Cerebrovascular Disease in Dogs and Cats

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KEYWORDS

• Stroke • Neurology • Dog • Cat

The term ''cerebrovascular disease'' is defined as any abnormality of the brain resulting from a pathologic process compromising its blood supply.[1] Pathologic processes of the blood vessel include occlusion of the lumen by a thrombus or embolus, rupture of a blood vessel wall, lesion or altered permeability of the vessel wall, and increased viscosity or other changes in the quality of the blood.[2] Cerebrovascular accident (CVA), also known as stroke, is the most common clinical presentation of cerebrovascular disease, defined as a sudden onset of nonconvulsive and nonprogressive focal brain signs secondary to cerebrovascular disease.[3] By convention, these signs must remain for more than 24 hours to qualify for the diagnosis of CVA, which is usually associated with permanent damage to the brain. If the clinical signs resolve within 24 hours, the episode is called a transient ischemic attack (TIA).[4]

CAUSES AND PATHOPHYSIOLOGY

From a pathologic point of view, the lesions affecting the cerebral blood vessels are divided into 2 broad categories, ischemic stroke and hemorrhagic stroke. Ischemic strokes result from occlusion of a cerebral blood vessel by a thrombus or embolism, depriving the brain of oxygen and glucose. Hemorrhagic strokes result from rupture of a blood vessel wall within the brain parenchyma or subarachnoid space, causing bleeding into or around the brain (**Fig. 1**).[2]

Ischemic Strokes

Ischemic strokes have been reported infrequently in the veterinary medical literature when compared with the human medical literature.[5–23] Most reports have been based on postmortem results in dogs that died or were euthanized as a result of the severity of the ischemic stroke or the suspected underlying cause of the stroke. This limitation may affect the prevalence and type of underlying causes, as it is likely that only the most severely affected dogs, or dogs in which infarction

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Vet Clin Small Anim 40 (2010) 65–79
doi:10.1016/j.cvsm.2009.09.001 **vetsmall.theclinics.com**
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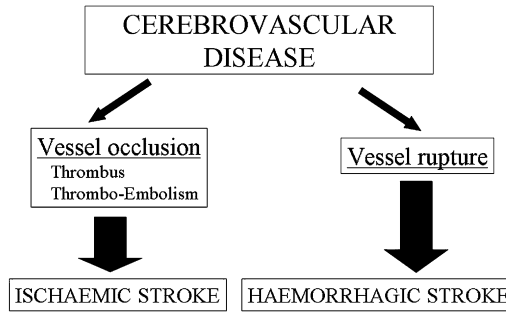

Fig. 1. Causes of cerebrovascular disease in dogs and cats.

occurred secondarily to a disease with a poor prognosis, would die or be euthanized. Suspected underlying causes identified in histopathologically confirmed cases include: septic thromboemboli associated with bacterial endocarditis or other sources of infection[13,24]; atherosclerosis associated with primary hypothyroidism and Miniature Schnauzers with hyperlipoproteinemia[8,9,11,25,26]; aberrant parasite migration (*Cuterebra*)[27,28] or parasitic emboli (*Dirofilaria immitis*)[6,7]; embolic metastatic tumor cells[11]; intravascular lymphoma[17]; fibrocartilaginous embolism[20]; and aortic or cardiac thromboembolism.[22,23]

In the author's study of magnetic resonance imaging (MRI) of dogs with brain infarct, a concurrent medical condition was detected in just over 50% of dogs, most commonly hyperadrenocorticism, chronic kidney disease, hypothyroidism, and hypertension.[22] The most commonly suspected causes of hypertension were chronic kidney disease and hyperadrenocorticism.[22] In human patients, infarcts of unknown cause are referred to as cryptogenic infarcts.[1] No age, sex, or breed predisposition was identified in that study, although Cavalier King Charles Spaniels (CKCS) and Greyhounds were overrepresented.[22]

Reports of ischemic strokes in cats are scarce. The term feline ischemic encephalopathy has been used to describe cases of peracute onset of clinical signs consistent with a unilateral cerebral or brainstem problem caused by ischemia. Although the cause remains unknown in most cases, some of them have been linked to *Cuterebra* migration.[27,28] It is believed that the migrating parasite or the host response leads to vasospasm in the cerebral vasculature, typically the middle cerebral artery.

