BLOOD PRESSURE: A CRITICAL FACTOR

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It has been stated that: "Systemic hypertension associated with kidney disease is a very real problem, and has been diagnosed in over 60% of cats with chronic renal disease. Hypertension can have multi-systemic effects if left untreated, including left ventricular hypertrophy and cardiac failure, retinal detachment and blindness, cerebrovascular hemorrhage, and progression of renal dysfunction." (Rosemary Henik, DVM, MS, DACVIM) While this is true, let's look at the applicability of measuring blood pressure, methods of assessment and the interpretation of results in clinical practice. These notes review the literature from 1990 up until the end of 2004. The interested reader is strongly urged to read the **ACVIM Consensus Statement** from **2007** entitled: **Guidelines for the Identification, Evaluation, and Management of Systemic Hypertension in Dogs and Cats**.[0]

Keypoints

1. Systemic arterial pressure is the pressure within the arteries and arterioles
2. Systolic pressure refers to the pressure when the aortic valve is open and the heart is ejecting blood (120 mmHg)
3. Diastolic pressure refers to the pressure when the aortic valve is closed and the heart is resting (80 mmHg)
4. Mean arterial pressure is closer to diastolic as the heart spends most of its time resting in diastole (90 mmHg)
5. Excitation, stress and pain can *transiently* raise the values, but as there are mechanisms in place to limit the elevations, consistent systolic values exceeding 170 mm Hg (range 168-180) are accepted as reflecting hypertension.[1-9]
6. To minimize the effects of "white coat syndrome", allow the patient to acclimate to the environment for ten minutes before measuring BP. Measure BP before performing any other evaluations (TPR, examination, etc.) Take measurements over several minutes until a series of five values are obtained that vary by no more than 10 mm Hg.
7. A mean arterial pressure of >60 mmHg are necessary to maintain perfusion to the brain, heart and kidneys.
8. Doppler measurement of systolic pressure underestimates values obtained by direct invasive measurement of arterial pressure. This may be corrected by the equation: Doppler + 14 mm Hg = direct systolic pressure.[10]

Whose blood pressure should we measure?

Non-invasive, indirect arterial measurements of blood pressure should be made in all anaesthetized, critical or high-risk patients to detect and monitor management of hypotension.[11] This technique should be used widely as a screening method for the pre-clinical detection of hypertension in patients with renal disease, hyperthyroidism, ocular changes consistent with hypertension, a cardiac murmur, or left ventricular hypertrophy, neurological dysfunction and all cats over eight years of age.[12]

How to measure

In an anaesthetized patient, Doppler or oscillometric methods are reliable.[13,14] In conscious cats, oscillometric measurements using devices reported in published papers do not correlate with radiotelemetrically obtained values; Doppler, PetMap or Memo methodology should be used. To minimize the effects of "white coat syndrome",[15] allow the patient to acclimate to the environment for ten minutes before measuring BP.[16] Measure BP before performing any other evaluations (TPR, examination, etc.).[3] Use of forelimb or hindlimb is equally valid. It is very important to use the appropriate cuff size. The cuff chosen must measure 40% of the circumference of the limb at the cuff placement site (see attached table). Shaving helps achieve good probe contact but is not essential.[17] In fact, I do not recommend shaving a conscious patient as this raises their fear level. Wetting the fur in the metatarsal or metacarpal area with alcohol is adequate. It is important to avoid alcohol touching the probe; use gel generously. Gentle inflation and deflation of the cuff will reduce strangeness of the experience for the patient. Use of a stereo headset will help reduce noise for the cat as well as make it easier for the operator to hear the signal. Take measurements over several minutes until a series of five values are obtained that vary by no more than 10 mm Hg.[2] Record the limb and cuff size used, for future comparisons, in the medical record.

Causes of artificially high values: fear, noise and the sensation of the cuff inflating and deflating.... be quiet, use headset and inflate gently; take the readings on the client's lap whenever possible. Using a cuff that is too small will also cause artificially high BP readings.

Other methods of measurement:
* Oscillometric measurement (Critikon™, Dinamap, Datascope Passport[17]) is not reliable in conscious cats and small dogs (<25 lbs). These are appropriate for monitoring anaesthetized patients.
* Central Venous Pressure (CVP) measurement:
CVP an easy, cheap and is an under-utilized technique and is the most accurate, but requires invasive procedure and is not an out patient procedure. While it reflects right atrial pressure associated with volume changes, arterial BP assesses adequacy of perfusion of vital tissues.[18]

