moderate following renal transplantation. Morphine is most commonly used for analgesia intraoperatively and is usually continued postoperatively by PCA.⁵⁰ Fentanyl or other opioids may also be used. Addition of regular paracetamol has an opioid sparing effect and will potentially reduce the incidence of opioid side effects. Should renal function deteriorate, the metabolites of morphine may accumulate. NSAIDs should be avoided in this group of patients due to their potential renal toxicity and GI tract erosions.

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CONCLUSION: Patients with CKD are complex medical cases and present unique challenges to the anaesthetist. They come with all the sequelae of CKD and of the diseases that caused CKD. As age is no longer a barrier to renal transplantation, increasing age with associated morbidity must also be considered. The perioperative care of these patients should be arranged and carried out by senior staff from the departments of surgery, anaesthesia, and nephrologist and in appropriate ward settings. Failure to care for these patients well has implications for graft survival in transplantees and morbidity in those patients with CRD.

As live related donation increases the multidisciplinary team must make allowances to care for otherwise healthy individuals with only 50% of their original renal capacity.

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Date of Submission: 06/02/2015.
Date of Peer Review: 07/02/2015.
Date of Acceptance: 23/02/2015.
Date of Publishing: 04/03/2015.