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ANESTHESIA FOR HEPATIC & RENAL DISEASED PATIENTS

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Keys to consider in the patient with hepatic dysfunction

- Hepatic function
  - Regulation of blood glucose
  - Synthesis of protein
  - Synthesis of clotting factors
  - Fat metabolism
  - Metabolism of drugs
- Hepatic blood flow
  - 20% of cardiac output
  - Hepatic artery
    - 30% of hepatic blood flow
    - 90% of oxygen deliver
  - Portal vein
    - 70% of hepatic blood flow
    - 10% of oxygen deliver
  - Anesthetics can alter hepatic perfusion by altering blood flow through either the hepatic artery, portal vein, or both
- Diagnosis of hepatic insufficiency
  - Ascites and distended abdomen
  - Enlarged liver
  - Depression
  - Seizuressjdclk
  - Weight loss
  - Jaundice
  - Laboratory analysis
    - "liver" enzymes
    - increased bleeding time
    - bile acids
- The hepatic dysfunction patients may have one or all of the following conditions:
  - Hypoproteinemia
  - Hypoglycemia
  - Bleeding problem
  - Slow to metabolize anesthetics
- Use anesthetics that can be antagonized or require less hepatic metabolism.
- Avoid long duration of action drug such as acepromazine.

Anesthetic management of hepatic dysfunction patients

Potential problems	*Management*
Low hepatic blood flow	• Avoid deep anesthesia • Maintain blood volume and blood pressure • Monitoring oxygenation and prevent hypoxemia by administering 100% oxygen
Prolonged recovery from anesthesia	• Use propofol induction or isoflurane mask induction • Reverse opioids if necessary • Use short half-life drugs (avoid high dose acepromazine or spare it all together)
Hemorrhage	• Pre-treat with vitamin K • Fresh whole blood transfusion • Give plasma to prevent clotting problem
Hypoglycemia	• Give 5% dextrose and other glucose supplements

A. Premedication:

- Depressed patients may not need preanesthetic premedication. Face mask induction with inhalation agents (isoflurane or sevoflurane)….note that 99% of isoflurane is eliminated from respiration and not the liver. Avoid premedication in severely debilitated patients.
- Avoid phenothiazine tranquilizers such as acepromazine:
  - Prolonged drug effect - prolonged recovery.
  - Vasodilation & thermoregulation disturbance and therefore hypothermia.
  - Lower seizure threshold
  - Reported isolated incidence of jaundice and hepatic injury in human following phenothiazine administration
- Avoid xylazine, or medetomidine to avoid hypotension and other profound cardiovascular depression.
- Agents of controversy
  - Benzodiazepines: have minimal tranquilizing effect in healthy animals but do have sedative effects in depressed patients. High dose of benzodiazepine may prolong recovery
  - Endogenous benzodiazepine like substance have been implicated with pathogenesis of hepatic encephalopathy
- Agents of choice: opioids +/- anticholinergics
  - Opioids:
    - provide analgesia
    - has minimal adverse effect on the liver
    - Reversible with opioid antagonists
  - Example
    - Oxymorphone 0.05-0.1 mg/kg IM, IV, or
    - hydromorphone 0.05-0.1 mg/kg IM, IV or
    - Morphine 0.25-0.5 mg/kg, IM, IV or
    - Butorphanol 0.1-0.4 mg/kg, IM, IV
    - with atropine 0.02-0.04 mg/kg, IM or glycopyrrolate 0.005-0.01 mg/kg IM, IV.

B. Induction

- Preoxygenation of 2-3 minutes prior to induction to prevent hypoxemia.
- Propofol, etomidate and thiobarbiturates can be used to induce mild to moderate liver dysfunctional patients. "titrate to effect" induction method is necessary. Avoid these in severe dysfunctional patients.
- Mask or chamber induction the animal with severe liver diseases.
- Cats may be induced with diazepam-ketamine combination or Telazol with minimal complication.
- Mild to moderate hepatic dysfunction dogs may be induced with diazepam-ketamine. Ketamine and Telazol (tiletamine) will have prolonged effects in dogs with severe hepatic dysfunction.

C. Maintenance and supportive therapy

- Isoflurane and sevoflurane are better choice for maintenance.
- Avoid halothane: higher metabolism and incidence of malignant hepatitis
- Portal vein blood flow decreases but portal arterial blood flow increases during isoflurane administration. However, decrease of portal venous blood flow is not offset by increases in hepatic arterial blood flow during administration of halothane. Therefore isoflurane is better choice as it can deliver more oxygen to the hepatic tissue.
- Lactated Ringer's solution with 5% dextrose if plasma glucose level is less than 70 mg/dl.
- In cases with albumin levels less than 2 g/dL, supplemental colloids such as plasma, dextran, or hetastarch are administered to increase plasma oncotic pressure.
- Avoid fluid overloading---less protein – and more susceptible to pulmonary edema.
- Balanced anesthesia using neuromuscular blocker: atracurium preferred over pancuronium

D. Recovery

- Allow recovering in a warm environment
- Under constant surveillance until fully recovered.
- Reverse opioids (with naloxone or partial reversal with butorphanol) and benzodiazepines (with flumazenil) if necessary.
- Keep patients warm and observe for bleeding.
- Closely monitor for signs of potential intra-abdominal bleeding
- Portal hypertension can cause severe discomfort as well as hemodynamic instability.
- Analgesia and symptomatic therapy

Keys to Anesthetizing Renal Dysfunction Patients

A. These patients may have one or some of the following conditions

- Hypoproteinemia
- Uremia
- Hyperkalemia
- Metabolic acidosis
- Dehydration
- Anemia

B. Anesthetic protocol considerations

- Anesthetic protocols must minimize changes in renal blood flow (blood flow: 25% of normal cardiac output)
- Anesthetic recovery at best is through liver metabolism or redistribution rather than renal excretion.
- Anesthetic metabolites should not be harmful to kidney (e.g., fluoride ions from methoxyflurane)
- Anesthesia and surgical stress results in decreased RBF, GFR and urine production due to the release of:
  - Aldosterone
  - Vasopressin (ADH)
  - Renin
  - Catecholamines
- Avoid drugs or condition (dehydration, hemorrhaging) that cause hypotension.

