

Managing Phosphorus & Magnesium Disorders

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You have asked...
What role do phosphorus and magnesium play in the health of veterinary patients?

The expert says...

Phosphorus is an important component of nucleic acids, phospholipids, and phosphoproteins and has a role in the metabolism of protein, fat, and carbohydrate and in processes requiring energy from adenosine triphosphate (ATP). Magnesium, meanwhile, is important for energy production, vascular smooth muscle tone, and protein synthesis; helps maintain appropriate intracellular potassium concentration; and regulates cytoplasmic calcium concentrations.

Phosphorus

Approximately 85% of total body phosphate is inorganic hydroxyapatite in bone and about 15% is in soft tissues. Phosphorus levels are regulated by the GI tract and kidneys under the influence of calcitriol, calcitonin, and parathyroid hormones.

Hypophosphatemia

Hypophosphatemia occurs when serum phosphorus concentrations are less than 2.5 mg/dL, although reference ranges vary (see **Causes of Hypophosphatemia**). Hypophosphatemia decreases ATP concentrations in RBCs, increasing erythrocyte fragility and leading to hemolysis (generally not observed until phosphorus concentration is <1 mg/dL). Hypophosphatemia

ATP = adenosine triphosphate

MORE ►

Causes of Hypophosphatemia

- | | |
|---|---|
| Decreased intake | <ul style="list-style-type: none"> ■ Phosphate binders ■ Vitamin D deficiency |
| Increased loss | <ul style="list-style-type: none"> ■ Hyperadrenocorticism ■ Primary hyperparathyroidism ■ Renal tubular disorders |
| Laboratory error | |
| Redistribution from extracellular fluid to intracellular space | <ul style="list-style-type: none"> ■ Hypothermia ■ IV dextrose administration ■ Refeeding syndrome (associated with enteral or parenteral nutritional supplementation after starvation or malnutrition) ■ Respiratory alkalosis ■ Treatment of diabetic ketoacidosis with insulin administration |

may also cause impaired oxygen delivery, shortened platelet survival time, weakness, pain (associated with rhabdomyolysis), vomiting, and proximal tubule bicarbonate wasting.

Hypophosphatemia should be anticipated in susceptible patients (ie, receiving insulin for diabetic ketoacidosis, at risk for refeeding syndrome). In these patients, phosphorous levels should be monitored closely or supplemented.

When hypophosphatemia develops, phosphorus should be supplemented in symptomatic patients *or* asymptomatic patients at risk for symptomatic hypophosphatemia. Phosphorus is best replaced by potassium phosphate CRI at 0.01 to 0.06 mmol/kg/hr IV mixed in saline or dextrose. Discontinue phosphorus supplementation when serum concentration normalizes. Monitor serum phosphorus concentration closely after discontinuing supplementation. Levels should be rechecked q6h to avoid oversupplementation, which may lead to hypocalcemia, soft tissue mineralization, hyperphosphatemia, or acute kidney injury. Oral phosphorus supplementation may be provided, although it is generally ineffective in vomiting patients or those with diarrhea. The underlying cause of hypophosphatemia should be investigated and addressed.

Hyperphosphatemia

Hyperphosphatemia occurs when serum phosphorus concen-

Causes of Hyperphosphatemia

Decreased excretion

- Renal insufficiency
- Hypoparathyroidism
- Prerenal or postrenal disease

Increased intake

- Hyperthyroidism phosphate enemas
- IV phosphorus supplementation
- Vitamin D intoxication

Laboratory error

Physiologic cause ■ Growing animals

Translocation

- Hemolysis
- Metabolic acidosis
- Rhabdomyolysis
- Tumor lysis syndrome

Physiologic cause ■ Growing animals

trations are greater than 6.5 mg/dL, but reference ranges may vary; like hypophosphatemia, the causes can vary (see **Causes of Hyperphosphatemia**). Increases in phosphorous concentration usually lead to decreased calcium concentration. Hyperphosphatemia may lead to hypocalcemia and soft tissue mineralization. Risk for soft tissue mineralization is higher when the calcium phosphorous ($\text{Ca} \times \text{PO}_4$) product is greater than 70.

IV fluid therapy usually decreases circulating phosphorus levels by increasing the glomerular filtration rate, hence phosphorus excretion, preferred for vomiting and/or anorexic patients. All oral sources of phosphorus should be evaluated and adjusted. Dietary phosphorus restriction should be initiated (usually with a protein-restricted diet [also low in phosphorus]). In patients with chronic renal insufficiency, intestinal phosphate absorption should be reduced by administration of oral phosphate binders with a meal. Common phosphate binders include aluminum hydroxide, calcium carbonate, and calcium acetate.

Magnesium

Magnesium is an intracellular cation found primarily in bone and muscle; only about 1% is located extracellularly. Extracellular magnesium is present in 3 forms: an ionized form that is biologically active, a protein-bound form, and a complex form. Magnesium is regulated in the GI tract and kidneys under the influence of parathyroid hormone and 1,25-dihydroxycholecalciferol. Increased morbidity and mortality can occur in critically ill patients with altered serum magnesium concentrations.

