Proceeding of the SEVC
Southern European Veterinary Conference

Oct. 2-4, 2009, Barcelona, Spain

http://www.sevc.info

Next conference:
October 1-3, 2010 - Barcelona, Spain

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MANAGING HYPERTENSION IN CATS WITH HYPERTHYROIDISM

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Hyperthyroidism has long been considered a top differential diagnosis for cats with systemic hypertension. Once considered an insignificant clinical problem, systemic hypertension has emerged as a common finding, especially in geriatric cats. Although many veterinary practitioners have yet to adopt the practice of routinely measuring blood pressure in cats, blood pressure measurement is becoming more and more commonplace. As a result our knowledge of hypertension is expanding, and questions about management of hypertension continually arise.

Diagnosis of Hypertension in Hyperthyroid Cats
The diagnosis of hypertension in cats with hyperthyroidism is not always straightforward. In normal cats, measurement of blood pressure is fairly reliable, whether using oscillometry or Doppler ultrasonography (Jepson et al. 2005). Both correlate well with intra-arterial measurements (Brown et al, 2007). Measurement of blood pressure requires experience, skill, and patience, and when blood pressure is measured in a relatively calm environment, and by a skilled operator, 150 mmHg is generally used as a cutoff for normal systolic pressure, and 95 mmHg is considered the upper limit of normal for diastolic pressure. Blood pressure classifications have been proposed in an American College of Veterinary Internal Medicine consensus statement (Brown et al. 2007), and are presented in Table 1.

<table>
<thead>
<tr>
<th>Table 1: Classification of Blood Pressure based on risk of target-organ damage (TOD), from Brown et al. 2007.</th>
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Prevalence of hypertension of effects of treatment of hyperthyroidism
The "white coat effect" is difficult to recognize in veterinary medicine, but it may be even more important in cats with hyperthyroidism. The earliest study on hypertension in cats with hyperthyroidism showed the prevalence of hypertension to be as high as 87% (Kobayashi et al. 1990). In that study, 34 of 39 cats with hyperthyroidism were hypertensive, but the cutoff values for definition of hypertension may have been unrealistically low. It should be noted, however, that the study was well-controlled, with hyperthyroid cats being compared to groups of both normal cats and cats with chronic renal failure, so the finding that cats with hyperthyroidism have significant elevations in blood pressure is difficult to dispute. While a decline in both systolic and diastolic pressure was documented in cats after treatment of hyperthyroidism, not all cats were re-evaluated, so strong conclusions could not be made.

Subsequent studies have shown much lower prevalence rates of hypertension in cats with hyperthyroidism (Stepien et al. 2003, Syme and Elliott 2003). Prevalence of hypertension was between 5% and 20%. Stepien et al. showed that the "white coat effect" is pronounced in cats with hyperthyroidism and no decrease in blood pressure was seen after treatment of hyperthyroidism. Syme and Elliott, however, showed a marked increase in the prevalence of hypertension after treatment of hyperthyroidism. For that reason, it is important that blood pressure be monitored carefully for the development of post-treatment hypertension.

In people with hyperthyroidism, hypertension is rarely a problem. When it occurs, the hypertension is usually systolic only. Thyroid hormone causes a pronounced decrease in peripheral vascular resistance. Hemodynamic effects of thyrotoxicosis include increased heart rate and increased stroke volume. It has been proposed that increased heart rate causes a summation of pressure in peripheral arteries with the pressure from systole, resulting in overall systolic hypertension (Biondi et al. 2002). This phenomenon may
exist also in cats with hyperthyroidism, but the reason for the increase in diastolic pressure in some hyperthyroid cats is unclear. The answer might be found in the kidney. Chronic renal insufficiency is common in cats with hyperthyroidism (Graves 1997), and hypertension is common in cats with renal insufficiency, evidence of which can be masked by hyperthyroidism.

It is difficult to tell if hyperthyroidism really does cause hypertension in cats. There is an association between the two, but a cause and effect has not been established. If hyperthyroidism is a significant cause of hypertension, it may not be as common a cause as some clinicians might believe. In one study, only 5 of 30 cats with hypertension were diagnosed with hyperthyroidism (Elliott et al. 2001). In a study of cats with hypertensive retinopathy, only 5 of 69 cats were hyperthyroid (Maggio et al. 2000). Conversely, another study found no evidence of ocular changes consistent with hypertensive damage in cats with hyperthyroidism (van der Woerdt and Peterson 2000).