C. Example of anesthetic combinations

- Premedications: oxymorphone 0.05-0.1 mg/kg, hydromorphone 0.05-0.1 mg/kg, or morphine 0.5-1 mg/kg, butorphanol 0.1-0.2 mg/kg, IV or IM with atropine 0.02 - 0.04 mg/kg or glycopyrrolate 0.005 - 0.01 mg/kg IV or IM.
- These opioids + anticholinergics can be combined with diazepam or midazolam (0.1- 0.2 mg/kg, IM or IV)
- Induction: mask or chamber with isoflurane or sevoflurane, or using propofol for induction.
- Maintenance: isoflurane or sevoflurane in oxygen, supplemental opioids for analgesia intraoperatively

Effects of Anesthetic Agents on Renal Function

A. Tranquilizers

- Phenothiazine and butyrophenone tranquilizers can produce hypotension due to peripheral vasodilation.
- Vasodilation reduces renal blood flow if normal blood volume and blood pressure is not maintained.
- May have prolonged effect in uremic patient.
- Benzodiazepines have minimal effect on renal function.

B. Xylazine or Medetomidine

- No direct effect on the kidney.
- May cause systemic hypotension or reduction of cardiac output and therefore lower renal perfusion
- Cause short duration of polyuria and glucosuria.

C. Opioids (morphine, hydromorphone, oxymorphone, butorphanol, fentanyl)

- Have no direct effect on the kidney.
- Stimulate ADH release and may produce transient oliguria, especially at high dose.
- Cause urinary retention due to increased tone of vesicle sphincter

D. Dissociative agents (ketamine, tiletamine)

- No direct effect on the kidney
- Sympathetic tone - cause a transitory decrease in renal blood flow.
- Cats eliminate ketamine predominantly unchanged through renal excretion.

E. Inhalation anesthetics

- Methoxyflurane:
  - Reduction of cardiac output, which would reduce renal blood flow.
  - Fluoride ion is released during the hepatic biotransformation.
  - Fluoride ion can produce proximal renal tubular necrosis.
    - Human >>> animals.
  - Fluoride induced nephrotoxicity
    - polyuria
    - hypernatremia
    - hyperosmolarity
    - increased plasma creatinine
    - inability to concentrate urine
  - Due to its nephrotoxicity this product was withdrawn and no longer in clinical use
- Halothane:
  - Renal function reduced due to reduction in cardiac output and ADH release.
  - Does not have a direct nephrotoxic effect.
- Isoflurane, sevoflurane, desflurane and nitrous oxide
  - Affects renal function minimally.
  - Sevoflurane reacts with carbon dioxide absorbents (soda lime, Baralyme) to form Compound A (fluoromethyl-2,2-difluro-1-(trifluoromethyl) vinyl ether)
    - It is nephrotoxic in rats.
    - The amount produced under clinical conditions has consistently been far below those concentrations associated with nephrotoxicity and the product is widely used in human anesthesia
    - Currently there is little evidence to contraindicate its clinical veterinary use due to concerns over nephrotoxicity.

Anesthetic agent selections

A. Premedication

- Premedication administered at a dose producing mild sedation enables easy handling of the patient (minimize stress and excitement) and is beneficial from low dose of phenothiazine or benzodiazepine tranquilizers, or a low dose of opioid may be given.
- Alpha 2 agonists can be used if cardiovascularly stable and can compensate but avoid these in severely debilitated renal failure patients
- Anticholinergics should be given in severely uremic patients since they are more susceptible to vagal-induced bradycardia and cardiac arrest.
- Depressed patients may not need preanesthetic premedication - simply mask with inhalation agents. Avoid heavy premedication in severely debilitated patients.

B. Induction

- Barbiturates should be used cautiously in renal dysfunction patients.
- Avoid barbiturates in severely uremic patients.
- Use of opioid agents induces narcosis which facilitates endotracheal intubation and safe induction.
- Midazolam with oxymorphone is suitable for dogs or cats induction.
- Reducing induction dose is necessary in mild-moderate renal dysfunction patients.

C. Maintenance

- Isoflurane or sevoflurane are better than halothane
- Monitor cardiovascular function- monitor arterial blood pressure intraoperatively - maintain mean arterial blood pressure at 70 mmHg with inotropic agents such as dopamine or dobutamine infusion.
- Fluid administration with crystalloid solution 10 ml/kg/hr, providing total protein and albumin are adequate.
- Blood loss should be replaced as it occurs- volume-for-volume basis using a colloidal solution or three times the volume of blood lost using a crystalloid solution.
- Arterial blood gas - acid-base monitoring.
- Urine output should be monitored - indication of renal perfusion.
    - Normal urine output 1-2 ml/kg/hr. If urine output reduces to 0.5 ml/kg/hr renal perfusion is inadequate.
- Low dose of dopamine 2-5 µg per kg per minute can be infused to patient to improve renal perfusion.

Recovering renal diseased patients

- Recover in a warm environment
- Under constant surveillance until fully recovered
- Maintain fluid volume and urine output until fully recovered
- Analgesia and symptomatic therapy