Anesthesia for renal transplants

JOYCE P. HOLDER, CRNA, BS
Brooklyn, New York

This article focuses on a comprehensive approach to the administration of anesthesia for renal transplants. The author examines the physiology and diseases which may exist concomitantly with end stage renal failure. Also, a description of the anesthetic management of the patient for renal transplant, with emphasis on altered responses to drugs, is provided.

In order to understand the various ramifications which must be considered while administering anesthesia for renal transplants, one must have a knowledge of the functional anatomy of the kidneys. Also, there must be an awareness of those conditions which may result from the existing pathophysiology in the patient with end stage renal failure.

Overview of functional anatomy

It is important to note that the kidneys are the organs of excretion for most of the end products of metabolism. Indeed, this includes the elimination of some anesthetic agents. The kidneys also have an endocrine function producing the enzymes renin and erythropoietin. The kidneys are among the “vessel rich” group receiving 20-25% of the total cardiac output through the renal circulation each minute. The nephron is the functional unit of the kidney; and within both kidneys, there is a total of more than 2 million nephrons.

Filtration and secretion reabsorption: These functions are the methods by which the plasma clears itself of unwanted substances, and reabsorbs or recycles those which are needed for use by the body. The waste products are eliminated in the form of urine.

The principle mechanism for plasma clearance by the nephrons is glomerular filtration. Glomerular filtration occurs at the rate of 125 ml/min. A drop in glomerular filtration rate (GFR) decreases the output of urine. Following glomerular filtration, the filtrate passes through the tubular system where secretion and reabsorption take place.

Autoregulation: Autoregulation is known to be the process which prevents the renal blood flow and GFR from undergoing a radical increase or decrease. There are many theories relating to the mechanism of autoregulation. One theory describes autoregulation as a tubuloglomerular feedback, which constricts the efferent arteriole and dilates the afferent arteriole.

Renin-Angiotensin System: It is believed that the renin angiotensin system plays an important role in conserving sodium and water to aid in tubular reabsorption. This system also adjusts nephron function to promote a balance in both kidneys, and plays an important role in vasoconstriction.
Conditions seen concomitant with renal failure

When the diseased kidneys are functioning ineffectively or are no longer capable of functioning, the pathophysiology which prevails results in some of the following conditions.

Water Retention: A patient with chronic renal failure may have both intracellular and extracellular edema dependent upon the salt and water intake. The elimination of these products is reduced, thus the renal failure patient should be dialyzed prior to surgery.

Acidosis: As a result of decreased urinary output, the normally excreted acid products are retained. The acidotic condition increases as renal failure becomes more severe.

Anemia: The normal kidney secretes the erythropoietic factor which stimulates the bone marrow to produce red blood cells. In the damaged kidney this factor is reduced, less blood cells are produced, and hence the renal failure patient suffers severe anemia. Other factors such as the retention of toxins may cause anemia in the renal failure patient.

Anemia in the kidney failure patient is compensated by an increase in plasma volume. Because of the severe anemia found in these patients, there is decreased oxygen carrying capacity and an increased cardiac output.

Hypertension: The most common cause of hypertension in the renal failure patient is clearly known, as these patients retain water and salt. Hypertension also occurs when there is an ischemic area in the kidney which secretes large amounts of renin. A larger amount of angiotension II is formed and consequently hypertension results.

Hypotension: On the other hand, in kidney failure resulting from interstitial kidney disease, increased quantities of water and salt are lost in the urine. Hypotension will eventually develop.

Osteomalacia: With prolonged renal failure, the diseased kidneys are unable to convert Vitamin D to 1,25-dihydroxycholecaliferol which enables calcium to be absorbed from the intestines. This situation produces a reduced availability of calcium to the bones. Bones become weakened, brittle and sometimes painful.

Hyperparathyroidism: Serum calcium levels are for the most part regulated by the parathyroid hormone. With renal disease, calcium is not effectively absorbed into the blood stream. Because of the low serum calcium levels, a feedback stimulation of the parathyroids results. This condition is known as secondary hyperparathyroidism. In extreme cases an intractable rash with severe itching may appear on the patient’s skin.

Uremia: Because there is malfunction of the kidneys, the end products of protein metabolism such as urea, uric acid and creatinine are not eliminated. In such a case there is an increase of these compounds in the blood, termed azotemia.

Another problem leading to uremia is failure of the kidneys to excrete potassium. If the serum potassium levels exceed 8 mEq/liter, cardiac dysfunction will result.

The uremic patient may also show evidence of nausea, vomiting and dehydration. Uremic retinopathy may be portrayed where there is excessive reddening of the eyes.

With end stage renal failure, the inhibition of platelet factor 3 by the uremic plasma seems to be the cause of bleeding tendencies. Coagulopathy, which is related to platelet dysfunction, is also frequently present.

Preanesthetic considerations

Laboratory data: An assessment of the preanesthetic considerations should include a careful evaluation of laboratory data.