Hypomagnesemia

Although the diagnosis of hypomagnesemia remains controversial and challenging, total and ionized magnesium levels can help evaluate patients with low magnesium concentrations. Total magnesium evaluation is widely available in reference laboratories, while ionized magnesium analysis is less common. Low total serum magnesium is usually significant in patients at risk for hypomagnesemia. However, total serum magnesium concentrations can be normal in patients with total body magnesium deficits.

Hypomagnesemia, commonly caused by depletion of total body stores of magnesium (see **Causes of Hypomagnesemia**), has been documented in critically ill dogs and associated with prolonged hospitalization and increased mortality.¹ Low magnesium may lead to cardiac arrhythmias (atrial fibrillation, supraventricular tachycardia, torsade de pointes), cardiac necrosis, systemic hypertension, dysphagia, and tetany. Hypomagnesemia may also cause refractory hypokalemia, hyponatremia, and hypocalcemia. Patients with concurrent refractory electrolyte abnormalities magnesium supplementation.

Causes of Hypomagnesemia

Changes in distribution

- Administration of insulin
- Idiopathic
- Massive blood transfusion
- Pancreatitis
- Sepsis
- Shock

Increased intake of magnesium

- Inadequate nutrition

Increased loss of magnesium

- Administration of aminoglycosides
- Chronic diarrhea
- Diabetic ketoacidosis
- Hyperthyroidism
- Inflammatory bowel disease
- Postobstructive diuresis
- Renal tubular acidosis

Laboratory error

Supplementation should be considered in at-risk patients with total magnesium concentrations of less than 1.5 mg/dL or if any signs consistent with hypomagnesemia are present. Patients requiring magnesium supplementation are typically treated with parenteral infusion of magnesium salts (magnesium chloride or sulfate) at 0.3 to 1 mEq/kg/q24h IV. The dose should be reduced in patients with underlying renal disease and cardiac conduction abnormalities.

Hypermagnesemia

Hypermagnesemia, not as clinically significant or as common as hypomagnesemia is commonly caused by renal insufficiency and pre- or postrenal azotemia. Recommended doses for magnesium supplementation are safe and rarely cause hypermagnesemia in veterinary patients. However, all patients supplemented with magnesium should be observed for changes in blood pressure or alterations on ECG.

Clinical signs associated with hypermagnesemia in humans include hypoventilation, hypotension, cutaneous flushing, and alterations in cardiac contractions. Hypermagnesemia, relatively easy to diagnose, is characterized by increased total serum magnesium or ionized magnesium concentration. Any value higher than laboratory reference range for magnesium suggests increased total body magnesium concentration.

Patients with hypermagnesemia should have discontinued parenteral magnesium supplementation, IV diuresis should be initiated (0.9% NaCl), and dialysis may be considered in patients with significant renal insufficiency. Calcium gluconate 10% (0.5–1.5 mL/kg IV over 10–15 min) may be administered to antagonize some of the effects of hypermagnesemia in patients with cardiac abnormalities. ■ **cb**

See **Aids & Resources**, back page, for references & suggested reading.

Advantage Multi® for Dogs and for Cats

(imidacloprid + moxidectin)

BRIEF SUMMARY: Before using *Advantage Multi® for Dogs* (imidacloprid+moxidectin) or *Advantage Multi® for Cats* (imidacloprid +moxidectin), please consult the product insert, a summary of which follows:

CAUTION: Federal (U.S.A.) Law restricts this drug to use by or on the order of a licensed veterinarian.

Advantage Multi for Dogs:

WARNING

- DO NOT ADMINISTER THIS PRODUCT ORALLY.
- For the first 30 minutes after application ensure that dogs cannot lick the product from application sites on themselves or other treated animals.
- Children should not come in contact with the application sites for two (2) hours after application.

(See Contraindications, Warnings, Human Warnings, and Adverse Reactions for more information.)

INDICATIONS:

Advantage Multi for Dogs is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis* and the treatment of *Dirofilaria immitis* circulating microfilariae in heartworm-positive dogs. **Advantage Multi for Dogs** kills adult fleas and is indicated for the treatment of flea infestations (*Ctenocephalides felis*). **Advantage Multi for Dogs** is indicated for the treatment and control of sarcoptic mange caused by *Sarcoptes scabiei var. canis*. **Advantage Multi for Dogs** is also indicated for the treatment and control of the following intestinal parasites species: Hookworms (*Ancylostoma caninum*) (*Uncinaria stenocephala*), Roundworms (*Toxocara canis*) (*Toxascaris leonina*) and Whipworms (*Trichuris vulpis*).

