

The Hope Line

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Managing the Anemic Azotemic Cat

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OVERVIEW

Chronic renal disease (CKD) is one of the most common conditions in geriatric felines and one of the major complications of CKD is non-regenerative anemia, affecting 35-68% of all cats with CKD. This is most commonly due to lack of erythropoietin (EPO) production but can also be due to chronic inflammation suppressing bone marrow progenitor cells, uremic effects on the erythron membrane and other yet-to-be-discovered mechanisms. Anemia causes lack of oxygen delivery to tissues and manifests as an overall impression of poor life quality in patients.

PATHOPHYSIOLOGY

EPO is produced in the tubular interstitial cells of the kidney and to a lesser extent, the liver. EPO production is triggered by hypoxia inducible factor and requires iron and oxygen to be produced. Once synthesized, EPO acts on red blood cell progenitor cells to release them into circulation and creates more hemoglobin within five days. When renal tubules are injured and degenerate, less oxygen is consumed, which increases the amount of available oxygen to the renal cells. This inhibits the synthesis of HIF and therefore, EPO production drops. Iron absorption may also be concurrently decreased in patients with gastrointestinal malabsorption as well. In addition, CKD is associated with interferon-alpha, beta, gamma and IL-1 production which decreases red blood cell survival and their responsiveness to EPO.

DIAGNOSIS

PCV/TS and ideally a full complete blood cell count with reticulocyte measurement will allow the clinician to assess if anemia is present and if so, if the anemia is regenerative (which indicates a blood loss or hemolytic cause) or non-regenerative (which is more commonly seen with chronic inflammatory diseases and CKD). It is implied that the pet will already fulfill the diagnostic criteria for renal disease as outlined by IRIS Guidelines.



TREATMENT

In patients who are clinically ill due to their anemia, a blood transfusion is necessary. There is no “cutoff” value for which a transfusion must be administered, but cats who have severe anemia (hematocrit <15%), a rapid decline in PCV, or lethargy, tachypnea, dyspnea or neurologic weakness would benefit from a transfusion.

Erythropoietin recombinant products have been developed for use in cats and dogs. Cats share 83% homology of EPO with humans, and epoetin-alfa was one of the first treatments available for anemic pets. EPO is given three times weekly and is associated with antibody formation leading to pure red cell aplasia (PRCA) and treatment failure.

Darbepoetin is a newer product and can be used in dogs and cats. It has a longer half life, so it only needs to be given once a week. It also has a decreased chance of PRCA when compared to EPO (10% compared to 25%). It is costly, but has been shown to increase quality of life and prolong survival in anemic azotemic cats (238 days compared to 136 days) compared to non-treated cats. The starting dose is 0.45 ug/kg SQ weekly until a PCV>25% is achieved. This can be repeated weekly, with monitoring of CBC and blood pressure recommended.

Iron should be administered to all cats and dogs receiving EPO stimulating agents, as iron is needed for formation of hemoglobin and therefore red blood cell production. Lack of iron availability is one of the leading causes of treatment failure in dogs and cats with anemia.

A newly released medication has been FDA approved for cats with CKD. Varenzin-CA1 (Molidustat) is an oral EPO stimulating agent (via inhibition of HIF hydroxylase) which has shown efficacy in limited studies. No data has yet been released on whether or not the incidence of antibody formation is higher than with Epoetin or Darbepoetin, but side effects appear to be very minimal.

Side effects of all EPO stimulating agents include hypertension, fever, PRCA and polycythemia. As new research occurs, we should hopefully look forward to an easier and more effective way to treat our anemic feline patients!

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| Treatment | <u>Epoetin</u> | <u>Darbepoetin</u> | <u>Varenzin-CA1 (Molidustat)</u> |
|---------------------------------|----------------|--------------------|----------------------------------|
| Cost | \$50/vial | \$250/vial | \$60/27ML bottle |
| Dose | 100IU/kg | 0.5-1ucg/kg | 5mg/kg |
| Frequency of Dosing | 3 x 1 week | weekly | daily |
| Incidence of Antibody Formation | 30-40% | <20% | Data not available |
| Route of Administration | SQ | SQ | oral |

References:

1. Managing Anemia in Chronic Kidney Disease. ACVIM proceedings 2015. Cathy Langston, DVM, DACVIM (SAIM)
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3. Use of molidustat, a hypoxia-inducible factor prolyl hydroxylase inhibitor, in chronic kidney disease-associated anemia in cats. JVIM Sept. 2023. Samuel Charles, Ricarda Süssenberger, Terry Settje, Catherine Langston, Chantal Lainesse

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