Renal blood flow is closely autoregulated in conscious, healthy patients. Anesthesia blunts or eliminates every patient’s ability to autoregulate renal blood flow. Maintenance of renal blood flow is imperative to preserve renal function in all patients, especially cats. An important goal is to maintain normal urine output during general anesthesia. Anesthetic drugs reduce renal blood flow, and therefore GFR, by causing arterial hypotension. Normal urine output in mammals is 1 to 2 ml/kg/min. Because renal chemistry values do not increase until as much as 80% of normal renal function is lost, it is difficult to evaluate if any renal damage has occurred during anesthesia. For patients with renal failure, any insult to renal function (renal blood flow) may cause all compensation to be lost, precipitating acute (anuric) renal failure.

Hypotension is one of the most common, if not the most common, anesthetic complication. Hypotension, even mild, can be devastating to a patient with renal failure. Preexisting hypovolemia exaggerates hypotension. Renal blood flow may be reduced by 50% due to hypovolemia alone, even before any anesthetic drugs are administered. Metabolic acidosis occurs frequently in renal patients. Renal excretion of drugs is usually impaired, causing delayed recoveries. Patients with an altered level of consciousness require reduced drug doses. PCV and TPP may be reduced and K+ may be increased or decreased. Most geriatric Patients have some degree of renal impairment, which may or may not be reflected by serum chemistry values. Urethral obstruction patients need analgesia and muscle relaxation in addition to unconsciousness (ketamine may not provide these). Bladder rupture patients will benefit from peritoneal lavage with K+ free fluids prior to anesthetic induction.

The aim of the anesthetic protocol is to maintain or increase renal blood flow and oxygenation, and to maintain GFR and urine output. The following protocols are some of the author’s favorites in renal patients:

Pre-procedure: place IV catheter and hydrate patients, check electrolytes and TPS
Premedication: benzodiazepine + opioid, +/- anticholinergic.
Induction is designed to maintain stroke volume and vascular tone
Maintenance: inhalant (isoflurane, sevoflurane, or desflurane)
Adjunct: local anesthetic nerve block (any number of techniques)
Supportive care: thermal support, eye lubricant, etc
IV fluids: buffered isotonic crystalloid at 3 ml/kg/hr for cats, 5 ml/kg/hr in dogs
Recovery: analgesia with opioids, local anesthetic blocks, (NSAIDs may pose nephrotoxicity risk)

**EXAMPLE INDUCTION COMBINATIONS**

<table>
<thead>
<tr>
<th>First IV drug mg/kg</th>
<th>Second IV drug mg/kg</th>
<th>Third IV drug to effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam 0.1</td>
<td>Alfaxan 1 to 2</td>
<td></td>
</tr>
<tr>
<td>Lidocaine 1</td>
<td>Propofol 1 to 3</td>
<td></td>
</tr>
<tr>
<td>Midazolam 0.05</td>
<td>Ketamine 0.5 to 1</td>
<td>Ketamine may be diluted to 10 mg/ml in saline</td>
</tr>
<tr>
<td></td>
<td>every 30 seconds</td>
<td></td>
</tr>
<tr>
<td></td>
<td>until intubateable</td>
<td></td>
</tr>
<tr>
<td>Midazolam 0.05</td>
<td>Ketamine 0.5 to 1</td>
<td>Propofol 1 to 2</td>
</tr>
<tr>
<td>Midazolam 0.05</td>
<td>Lidocaine 1</td>
<td>Etomidate 0.5 to 2</td>
</tr>
</tbody>
</table>

**RENAAL PROTECTION: CONTROVERSIES**

The renal system serves the three primary functions of filtration, reabsorption, and secretion and many secondary functions. In healthy patients, the kidneys receive approximately 20% to 25% of cardiac output, which is unequally distributed between the cortex and medulla. The renal cortex receives more than 90% of the total renal blood flow. Despite receiving a large distribution of cardiac output, the kidney is highly sensitive to hypotension and hypoperfusion. Evidence suggests the thick ascending limbs and straight proximal S3 segments of the loop of Henle are highly susceptible to hypoxic injury due to the high oxygen requirements of sodium and chloride reabsorption. Acute tubular necrosis can be induced with as little as a 40% to 50% reduction in total renal blood flow.

Control of medullary blood flow is complex and involves a number of mediators which include nitric oxide, prostaglandin E2, adenosine, dopamine, urodilatin, endothelin, angiotensin II, ADH, insulin-like growth factor I, epidermal growth factor, and tumor necrosis factor. There is also a tubulo-glomerular feedback mechanism which activates when there is insufficient reabsorption of sodium by the renal tubules. This reflex leads to glomerular afferent vasoconstriction, reducing filtration and the delivery and reabsorption of tubular solute.

Medullary hypoxic injury is characterized by necrosis of the tubules farthest away from the blood vessels. The injury associated with hypoxia alone will be worsened by the presence of aminoglycoside or other nephrotoxic antibiotics, NSAIDs, calcium ions, myoglobin, hyperbilirubinemia, and radiocontrast media.
The most significant risk factors for development of renal tubular necrosis seem to be hypotension, hypovolemia, and/or dehydration. Other risk factors identified in people undergoing cardiac surgery include: age greater than 75% of life expectancy, diabetes mellitus, congestive heart failure, low cardiac index, preexisting renal dysfunction, and more complex surgical procedures.

Acute Kidney Injury (AKI) does not represent a single clinical entity; rather, it is a constellation of many disease processes and pathophysiology. Acute Kidney Injury is defined different ways. The Society of Thoracic Surgeons describes two separate clinical entities: postoperative renal insufficiency is defined as a 2-fold or greater elevation of serum creatinine and renal failure as AKI requiring dialysis. Other groups use different criteria to grade or define AKI and there is no clear consensus.

Assessment or measurement of renal function in the peri-anesthetic and postoperative period most often includes serum BUN, serum creatinine, and urine output as predictors of GFR. None of these tests are fully specific for renal function. Of the three, serum creatinine is the most specific indicator of renal function. Other tests used to assess renal function include urine specific gravity, urine protein quantitation, urine osmolality, urine/plasma creatinine ratio, urine/plasma urea ratio, urinary sodium excretion, fractional excretion of sodium, free water clearance, creatinine clearance, and renal blood flow. The most recent serum chemistry value used to indicate real status is Symmetric Dimethylarginine (SDMA) a methylated arginine amino acid. SDMA is specific for kidney function. SDMA is not affected by other diseases if kidney function is not affected. SDMA is a biomarker of kidney function. It reportedly correlates extremely well with glomerular filtration rate (GFR). SDMA increases earlier than creatinine in chronic kidney disease. SDMA increases when approximately 40% of kidney function is lost. This may prove an additional indicator of anesthesia/surgery induced AKI.

Treatment aims for the prevention of post-operative renal dysfunction include

1. Maintaining adequate oxygen delivery
2. Avoidance of renovascular constriction
3. Renal vasodilation
4. Maintaining renal tubular flow
5. Decrease oxygen demand

Non-controversial recommendations to protect renal function include optimization of renal perfusion and avoidance of nephrotoxic substances. In patients with pre-existing renal dysfunction, stabilization and diuresis in the pre-operative period are
recommended. For at risk patients, recommendations include maintaining adequate vascular volume by the administration of IV fluids. Isotonic crystalloids may be preferable to colloids for volume loading as the renal effects of different colloids have not yet been fully elucidated.

The use of dopamine at "renal" doses (0.5 to 4 mcg/kg/min IV) is controversial and there are many studies with conflicting results as to the validity of this practice. Two large, independent meta-analytical papers covering 39 studies and 1,970 human patients found no benefit to the administration of “renal” doses of dopamine at preventing AKI. These studies included both surgical patients and patients in the ICU. In healthy, non-anesthetized patients, low dose dopamine (0.05 to 2.5 mcg/kg/min) results in renal vasodilation and predominantly reduces the activity of the Na+/K+ ATPase in the proximal tubule, thereby reducing proximal tubular reabsorption of sodium. At higher doses (5 to 10 mcg/kg/min) cardiac output increases, increasing renal blood flow, GFR, and natriuresis. However, these effects in anesthetized patients are less clear. Dopamine also has inotropic effects and can cause tachycardia and arrhythmia through its alpha and beta adrenoceptor effects.

Fenoldopam is a selective DA1 receptor agonist introduced as an antihypertensive drug. Fenoldopam has no alpha or beta adrenoceptor effects. It reduces blood pressure in a dose dependent manner while preserving renal blood flow and GFR. More recently it has gained favor for use as a renal protectant (0.03 to 0.05 mcg/kg/min IV) in people undergoing cardiovascular surgery. In dogs, fenoldopam acts to increase both medullary and cortical blood flow, decreases sodium transport in the thick ascending loop, reducing medullary oxygen requirements. Although promising in people and dogs, there are few trials of fenoldopam in renal protection and scant information about fenoldapam in cats. Cats do not have the same populations of dopamine receptors in their kidneys as dogs and people do, therefore may not respond the same to this drug.

Other techniques postulated as useful for renal protection are controversial and there is little objective evidence to support their routine use.

The use of low dose mannitol may be of benefit in some patients. Mannitol exerts its actions via several mechanisms. It is an osmotic diuretic, it causes renal vasodilation through a prostaglandin mediated effect, and acts as a free radical scavenger. To be effective, mannitol must be given prior to the ischemic episode and at high doses it can cause renal vasoconstriction.
Prophylaxis with loop diuretics, such as furosemide, is effective for preventing pigment nephropathies. The use of furosemide can cause renal vasodilation, increased urine output and creatinine clearance. However, it may also precipitate renal impairment in some patients.

Dopexamine is a synthetic sympathomimetic agonist having mostly beta-2 effects. It acts as a positive inotrope, increasing heart rate and decreasing systemic vascular resistance. Dopexamine may increase renal blood flow through DA1 agonism, leading to intra-renal vasodilation. This results in increased cortical, but not medullary, blood flow. The increased renal blood flow will increase GFR and urine production.

Calcium channel blockers such as verapamil or diltiazem may have beneficial effects in renal protection. Alveolar vasoconstriction is mediated by increases in cytoplasmic calcium. Calcium antagonists may affect renal vascular tone and GFR.

Investigations currently underway are examining the systemic administration of erythropoietin and minocycline, a second-generation tetracycline. Intra-renal infusion of fenoldopam, the calcium antagonist nimodipine, acetylcholine, and erythropoietin are also being investigated for their renal protective potential.

REFERENCES