The pathophysiology of ischemic stroke is based on the principle that with limited energy stores, the brain relies on a constant supply of glucose and oxygen to maintain ionic pump function. When perfusion pressure falls to critical levels, ischemia develops, progressing to infarction if it persists long enough or is severe enough. An infarct is an area of compromised brain parenchyma caused by a focal occlusion of one or more blood vessels. An infarct may be due either to vascular obstruction that develops within the occluded vessels (thrombosis) or to obstructive material that originates from another vascular bed and travels to the brain (thromboembolism).[2] Infarcts can be a consequence of small vessel disease (ie, superficial or deep perforating artery) that gives rise to a lacunar infarct, or large vessel disease (ie, a major artery of the brain or its main branches) that gives rise to a territorial infarct.[1] Two distinct regions can be distinguished, the core where ischemia is severe and infarction develops rapidly, and the surrounding penumbra containing a more moderate decrease of cerebral blood flow (CBF) that allows longer duration of ischemic stress to be tolerated.[29] The relative volume of these 2 regions changes as the infarct evolves. The factors causing the evolution of the penumbra to irreversible injury are

multiple and complex, and include the degree of blood flow reduction, the region of the brain involved, and the individual patient. In the penumbra, neurons are still viable but at risk of becoming irreversibly injured.[29] Tissue within the penumbra has the potential for recovery and therefore is the target for therapy in acute ischemic stroke.[30] At the cellular level, the ischemic neuron becomes depolarized as adenosine triphosphate is depleted and the Na^+/K^+ adenosine triphosphate pump and other ionic membrane pumps fail, leading to loss of fluid-electrolyte homeostasis.[31,32] This process results in loss of ionic gradients and a net translocation of water from the extracellular to the intracellular compartment, causing the cell to swell (cytotoxic edema).[33] Over time the ischemic cascade progresses, resulting in cell lysis, increased macrophage activity, and disruption of the blood-brain barrier, leading to vasogenic edema.[34–37] Vasogenic edema typically takes 4 to 6 hours to develop once blood flow decreases to ischemic levels, and may continue to progress for 24 to 48 hours. Because neurons have the highest demand for oxygen, neuronal function is first affected; this is followed, in declining order of vulnerability, by the function of oligodendrocytes, astrocytes, mesodermal microglia, and fibrovascular elements.[34] If sufficient perfusion is not reestablished, severe ischemia results in an area of dead tissue described as an infarct.[38] Ischemia is thus a continuum between normal cellular function and cell death.

Hemorrhagic Stroke

In contrast to the high incidence in man, intracerebral hemorrhage resulting from spontaneous rupture of vessels is considered rare in dogs.[16,39] Secondary hemorrhage has been reported in dogs in association with rupture of congenital vascular abnormalities,[11,40–42] primary and secondary brain tumors,[5,43–45] intravascular lymphoma (malignant angioendotheliomatosis),[46,47] cerebral amyloid angiopathy[48] and inflammatory disease of the arteries and veins (necrotizing vasculitis),[49] brain infarction (hemorrhagic infarction),[10,15] and impaired coagulation (extracranial diseases predisposing for disseminated intravascular coagulation such as neoplasia, von Willebrand disease, or *Angiostrongylus vasorum*).[11,44,50] Nontraumatic subdural or subarachnoid hemorrhage has been reported in dogs[51,52] but remains very rare when compared with its occurrence in man, where aneurysmal rupture is the most common underlying cause.

In hemorrhagic stroke, blood leaks from the vessel directly into the brain, forming a hematoma within the brain parenchyma, or into the subarachnoid space.[19] The mass of clotted blood causes physical disruption of the tissue and pressure on the surrounding brain.[53] This process alters intracranial volume/pressure relationships, and can lead to increased intracranial pressure (ICP) and decreased CBF. Initially, ICP may remain normal due to a system of compensation.[19] Within the closed space of the skull are 3 noncompressable constituents, brain tissue, blood, and cerebrospinal fluid (CSF). A change in the volume of one constituent will be balanced by a compensatory change in another. This principle is called the Monroe-Kellie doctrine. As the hematoma continues to expand, this compensatory system becomes exhausted and ICP starts to increase; this can be clinically associated with herniation. Due to mechanical autoregulation, CBF remains constant even though the cerebral perfusion pressure (CPP) may vary between 40 and 120 mm Hg.[54] The normal autoregulation of CBF may be impaired following cerebrovascular accidents, causing blood flow to damaged regions to become directly dependent on systemic blood pressure. Such animals may be unable to compensate for reductions in mean arterial blood pressure (MABP), causing decreased CPP in the presence of increased ICP.[54] This anomaly emphasizes the importance of maintaining systemic blood pressure. In these

circumstances, systemic hypotension can result in inadequate perfusion of the brain, which leads to cerebral ischemia and secondary neuronal injury.

CLINICAL PRESENTATION

In ischemic or hemorrhagic stroke, the denominative feature is the temporal profile of neurologic events.[55] It is the abruptness with which the neurologic deficits develop that is highly suggestive of the disorder as being vascular.[2] This event is then followed by a plateau and then resolution of the neurologic deficit in all except the fatal strokes. Worsening edema can result in progression of neurologic signs for 24 to 72 hours.[19] Intracranial hemorrhage can be an exception and cause rapid progressive onset over a very short period of time. Clinical signs usually improve after 24 to 72 hours due to a decrease in size of the hematoma and edema.[19,56]

Neurologic deficits usually refer to a focal anatomic diagnosis and depend on the neurolocalization of the vascular insult (telencephalon, thalamus, midbrain, pons, medulla, cerebellum).[55] Infarction of an individual brain region is associated with specific clinical signs that reflect the loss of function of that specific region.[21] In its mildest form, the impaired regional CBF causes a TIA. The cause of TIA in humans is usually small emboli from the heart or atherosclerotic plaques in the carotid or vertebrobasilar arteries. Similar paroxysmal events have been reported in dogs with suspected or histologically proven infarction,[16,21,23] but the underlying cause remains undetermined. With hemorrhagic stroke, the clinical picture is different, as the hemorrhage usually involves the territory of more than one artery and pressure effects cause secondary signs. Neurologic signs are largely related to raised ICP, which gives rise to nonspecific signs of forebrain, brainstem, or cerebellar disturbance.[19]

CONFIRMATION OF DIAGNOSIS

Initial evaluation of animals with suspected stroke should focus on the differential diagnosis, including traumatic, metabolic, neoplastic, inflammatory/infectious, and toxic encephalopathies.[57] Fundus examination should be considered in all animals and may reveal tortuous vessels (suggestive of systemic hypertension), hemorrhage (suggestive of coagulopathy or systemic hypertension), or papilledema (suggestive of elevated ICP). Imaging studies of the brain (computed tomography, conventional and functional MRI) are necessary to confirm stroke, define the vascular territory involved, determine the extent of the lesion, and distinguish between ischemic and hemorrhagic stroke. Imaging studies are also necessary to rule out other causes such as tumor, trauma, and encephalitis. Once stroke is confirmed, diagnostic tests focus on identifying an underlying cause (**Boxes 1** and **2**).

Confirmation of the Diagnosis of Stroke

Ischemic stroke

Computed tomography (CT) images are frequently normal during the acute phase of ischemia; therefore the diagnosis of ischemic stroke using CT relies on the exclusion of mimics of stroke. Early CT signs of ischemia can be subtle and difficult to detect even by experienced readers, and include parenchymal hypodensity, loss of gray-white matter differentiation, subtle effacement of the cortical sulci, and local mass effect.[15,58–60]

Conventional MRI can detect ischemic stroke within 12 to 24 hours of onset and can distinguish hemorrhagic lesions from infarction.[21,23] T2-weighted and fluid-attenuated inversion recovery (FLAIR) images are particularly useful in imaging of ischemic stroke to give a more anatomic image of the brain and depict edema, old infarcts,

Box 1
Ancillary diagnostic tests in cases of ischemic stroke

- Serial blood pressure measurements
- Complete blood count
- Serum biochemistry profile
- Urinalysis
- Urine protein/creatinine ratio
- Serum antithrombin III activity
- D-dimers
- Endocrine testing for hyperadrenocorticism, thyroid diseases, and pheochromocytoma
- Thoracic radiographs
- Abdominal ultrasound
- Echocardiography and electrocardiography

microangiopathic changes, tumors, and other abnormalities. With these sequences, ischemic infarction appears as a hyperintense lesion.[21] Differentiation of the core from the surrounding penumbra is, however, not possible. T2*-weighted (gradient echo) images are used to identify or exclude hemorrhage.[55,61,62] Although infarcts are sometimes difficult to differentiate from other lesions such as inflammatory diseases, they tend to have certain distinguishing characteristics on conventional MR images[21,63]:

- The conformity of an ischemic infarct to a vascular territory is an important element in the diagnosis that helps in distinguishing these lesions from brain tumors, inflammation, and trauma. Because infarcts are caused by occlusion of a blood vessel, they conform to a vascular territory with sharp demarcation from the surrounding normal brain tissue and minimal or no mass effect.
- Ischemic infarcts are caused by failure of perfusion and therefore energy depletion. This depletion results in failure of the Na^+/K^+ pump and accumulation of Na^+ and water within the cell, that is, cytotoxic edema. The MRI changes rely on an increase in tissue water content. The T2-weighted or FLAIR images gradually become more hyperintense because of T2 prolongation that increases signal intensity, particularly over the first 24 hours.

Box 2
Ancillary diagnostic tests in cases of hemorrhagic stroke

- Serial blood pressure measurements
- Complete blood count
- Serum biochemistry profile
- Buccal mucosa bleeding time
- Prothrombin time (PT)
- Activated partial thromboplastin time (APTT)
- Thoracic radiographs
- Abdominal ultrasound

- MRI changes are best appreciated in the gray matter and are well visualized in deep gray matter structures such as the thalamus and basal ganglia, which are more vulnerable to ischemia.
- Contrast-enhancement, associated with reperfusion, is not usually seen until at least 7 to 10 days.

Several functional magnetic resonance imaging (fMRI) techniques improve the early diagnosis of stroke and evaluation of treatment in human patients. These methods include diffusion and perfusion imaging and magnetic resonance angiography (MRA). Diffusion and perfusion MRI are new techniques that monitor water transport in the microenvironment at cellular or capillary levels. These techniques provide complementary information about the pathophysiological processes following cerebral ischemia.[64] Diffusion-weighted imaging (DWI) is used commonly in human patients to improve the sensitivity and specificity of the diagnosis of acute stroke, making it an ideal sequence for positive identification of hyperacute stroke.[65,66] The temporal evolution of the DWI signal also allows the discrimination of acute versus chronic lesions.[21,23] MR perfusion-weighted imaging is employed to depict brain regions of hypoperfusion and identifies the tissue at risk by comparing the results with the findings on DWI.

In addition to its use for tissue evaluation, MRA can noninvasively assess the intracranial vascular status of stroke patients. Two techniques can be used: time-of-flight (TOF) MRA and contrast-enhanced MRA. One of the main limitations of MRA is its lower resolution compared with conventional angiography. This limitation becomes progressively worse as the luminal size decreases.[55] In human patients, angiographic techniques are particularly used for screening of carotid artery stenosis, vascular malformation (such as arteriovenous malformation, venous angioma) and aneurysms. The use of MRA in dogs has been described, and may allow identification of underlying vascular lesions in cases of canine stroke.[17,55]

Hemorrhagic stroke

CT is exquisitely sensitive at detecting acute hemorrhage, which is evident as increased density due to attenuation of X-ray beam by the globin portion of blood.[67] The attenuation gradually decreases until the hematoma is isodense at about 1 month after the onset. The periphery of the hematoma enhances with contrast at 6 days to 6 weeks due to revascularization.[67] Until recently, CT was the preferred imaging modality in human patients to determine the presence of hemorrhage in early stroke. Recent developments in MRI mean that CT now offers no advantage in the diagnosis of ischemic stroke.[67,68]

With conventional MRI, the signal intensity of intracranial hemorrhage is influenced by several intrinsic (time from ictus, source, size and location of hemorrhage) and extrinsic (pulse sequence and field strength) factors.[69] The exact effect of these various factors is difficult to evaluate with clinical studies because it is frequently impossible to ascertain the precise interval between hemorrhage and MR imaging. As the hematoma ages, oxyhemoglobin breaks down sequentially into several paramagnetic products: first deoxyhemoglobin, then methemoglobin, and finally, hemosiderin.[19] The 2 most important biophysical properties are the paramagnetic effects of iron as the hemoglobin oxygenation states change and the integrity of red blood cell membranes that compartmentalize the iron.[69] The earliest detection of hemorrhage depends on the conversion of oxyhemoglobin to deoxyhemoglobin, which occurs after the first 12 to 24 hours.[69] In oxyhemoglobin, iron is shielded from surrounding water molecules and the MR signal is similar to that of normal brain parenchyma. In deoxyhemoglobin, iron is exposed to surrounding water molecules, which

creates a signal loss that makes it easy to identify on T2-weighted and susceptibility-weighted sequences.[19] Details of time-related changes on MR images relative to the stage of advancement of hematoma from hyperacute to chronic have been reviewed elsewhere.[16,19,70] Gradient-echo sequences have been proven to be the most accurate of all of the MR pulse sequences, and more accurate than CT in predicting the extent of hemorrhage on pathologic examination in a dog model.[71] Compared with other sequences, gradient-echo scans demonstrate readily detectable hypointensity regardless of the time from ictus, the source and location of hemorrhage, or the field strength. Due to the progressive centripetal increase in the deoxyhemoglobin concentration, the periphery of the hematoma is often initially more hypointense on susceptibility-weighted images than on T2-weighted images.[19] Hypointensity on gradient-echo images is, however, not specific for hemorrhage and may also be seen with calcification, air, iron, foreign bodies, and melanin. However, air, calcification, and many foreign bodies are also hypointense on other pulse sequences.[23]

Cerebrospinal Fluid Analysis

CSF analysis is unlikely to confirm a diagnosis of stroke but may help to rule out inflammatory disease. In most cases of stroke it is either normal, or reflects a mild mononuclear or neutrophilic pleocytosis, occasionally with elevated protein.[18,21,72]

Identification of Underlying Causes of Stroke

Patients with ischemic stroke should be evaluated for hypertension (and its potential underlying causes), endocrine disease (hyperadrenocorticism, hypothyroidism, hyperthyroidism, diabetes mellitus), kidney disease (especially protein-loosing nephropathy), heart disease, and metastatic disease.[22,55] Despite thorough investigations, concurrent medical conditions were not identified in almost half of the dogs with ischemic stroke in one of the author's studies.[22] This finding parallels the prevalence of cryptogenic infarction in human patients.[3] This percentage is only slightly higher than that previously reported for histopathologically confirmed brain infarcts of unknown cause in dogs (39%).[5–8,10–18,20] Antemortem diagnostic investigations, such as angiographic studies of the vertebrobasilar and carotid system, and lipid and hemostatic profiles would be necessary in the future to investigate potential causes of ischemic stroke in dogs.

Diagnostic tests of presumed/confirmed cases of hemorrhagic stroke focus on screening the animal for coagulopathy, hypertension (and potential underlying causes), and metastatic disease (particularly hemangiosarcoma). Recommended ancillary diagnostic tests are listed in **Boxs 1** and **2**.

TREATMENT

Once the diagnosis of a stroke is made, any potential underlying disease is identified and treated accordingly. The general aim is to provide supportive care, maintain adequate tissue oxygenation, and manage neurologic and nonneurologic complications. Nursing management of a recumbent dog is vital to the success of more specific therapies. This management includes prevention of decubital ulceration, aspiration pneumonia, and urine scald, in addition to physical therapy and enteral nutrition. More specific therapies are aimed at preventing further neurologic deterioration.

Ischemic Stroke

Most cases of ischemic stroke recover within several weeks with only supportive care.[22] Potential underlying causes should be investigated and treated accordingly to limit the risk of recurrences. Treatment revolves around 3 principles: (1) monitoring

and correction of basic physiologic variables (eg, oxygen level, fluid balance, blood pressure, body temperature); (2) inhibition of the biochemical and metabolic cascades subsequent to ischemia to prevent neuronal death (neuroprotection); and (3) restoration or improvement of CBF by thrombolysis in cases of thrombus.[73] The potentially salvageable penumbra is the target for both thrombolytic and neuroprotective therapy.[74] The time period during which injury may be reversible is called the therapeutic window.[75] This "window of opportunity" is approximately 6 hours before irreversible neurologic damage occurs.

Monitoring and correction of basic physiologic variables

Fortunately, the vast majority of ischemic stroke patients have no major difficulty maintaining adequate airways, breathing, and circulation early in their clinical course.[76] Some controversies exist surrounding the management of hypertension in the setting of an ongoing acute ischemic stroke. As well as being a potential risk factor for stroke, hypertension can occur as a physiologic response to ensure adequate CPP in the penumbra of the infarct for up to 72 hours after onset.[77,78] Maintaining normal systemic arterial blood pressure is essential, and aggressive lowering of blood pressure is avoided during the acute stages unless the patient is at a high risk of end-stage organ damage (systolic blood pressures remaining above 180 mm Hg).[76,79] In such cases, hypertension can often be controlled with an angiotensin-converting enzyme inhibitor such as enalapril (0.25–0.5 mg/kg twice a day) or benazepril (0.25–0.5 mg/kg twice a day), or calcium channel blockers such as amlodipine (0.1–0.25 mg/kg once a day), which tends to be more effective.[73] Treatment with these oral antihypertensives is preferred, but parenteral medications such as nitroprusside, intravenous β-blockers, calcium channel blockers, or diuretics may be necessary in animals that cannot tolerate oral medications.[80]

Neuroprotection

There is no evidence that glucocorticoids provide any benefit in stroke.[81] Aside from the lack of proven benefit in veterinary stroke patients, the use of glucocorticoids may increase the risk of gastrointestinal complications and infection.[82] Treatment strategies for ischemic stroke considered in man using other neuroprotective agents (*N*-methyl-D-aspartate [NMDA] antagonists, Ca^{2+} channel blockers, sodium channel modulators) or antiplatelets and thrombolytic therapy have not been evaluated clinically in dogs. Although the aforementioned neuroprotective agents have resulted in a dramatic decrease in the size of stroke lesion in experimental animal models, these agents have either failed to prove their efficacy in clinical trials or are awaiting further investigation.[83,84]

Thrombolytic therapy

At present, there are no definitive data in humans or animals to confirm a benefit of thrombolysis using unfractionated heparin in patients with acute ischemic stroke. Despite conflicting results regarding its efficacy, intravenous recombinant tissue plasminogen activator (tPA) is sometimes used in human stroke patients if it can be given within the first 3 hours after the onset.[85] This critical time window makes thrombolytic treatment unrealistic in veterinary neurology. Furthermore, this type of treatment carries a significant risk of intracranial hemorrhage.[86] Antiplatelet therapy with low-dose aspirin (0.5 mg/kg by mouth once a day) can be used prophylactically to prevent clot formation in proven cardiac sources of an embolus.[80,87] No controlled studies in veterinary medicine have assessed these treatments.

Hemorrhagic Stroke

The most important consideration in hemorrhagic stroke is maintaining cerebral perfusion by treating hypotension and elevated ICP, and treating any underlying cause. Management includes stabilization of the patient by protecting the airway and monitoring and correction of vital signs; monitoring neurologic status; identifying and treating any underlying cause; and specific treatments such as managing raised ICP.[73] The risk of neurologic deterioration and cardiovascular instability is highest during the first 24 hours after the onset, as the space-occupying lesion slowly expands and cerebral vasogenic edema develops.[82] The initial focus is extracranial stabilization, closely followed by therapies directed toward intracranial stabilization and treatment of any identified underlying cause. Careful monitoring is essential during the initial period and includes assessment of vital parameters as well as neurologic status.

Extracranial stabilization

Extracranial stabilization involves careful monitoring of vital parameters (oxygen levels, fluid balance, blood pressure, body temperature) and correction of any abnormalities. Hypoxia should be avoided, as with any other intracranial disease. However, there is no evidence in human patients to support the routine use of oxygen for the treatment of hemorrhagic stroke in the absence of hypoxia.