Advantage Multi for Cats is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis*. **Advantage Multi for Cats** kills adult fleas (*Ctenocephalides felis*) and is indicated for the treatment of flea infestations. **Advantage Multi for Cats** is also indicated for the treatment and control of ear mite (*Otodectes cynotis*) infestations and the intestinal parasites species Hookworm (*Ancylostoma tubaeforme*) and Roundworm (*Toxocara cati*). **Ferrets:** **Advantage Multi for Cats** is indicated for the prevention of heartworm disease in ferrets caused by *Dirofilaria immitis*. **Advantage Multi for Cats** kills adult fleas (*Ctenocephalides felis*) and is indicated for the treatment of flea infestations in ferrets.

CONTRAINDICATIONS: Do not administer this product orally. (See **WARNINGS**). Do not use the Dog product (containing 2.5% moxidectin) on cats.

WARNINGS:

Advantage Multi for Dogs: For the first 30 minutes after application: Ensure that dogs cannot lick the product from application sites on themselves or other treated dogs, and separate treated dogs from one another and from other pets to reduce the risk of accidental ingestion. Ingestion of this product by dogs may cause serious adverse reactions including depression, salivation, dilated pupils, incoordination, panting, and generalized muscle tremors. In avermectin sensitive dogs¹, the signs may be more severe and may include coma and death².

¹ Some dogs are more sensitive to avermectins due to a mutation in the MDR1 gene. Dogs with this mutation may develop signs of severe avermectin toxicity if they ingest this product. The most common breeds associated with this mutation include Collies and Collie crosses.

² Although there is no specific antagonist for avermectin toxicity, even severely affected dogs have completely recovered from avermectin toxicity with intensive veterinary supportive care.

Advantage Multi for Cats: Do not use on sick, debilitated, or underweight cats. Do not use on cats less than 9 weeks of age or less than 2 lbs. body weight. Do not use on sick or debilitated ferrets.

HUMAN WARNINGS: Not for human use. Keep out of the reach of children. Dogs: Children should not come in contact with the application sites for two (2) hours after application. Cats: Children should not come in contact with the application site for 30 minutes after application.

Causes eye irritation. Harmful if swallowed. Do not get in eyes or on clothing. Avoid contact with skin. Wash hands thoroughly with soap and warm water after handling. If contact with eyes occurs, hold eyelids open and flush with copious amounts of water for 15 minutes. If eye irritation develops or persists, contact a physician. If swallowed, call poison control center or physician immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by the poison control center or physician. People with known hypersensitivity to benzyl alcohol, imidacloprid or moxidectin should administer product with caution. In case of an allergic reaction, contact a physician. If contact with skin or clothing occurs, take off contaminated clothing. Wash skin immediately with plenty of soap and water. Call a poison control center or physician for treatment advice. The Material Safety Data Sheet (MSDS) provides additional occupational safety information. For a copy of the Material Safety Data Sheet (MSDS) or to report adverse reactions call Bayer Veterinary Services at 1-800-422-9874. For consumer questions call 1-800-255-6826.

PRECAUTIONS: Do not dispense dose applicator tubes without complete safety and administration information. Use with caution in sick, debilitated or underweight animals. The safety of **Advantage Multi for Dogs** has not been established in breeding, pregnant, or lactating dogs. The safe use of **Advantage Multi for Dogs** has not been established in puppies and dogs less than 7 weeks of age or less than 3 lbs. body weight. **Advantage Multi for Dogs** has not been evaluated in heartworm-positive dogs with Class 4 heartworm disease.

Cats may experience hypersalivation, tremors, vomiting and decreased appetite if **Advantage Multi for Cats** is inadvertently administered orally or through grooming/licking of the application site. The safety of **Advantage Multi for Cats** has not been established in breeding, pregnant, or lactating cats. Use of this product in geriatric cats with subclinical conditions has not been adequately studied. Ferrets: The safety of **Advantage Multi for Cats** has not been established in breeding, pregnant, and lactating ferrets. Treatment of ferrets weighing less than 2.0 lbs. (0.9kg) should be based on a risk-benefit assessment. The effectiveness of **Advantage Multi for Cats** in ferrets weighing over 4.4 lbs. (2.0 kg) has not been established.

ADVERSE REACTIONS: **Heartworm Negative Dogs:** the most common adverse reactions observed during field studies were pruritus, residue, medicinal odor, lethargy, inappetence and hyperactivity. **Heartworm Positive Dogs:** the most common adverse reactions observed during field studies were cough, lethargy, vomiting, diarrhea, (including hemorrhagic), and inappetence. **Cats:** the most common adverse reactions observed during field studies were lethargy, behavioral changes, discomfort, hypersalivation, polydipsia and coughing and gagging. **Ferrets:** the most common adverse reactions observed during field studies were pruritus/scratching, scabbing, redness, wounds and inflammation at the treatment site, lethargy and chemical odor.

For a copy of the Material Safety Data Sheet (MSDS) or to report adverse reactions call Bayer Veterinary Services at 1-800-422-9874. For consumer questions call 1-800-255-6826.

Advantage Multi is protected by one or more of the following U.S. patents: 6,232,328 and 6,001,858.

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