Causes of hypertension
Chronic renal insufficiency (of unspecified types) and hyperthyroidism are undisputedly the most common disease conditions associated with hypertension in older cats. In sixteen studies,[1,2,5-7,15,16,19-27] the percentage of hypertensive patients with these two underlying causes varies quite widely. For hypertensive cats the incidence of CRI is between 41 and 92%. Hyperthyroidism is found in 8-87% of hypertensive cats. The corollary of this is that approximately 60% of cats with CRI and 40-60% of cats with hyperthyroidism are hypertensive. Thus, it is logical to recommend that blood pressure monitoring be part of the examination of any feline patient with renal disease, hyperthyroidism, ocular changes reflective of hypertension, a cardiac murmur or echocardiographic changes shown to be associated with increased afterload, epistaxis, or neurological dysfunction as well as all cats over 8 years of age.[4] Less common causes of hypertension include excessive dietary sodium,[28] pheochromocytoma[29] and as an uncommon adverse effect in erythropoeitin therapy.[30] Whether idiopathic[25] or "essential" hypertension occurs in cats is unknown. Unlike humans, diabetes mellitus does not appear to predispose cats to hypertension.[8]

While there is an increased incidence of hypertension inducing disease in senior cats, an increase in blood pressure has also been shown to occur in healthy cats associated with increasing age.[5, 26, 31]

Pathogenesis of hypertension
When hypertension occurs in feline chronic renal disease (CRD), the speculated mechanism of action involves the renin-angiotensin-aldosterone (RAA) axis. Interestingly, in the few studies that have looked at this, results, and therefore, interpretation, vary. One paper speculates that the cause for hypertension is due to RAA[27] changes. Another[24] shows a lack of difference in plasma renin activity as well as angiotensin levels between cats with CRD and normal cats. This same paper reports a significantly higher aldosterone level in hypertensive CRD cats. A third paper,[32] which compared a small number of Persian cats with polycystic kidney disease (PKD) to normal cats cites a higher aldosterone: renin ration in half of the PKD cats. Of interest is the finding in this paper that the cats with PKD had only slightly higher BP levels than normal cats. A different paper studying PKD patients showed normotension in both PKD and normal cats. This implies, albeit in a very small number of patients, that PKD does not result in hypertension, a situation that is different from other forms of chronic renal disease.[33]

In hyperthyroid cats, the mechanism of hypertension appears to be due to high cardiac output. In fact, unless hyperthyroidism is accompanied by chronic renal insufficiency, the degree of hypertension is mild. Therapy directed towards controlling hyperthyroidism is usually all that is required to control hypertension in these cats. If inadequate, then the hyperdynamic state should be addressed using a beta-blocker to dampen the inotropic effect and tachycardia induced by thyroid hormones.

When renal insufficiency is part of, or the sole cause of, the hypertension, reduction of arteriolar constriction may be achieved using amlodipine through its action blocking calcium channels in peripheral vasculature.[7]

The most obvious clinical effects of hypertension are those affecting the ocular structures: retinal hemmorhage, hyphema and retinal detachment resulting in visibly obvious changes in the appearance of the cat's eye (persistent papillary dilation or hyphema) or an acute onset of blindness. Hypertension affects other tissues, which also have a rich arteriolar supply, cardiovascular and renal structures.[3]

Persistence in hypertension results in an increased afterload for the heart. This results in concentric hypertrophy. If the hypertrophy is more than mild, especially if it is severe, then the trophic effect of hyperthyroidism should be suspected. Indeed, two papers evaluating the effects of systemic hypertension on cardiovascular parameters showed mild left ventricular hypertrophy, subtle asymmetrical hypertrophy with thicker interventricular septum, and distal aortic root measurements that were greater in hypertensive cats compared to age-matched, older healthy cats.[9, 26]

The effects of hypertension on the kidneys of cats appear to be somewhat different than what has been recognized in dogs and humans. The feline pre-glomerular vessels are more resistant to the detrimental effects of hypertension and are able to compensate better than in those other species. While albuminuria (but not increases in urine protein: creatinine ratios) correlates with hypertension in experimentally induced renal failure (9/10 nephrectomy remnant kidney model[34]), this effect has not been documented in hypertensive cats to date.

The situation with chronic renal insufficiency (CRWSAVAI) as a cause of hypertension is being studied intensively. Cats with CRI lose the normal auto regulatory capacity of the glomerular arterioles. This may not only cause systemic hypertension (50-60% of cats with CRI?) but also promote progression of renal insufficiency through glomerular injury. Treatment of hypertension should be considered in cats whose systolic BP is consistently > 170 mm Hg. Amlodipine is the most efficacious agent (0.625 mg/cat PO q24h, titrate up as needed) as it has a direct effect on the calcium channels of the peripheral vasculature. Angiotensin-converting enzyme inhibitors (ACEI) will have overall effect of reduced vasoconstriction of efferent arteriole that can increase overall renal flow, reduce glomerular hypertension (beneficial in the case of renal protein loss) but can at the same time reduce driving force for GFR by which we may create, in essence, a pre-renal azotemia. If ACEI are used, monitor BUN and creatinine after 1 or 2 doses and respond accordingly. Beta-blockers reduce renin secretion, which will have same net effect. Combination therapy using amlodipine along with an ACEI may be advantageous by reducing BP via the systemic vasodilation (preglomerular) while also dilating efferent arterioles (post-glomerular), thereby balancing the effects on GFR and on glomerular capillary pressure.