Hypoventilation may occur as a result of damage to the respiratory center in the brainstem following raised ICP. The impaired respiratory drive results in elevated $PaCO_2$ and resultant cerebral vasodilation, which in turn aggravates intracranial hypertension. $PaCO_2$ should be maintained within a normal range and not allowed to exceed 40 mm Hg, including intubation and ventilation if necessary.[82]

Maintaining adequate tissue perfusion is important in any patient with hemorrhagic stroke. The primary goal of fluid therapy is rapid restoration of blood pressure, such that CPP is maintained greater than 70 mm Hg. Hypovolemia should be recognized and treated with volume expansion using artificial colloids or hypertonic saline (7.5%) to achieve rapid restoration of blood volume and pressure while limiting the volume of fluid administered. Hypertonic saline has many properties that may make it a superior resuscitation fluid for patients with intracranial disease such as hemorrhagic stroke. The recommended dose of hypertonic sodium chloride (7%–7.5%) for volume expansion is 3 to 5 mL/kg administered over 10 to 15 minutes. The use of glucose-containing solutions is discouraged, as hyperglycemia has been shown to correlate with poor outcome in human stroke patients.[88] Therefore, blood glucose should be monitored from the time of presentation. Hypotonic fluids should also be avoided.

As for ischemic stroke, attempts to lower and normalize blood pressure should be reserved for animals at a high risk of end-stage organ damage (systolic blood pressures remaining above 180 mm Hg) or animals with severe ocular manifestations of hypertension such as retinal detachment or intraocular hemorrhage.[76,82] However, moderate levels of hypertension should not be treated, as systemic hypertension may be secondary to the intense reflex sympathetic response to intracranial hypertension, which is a compensatory mechanism to maintain cerebral perfusion. Treatment recommendations for lowering blood pressure are detailed in the previous section on the treatment of ischemic stroke.

Intracranial stabilization

Once initial assessment and extracranial stabilization have occurred, medical intervention to address intracranial issues focuses on decreasing ICP.[73] Three principles

can be applied: (1) reducing cerebral edema associated with intracranial hemorrhage; (2) optimizing cerebral blood volume; and (3) eliminating space-occupying mass.

Osmotic diuretics such as mannitol are useful for treating cerebral edema and resultant intracranial hypertension associated with disorders such as head trauma, brain tumors, or encephalitis. There is no compelling evidence that mannitol exacerbates intracranial hemorrhage. Although the efficacy is still controversial, osmotic diuretics are routinely used in the control of ICP in human patients with known intracranial hemorrhage.[89] Mannitol (0.25–1.0 g/kg intravenous over 10 to 20 minutes up to every 8 hours) may be used to treat elevated ICP secondary to hemorrhagic stroke.[54] Mannitol's main effect is to enhance CBF by reducing blood viscosity.[54] It should, however, be avoided in hypovolemic patient.

Cerebral blood volume is another intracranial component that contributes to ICP. In a rapidly deteriorating animal, hyperventilation can be used to temporarily reduce ICP with a target $PaCO_2$ of less than 35 mm Hg. The aim of hyperventilation is to reduce cerebral blood volume and hence ICP, by causing cerebral vasoconstriction. However, excessive hyperventilation can be accompanied by a reduction in global CBF, which may drop below ischemic thresholds; therefore it is not recommended unless the $PaCO_2$ is closely monitored with capnography or arterial blood gas analysis.[90]

Elimination of the space-occupying mass within the cranial vault is the third method to reduce ICP. Surgical evacuation of the hematoma can therefore be employed in dogs with large hematomas (mostly subarachnoid) and a deteriorating neurologic status.

PROGNOSIS

The prognosis for ischemic or hemorrhagic stroke depends on the severity of the neurologic deficit, the initial response to supportive care, and the severity of any underlying cause. Fortunately, most cases of ischemic stroke recover within several weeks with only supportive care. In a recent retrospective study of 33 dogs with MRI or necropsy evidence of brain infarction, there was no association between the region of the brain involved (telencephalic, thalamic/midbrain, cerebellum), the type of infarction (territorial or lacunar), and the outcome.[22] However, dogs with a concurrent medical condition had a significantly shorter survival time than those dogs with no identifiable medical condition. Dogs with a concurrent medical condition also were significantly more likely to suffer from subsequent infarcts.[22] Hemorrhagic stroke is far less common than ischemic stroke, but is associated with higher mortality.[23,91]

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