Serum creatinine (normal 0.6-1.3 mg/100 ml) and creatinine clearance (normal 85-140 ml/min) tests show increases or decreases in GFR.

BUN (blood urea nitrogen) (normal 8-20 mg/100 ml) is also indicative of glomerular filtration rate, but is not as reliable as the tests previously mentioned. A BUN of more than 50 mg/100 ml is usually significant of a decreased GFR.

Serum creatinine may increase as much as ten fold in renal disease. Serum creatinine clearly indicates a measure of glomerular filtration rate, in that when the serum creatinine is doubled, the GFR may be decreased by 50%. Studies which reflect GFR are important to the anesthetist, since a decrease in arterial pressure causes a decrease in GFR, and hence, a decrease in urinary output.

Serum potassium levels may be high (normal 3.5-5 mEq/L). Hyperkalemia (increased serum potassium levels) may exist, as the kidneys cannot excrete potassium. Most authorities recommend that elective surgery be postponed if the serum potassium is above 5.5 mEq/L. In an elective operation the potassium may be lowered by oral or rectal administration of Kayexalate® (sodium polystyrene sulfonate) which is a potassium exchange resin. In cases of emergency, a rapid reduction of potassium can be achieved by intravenous injection of 25-50 gm of 50% dextrose, together with 12-24 units of soluble insulin.

Hemoglobin (normal 12-18 gm/100 ml) and hematocrit (normal 36-50 ml/100 ml) are usually low because of the previously explained pathophy-
siology. This anemia is of gradual onset and may fall as low as 5-8 gm/100 ml. No attempt should be made to treat the anemia preoperatively. The renal failure patient compensates for anemia with increased plasma volume and increased cardiac output. Clearly, there is danger of fluid overload with preoperative transfusions. Blood transfusions may also stimulate antibodies or cause serum hepatitis which may initiate kidney rejection.

Regarding urinalysis, osmolality and specific gravity are tests which reflect renal tubular function.

Glucose in the urine may occur in renal failure patients. When there is a disorder in the renal tubules in which the transport mechanism is deficient, serum glucose may be normal, but excess glucose may be excreted in the urine. This condition is termed glycosuria.

There is evidence of proteinuria in renal failure. The proteinuria found in renal disease is diagnosed by the presence of albumin and casts in the urine. These casts contain particles of tubule cells, pus cells and erythrocytes. The casts characteristic of advanced renal failure are known as broad casts or renal failure casts. Best and Taylor describe proteinuria as being present when the total daily excretion exceeds 150 mg/day, which is the upper limit of urinary protein excretion in normal humans (normal 40-150 mg/day).

Premedication

Levels of renal excretion of drugs: Since most kidney transplants are emergency procedures, premedication is not routinely administered. If premedication is considered necessary, the dosages should be reduced.

Demerol® (meperidine) is 5-10% excreted by the kidneys. Morphine is excreted by the kidneys to a larger extent than Demerol®. Valium® (diazepam) forms metabolites, and 70% of the metabolites are excreted in the urine. Atropine is eliminated one-third to one-half unchanged in the urine. Scopolamine is almost completely metabolized before renal excretion. Ativan® (lorazepam) terminates as a metabolite which is more than 65% excreted 72 hours after intramuscular injection.

Preparation of the patient and equipment

With this profile of the renal failure patient in mind, the next step for the anesthetist is the preparation of the patient and equipment for anesthetic management. A good working intravenous line with a wide-gauge cannula should be secured, avoiding sites of grafts or fistula for infusion. Do not place the blood pressure cuff or apply any pressure to the arm where there is a graft, shunt or fistula. This arm must be protected in order to keep blood vessels patent in case the transplanted kidney is rejected. In the event of rejection, the arm will again be needed for dialysis.

The anesthesia machine must be prepared for intubation and resuscitation regardless of whether regional or general anesthesia is planned.

In the text *Medicine for Anesthetists* (1979), Vickers suggested that anesthetic equipment should be sterilized and used in such fashion so as to reduce the amount of bacteria being introduced to the patient. Indeed, the intravenous cannula should be inserted with sterile technique, as these patients are very prone to infection.

The equipment and supplies should include paraphernalia for intraoperative transfusions; diuretics which may be given after the vasculature is anastomosed; steroids to assist in the suppression of the thymus gland activity; and intravenous fluids. Some authorities suggest 5% dextrose with Ringer's Lactate solution. Others agree that 5% dextrose with 0.45%, normal saline and sodium bicarbonate added is better since studies have found that this solution most closely approximates the average urinary concentration of sodium and bicarbonate.

Anesthesia course

Altered responses to drugs: Many techniques have been used successfully for the anesthetic management of kidney transplantation. Whatever the technique selected, the reduced dose is emphasized. Proteinuria results in a reduction of serum albumin levels and a decrease in protein binding of drugs. Because of the decreased protein binding, more drug is available to bind to tissues. Goodman and Gilman state that "drugs that bind to protein usually also bind to tissues;" and when drugs accumulate in the tissues, this may act as a storage area which prolongs the effects of the drug. Thus, there may be an increased response to normal doses of drugs. In addition, renal failure patients are usually treated with large doses of antibiotics which may potentiate nondepolarizing muscle relaxants if used during maintenance.