Treating Hypertension in Hyperthyroid Cats

While the diagnosis of hypertension in cats with hyperthyroidism may sometimes be difficult, once the diagnosis is established, the need for treatment is clear. Persistent hypertension damages the kidneys (Brown et al. 2007), and the co-morbid condition of hyperthyroidism and renal failure is well-documented in cats. Drugs used to treat hypertension in cats are presented in Table 2. Drugs used to treat hypertension in cats fall into 3 categories: angiotensin-converting enzyme (ACE) inhibitors, calcium-channel antagonists, and beta adrenergic antagonists.

Amlodipine

Amlodipine is a calcium channel antagonist, and it probably the most frequently used anti-hypertensive drug in cats. It is considered the drug-of-choice for treatment of severe hypertension. The drug acts by inhibiting calcium entry into smooth muscle cells, resulting in arterial muscle relaxation. As evidence of the importance of hypertension in the progression of renal disease in cats, a large study of 141 cats with systolic hypertension showed that treatment with amlodipine causes a significant reduction in pathologic proteinuria (Jepson et al. 2007). It is interesting to note that proteinuria is associated with decreased survival times in hypertensive cats, but a concurrent diagnosis of hyperthyroidism is not.

Table 2: Drugs used to treat hypertension in cats

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Notes</th>
</tr>
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<tbody>
<tr>
<td>Amlodipine</td>
<td>0.625 mg/cat Every 24 hours</td>
<td>Calcium channel antagonist. Useful for severe hypertension. Decreases proteinuria. Well-tolerated</td>
</tr>
<tr>
<td>Benazapril</td>
<td>0.5 mg/kg Every 12-24 hours</td>
<td>ACE Inhibitor Not as effective as amlodipine Decreases proteinuria Delays progression of renal disease Well-tolerated</td>
</tr>
<tr>
<td>Enalapril</td>
<td>0.5 mg/kg Every 12-24 hours</td>
<td>ACE Inhibitor Not as effective as amlodipine No negative effects on kidneys Well-tolerated</td>
</tr>
<tr>
<td>Ramipril</td>
<td>0.125 mg/kg Every 24 hours</td>
<td>ACE Inhibitor Effective in controlling hypertension Hepatic metabolism Renal effects unknown Well-tolerated</td>
</tr>
<tr>
<td>Atenolol</td>
<td>3.125-6.25 mg/cat Every 12 hours</td>
<td>Selective Beta-1 antagonist Controls tachycardia Useful in hyperthyroidism Limited use for hypertension</td>
</tr>
</tbody>
</table>

ACE Inhibitors

The use of ACE inhibitors in treating hypertension in cats with hyperthyroidism seems compelling. There is evidence that benazapril has highly beneficial effects on the kidneys (Lefebvre et al. 2007, Mizutani et al. 2006, Watanabe et al. 2007). Like amlodipine, it is associated with decreased proteinuria, and it has
Beta Adrenergic Antagonists

Beta blockers have long been used in cats with hyperthyroidism. Propanolol has not been shown to be effective in the control of hypertension in cats (Jensen et al. 1997). Atenolol, is a beta-1 selective adrenergic antagonist recommended for treatment of tachycardia in cats with hyperthyroidism (Trepanier 2007). If, as in some human patients, cats with hyperthyroidism have systolic hypertension due to tachycardia, the use of atenolol would be ideal. A question arises in the use of atenolol in a hypertensive hyperthyroid cat with underlying renal disease. ACE inhibitors and beta blockers have been compared in human patients with non-diabetic nephropathies. Some studies have shown ACE inhibitors to be superior for use in patients with renal failure (Himmllmann et al. 1996), whereas other studies have shown no difference (van Essen et al. 1997). Because the effects of beta blockers on renal function in cats, and especially those with hyperthyroidism and renal disease, have not been reported, atenolol should probably be used with caution in hypertensive cats with hyperthyroidism.

References: