

CHAPTER 32 (L+J 2015)

- Azotemia is associated with a decrease in plasma pH and can decrease protein binding of administered drugs
 - Results in higher concentrations of active free drug and increased risk of relative overdose
- All anesthetics are likely to decrease the rate of glomerular filtration
- Anesthetic drugs may directly affect RBF or they may indirectly alter renal function via changes in cardiovascular and/or neuroendocrine activity.
- Sedative and analgesic drugs have varying effects on RBF and GFR and generally relate to individual drug effects on cardiac output and vasomotor tone
 - Most anesthetics that decrease GFR do so as a consequence of decreased RBF.

Table 32.4 Effects of anesthetics on renal blood flow (RBF) and glomerular filtration rate (GFR).

Drug	RBF	GFR
Isoflurane	Slight decrease	Decrease
Sevoflurane	Slight decrease	Decrease
Thiopental	No change	No change or slight decrease
Ketamine	Increase	Decrease or no change
Propofol	No change	No change
Etomidate	No change	No change

Source: adapted from Green SA, Grauer GF 2007. Renal disease. In: Tranquilli WJ, Thurmon JC, Grimm KA, eds. *Lumb and Jones' Veterinary Anesthesia and Analgesia*, 4th edn. Ames, IA: Blackwell Publishing, 2007; 915–919. Reproduced with permission of Wiley.

α2-Adrenergic agonist drugs

- Can have significant dose-dependent depressant effects on heart rate and cardiac output and increase systemic vascular resistance
- These effects could be expected to reduce RBF and subsequently GFR – decreases RBF by 30%.
- Cause profound diuresis
 - The mechanism is multifactorial including inhibition of vasopressin (AVP) release, inhibition of cAMP formation in the kidney, redistribution of aquaporin-2 receptors, inhibition of renin release, increased atrial natriuretic peptide, inhibition of renal sympathetic activity, osmotic diuresis due to increased plasma glucose, and inhibition of tubular sodium reabsorption
 - The increased production of dilute urine may be detrimental in patients with postrenal urinary tract obstruction or dehydration and hypovolemia

Benzodiazepines

- Diazepam and midazolam have minimal effects on cardiac output, systemic vascular resistance, and blood pressure. Consequently, their use probably has little impact on RBF and GFR
- Protein bound in the plasma
- Reduction in initial dosage is probably warranted in patients with acute kidney disease or which are severely acidotic, azotemic, or hypoproteinemic

Opioids

- Provide sedation and analgesia to patients with minimal impact on cardiac output and RBF as a result
- Opioids can cause urine retention when administered systemically or as an epidural injection

Barbiturates

- Highly protein bound
- Avoid use of thiopental in patients with azotemia or renal disease

Ketamine

- Increases RBF and renal vascular resistance
- Ketamine and its metabolites are highly dependent on renal excretion
 - In cats majority of the drug is excreted unchanged and should be avoided in cats with renal insufficiency

Propofol

- Propofol demonstrates a dose and rate-dependent reduction in arterial blood pressure
- At moderate to low doses it has minimal effects on RBF and GFR
- Suitable agent for induction and total intravenous anesthesia in human patients with uremia

Etomidate

- Minimal effects on heart rate, blood pressure, and cardiac output
- Does not significantly affect GFR in dogs

Inhalant anesthetics

- Can cause systemic hypotension, especially during excessive depth
 - Can cause renal ischemia secondary to reduced RBF and GFR
- Depress myocardial contractility and cardiac output in a dose-dependent manner
- Decrease RBF and GFR in a dose-dependent manner
- Light planes of inhalation anesthesia preserve renal autoregulation of blood flow, whereas deep planes are associated with depression of autoregulation and decreases in RBF
- Effects of inhaled anesthetics on renal function are reversed at the termination of anesthesia
 - Some patients may not regain the ability to regulate urine production for several days

Anesthetic management of patients with kidney disease

- Premedication: opioid–benzodiazepine combination
- Induction: propofol, thiopental, etomidate, benzodiazepine-dissociative, or benzodiazepine–opioid combinations.

Table 32.5 Example of an anesthetic plan for a small animal patient with renal disease.

Drug	Dose	Route
<i>Premedication:</i>		
Opioid of choice:		
Butorphanol	0.2–0.4 mg/kg	Intramuscular
Hydromorphone	0.1–0.2 mg/kg	Intramuscular
Morphine	0.1 mg/kg (cats)	Intramuscular
	0.25–1.0 mg/kg (dogs)	Intramuscular
Midazolam ^a	0.2–0.4 mg/kg	Intramuscular
<i>Induction:</i>		
Propofol	4–6 mg/kg (to effect)	Intravenous
or		
Etomidate	1–2 mg/kg (to effect)	Intravenous
<i>Maintenance:</i>		
Isoflurane	1–2% (to effect)	Inhalation
or		
Sevoflurane	2–3% (to effect)	Inhalation
<i>Adjunctive to maintenance:</i>		
Remifentanyl	0.005–0.02 mg/kg/h	Intravenous infusion
or		
Fentanyl	0.005–0.02 mg/kg/h	Intravenous infusion
<i>Supportive treatments:</i>		
Replacement crystalloid fluid (lactated Ringer's, Normosol-R, or Plasma-Lyte A)	10–20 mL/kg for first hour	
Mannitol (20–25% solution) ^b	5–10 mL/kg/h thereafter	
	Loading dose 500 mg/kg	
	Infusion 1 mg/kg/min	

^aIn healthy cats and dogs, midazolam may elicit aggressive or excitable behavior and can be removed from the plan.

^bMannitol is prone to crystallization at room temperatures and should be warmed prior to administration and delivered through a filter.

- RBF and GFR (and therefore urine production) are generally decreased with surgery in any patient due to release of aldosterone, vasopressin, renin, and catecholamines associated with stress
 - In the face of appropriate intravenous fluid administration (10 mL/kg/h) during anesthesia, dogs with normal kidney function will have a urine output less than the usual range of 1–2 mL/kg/h in awake animals
- Most important parameters for a patient with renal disease are hydration status and circulating blood volume
- IV fluid therapy through anesthetic period will maintain fluid volume and hydration
 - Rate of 20 mL/kg for the first hour then 10 mL/kg/h should be maintained if the patient does not have heart disease, hypoproteinemia, or severe anemia

Questions

1. In an animal with a negative fluid balance, how can using an alpha 2 adrenergic agonist worsen dehydration?
2. True or False. Medetomidine in combination with anticholinergic and opioid drugs increases GFR in dogs.

3. Which of the following drugs have a significant effect on GFR when used at moderate doses?
 - a. Etomidate
 - b. Propofol
 - c. Diazepam
 - d. Isoflurane

Answers

1. In an animal with a negative fluid balance, how can using an alpha 2 adrenergic agonist worsen dehydration?
 - a. Void large volumes of dilute urine. Block vasopressin receptors located within the collecting ducts, preventing water reabsorption
2. True or **false**. Medetomidine in combination with anticholinergic and opioid drugs increases GFR in dogs.
 - a. *There is evidence that medetomidine in combination with anticholinergic and opioid drugs has minimal effects on GFR in dogs*
3. Which of the following drugs have a significant effect on GFR when used at moderate doses?
 - a. Etomidate
 - b. Propofol
 - c. Diazepam
 - d. **Isoflurane**