If management by inhalation anesthesia is planned, the patient should be thoroughly preoxygenated to prevent tissue hypoxia. Tissue hypoxia may result from decreased oxygen carrying capacity due to anemia.

Induction

Sodium thiopental may be used for induction, followed by succinylcholine or a nondepolarizing...
muscle relaxant for intubation. In the case of a patient with a full stomach, rapid induction with cricoid pressure should be employed. Succinylcholine (Anectine®) must be used prudently with the renal failure patient. This drug causes a release of serum potassium, about 0.5-1 mEq/L. Therefore, its use may be contraindicated if potassium levels are very high. (Studies have found that precurarization does not significantly reduce the release of potassium during induction.) Succinylcholine is metabolized by plasma cholinesterase and does not require the kidneys to be functioning normally for termination of action. However, in patients with end stage renal failure, the plasma cholinesterase levels are reduced. The amount of succinylcholine used should be reduced.

**Maintenance**

Since inhalation agents do not depend entirely on renal excretion for termination of action, they may serve as one of the best techniques of choice for kidney transplant operations. Nevertheless, the end products of inhalation agents must be considered.

Enflurane (Ethrane®) is not recommended in the presence of renal disease, as its end products of metabolism, inorganic fluorides, may cause nephrotoxicity. Methoxyflurane is known to cause nephrotoxicity which is characterized by a high output renal failure.

Nitrous oxide is almost completely eliminated via the lungs. Fluothane® (halothane) may be used for maintenance, but should be used in small percentages in order to avoid hypotension. Thus, the need for muscle relaxants manifests itself.

Either d-Tubocurarine or pancuronium may be used for renal transplants, although with non-depolarizing muscle relaxants, about 60-80% of them are eliminated unchanged via the kidneys. d-Tubocurarine has an alternate method of terminating its action, that is by biliary excretion. Pancuronium has some termination of action by hepatic biotransformation. d-Tubocurarine may be the better choice in the presence of hypertension and tachycardia. Pancuronium may be the better choice in the presence of hypotension and bradycardia. Gallamine is not recommended for use in renal failure patients since it is found to be completely excreted by the kidneys. Metocurine (Metubine®) is eliminated somewhat similar to d-Tubocurarine.  

Whatever the choice of muscle relaxant, it should be used judiciously and sparingly. To assess the level of relaxation, the use of a peripheral nerve stimulator is imperative.

**Fluid therapy**

In the patient with end stage renal failure, a uremic condition may exist. Do not overload the patient with fluids. Replace blood loss when indicated. A central venous pressure line will assist in the assessment for replacement of fluid volume.

**Blood gas application**

Do not hyperventilate nor hypoventilate the renal failure patient. These patients already have an increased cardiac output, possible increased potassium levels and uremia. Hypoventilation produces acidosis which may increase serum potassium. Hyperventilation results in alkalosis, increasing the hemoglobin oxygen affinity. Increased workload on the heart and tissue hypoxia may be the result.

It follows, therefore, that arterial blood gases should be measured intraoperatively to offer guidelines for ventilation.

**Reversal and emergence**

At the end of the procedure, the effects of a non-depolarizing muscle relaxant may be reversed with a neostigmine (Prostigmin®) and atropine or a pyridostigmine and glycopyrrolate combination. The choice of reversal technique should depend on the onset, duration of action, and side effects of the drugs. Neostigmine has a faster onset and the duration of action is less; while pyridostigmine is of slower onset with a longer duration of action than neostigmine.

Do not be too quick to extubate the renal failure patient. Reports have been made where recurarization has occurred in renal failure patients who were previously thought to be adequately reversed. It is better judgment to leave the endotracheal tube in place if there is any doubt. Carefully evaluate the degree of reversal of the muscle relaxant with the help of a blockaid monitor; and measure respiratory status, employing all available techniques before extubation.

In summary, as an alternative to inhalation agents, many techniques such as neurolept, regional blocks and narcotics have been used successfully for renal transplant operations. Whatever the method chosen, it is essential that altered responses to drugs be known, and that good judgment and reduced dosages of drugs be used for the end stage renal failure patient.

**REFERENCES**


AUTHOR

Joyce P. Holder, CRNA, BS, is a graduate of Harlem Hospital School of Anesthesia, New York. She received a Bachelor of Science Degree in Health Care Administration from St. Francis College, New York. Ms. Holder is currently an Anesthetist on the Staff of State University Hospital, Downstate Medical Center; Didactic Instructor and Associate Director at Kings County Hospital, School of Anesthesia, which is affiliated with Downstate Medical Center. She is currently in a Master's Degree program at Brooklyn College, New York.