Benazepril (an ACEI) is currently undergoing a large, multi-institutional study to assess its effects on CRI in cats. Interim results for this study (presented September, 2001, WSAVA, ACVIM 2002) show that using benazepril or placebo didn't make any significant difference in survival time for all CRI cats. For cats with urinary protein loss (urine protein/creatinine), benazepril treated cats had longer survival times and better appetite than placebo treated urinary protein losing cats. Benazepril was well tolerated by all cats. Subsequent studies have not shown compelling reasons to use this agent routinely in CRI.

When to treat

Normal values are ~120mm Hg systolic, but due to fear-induced hypertension, reassess when the values are consistently above 170 mmHg.

How to treat

1) identify and treat the underlying cause;
2) medical management? ONLY if you can and will monitor the BP. Classes of drugs used in the treatment of hypertension include diuretics, ACE inhibitors, beta-blockers, calcium channel blocker, and vasodilators. The drug chosen must depend on the underlying cause as well as the hydration status, renal and cardiac function and response to therapy. Of ten papers reporting studies of therapies for the treatment of hypertension in cats, eight evaluated efficacy or safety and efficacy of amlodipine. Three evaluated other agents (propranolol, enalapril, captopril, furosemide).[29,33,34] The conclusion can be made that amlodipine is safe and effective when used long-term at a dose of 0.625 mg/cat/day (or 1.25 mg/cat/day to effect in cats weighing more than 5 kg) at the average dose of 0.18 +/- 0.03 mg/kg PO q24h.[2-4,7,25,34,35] The other agents had a high incidence of side effects and were not reliably effective in reducing blood pressure.
3) sodium restriction in diet? (This is discussed later in this paper.)
4) weight reduction if obese or overweight

MONITOR! after 5-7 days and adjust dose if necessary, check again in 2-3 weeks ....then every two to three months. Monitoring is ***essential***, as over treatment, causing hyPOtension could cause acute renal failure or

cardiac collapse and coma. Recheck appointments should include assessment of heart rate and function, hydration, body weight, general condition and quality of life, renal values, urinalysis, ophthalmic and neurologic status.

Causes of hypotension

Anaesthesia commonly causes hypotension.[36] Mean arteriolar BP must be above 60 mm Hg (approx 80-90 systolic BP) to provide adequate perfusion to the brain, heart and kidneys. If this is not achieved, organ dysfunction will result. Monitoring the blood pressure of anaesthetized patients along with other parameters allows for appropriate and timely adjustment of anaesthetic depth, fluid support and the use of supportive drugs. One paper showed a dramatic decrease in cardiac parameters along with blood pressure when 2.0 minimum alveolar concentration (MAC) isofluorane was compared to 1.30 MAC in cats. Despite assisted ventilation, cardiac indices remained impaired.[37]

Other causes of hypotension include hypoperfusion due to pain,[38] hypovolemia[39,], cardiac arrhythmias, heart failure, blood loss, sepsis,[40-42] DIC. *Causes of artificially low values*: using a cuff that is too large and is occluding the artery, taping the cuff too snugly.

Treatment of hypotension: treat the underlying cause (provide analgesia, reduce the inhalant anaesthetic flow, use appropriate antibiotics, etc.) and support hypovolemia with oxygen, fluids (crystalloids, colloids), dopamine or dobutamine.[39, 41,42] Refractory hypotension, with or without cardiovascular collapse, development of respiratory disease, or disseminated intravascular coagulation (DIC) are all associated with a poor prognosis in patients with septic peritonitis, thus recognition, treatment and monitoring of hypotension is of critical importance in caring for these patients.[40]

What about dietary sodium?

Recent papers have looked at the role of dietary sodium in lower urinary tract disease, renal disease and blood pressure in cats. Increasing dietary sodium has been evaluated as a way to increase urine output and reduce specific gravity, hereby not only increasing frequency of voiding, but also reducing the relative supersaturation of solutes to risk of urolith formation. [43]

As far as renal disease goes, there is much conflict in results. In one study, cats eating a higher sodium diet had an increase in creatinine, BUN and serum phosphorus compared to cats on a lower Na diet.[44] Another study showed that a low Na diet resulted in a reduced glomerular filtration rate, increased urinary potassium loss, activation of RAA.[45] A third study showed that feeding higher levels of Na, along with Mg, protein and dietary fiber resulted in a lower risk for development of chronic renal failure.[46] Finally, feeding a classic restricted protein, phosphorus and Na diet to cats in renal insufficiency resulted in fewer renal related deaths in a fourth study.[47]

There is no strong evidence that increased dietary sodium increases the risk of hypertension in dogs and cats, and the current recommendation for hypertensive animals is to avoid high dietary salt intake without making a specific effort to restrict it as restriction may, in fact, activate the RAA system.[43] Reduction of Na has not been shown to have an effect on blood pressure (systolic, diastolic, mean)[44, 45] and may, in fact, result in hypotension in cats, especially if these cats are on an ACE inhibitor. [48]

It is important to recognize that these studies vary with respect to diet composition and what constituted high vs. low Na levels. The studies reported in these six papers are designed differently, so drawing conclusions relative to the other papers is not really possible.

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