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Heat stroke in dogs: Literature review

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Abstract: Heat stroke is a clinical emergency secondary to a severe temperature increase due to the inefficiencies of heat dissipation mechanisms, causing central nervous system dysfunctions, which may lead to multiple organ dysfunction syndrome. Heat disturbances can be classified as "classic" or "exertional" ones and several predisposing factors are involved in their development. This review provides a broad approach to the pathophysiological mechanisms of this syndrome, and the diagnostic and treatment methods to facilitate their approach in clinical routine and increase the survival rate of patients.

Keywords: cytotoxicity; hyperthermia; thermoregulation

Introduction

Heat stroke is a heat disorder with a high level of severity, characterised as an acute emergency secondary to a body temperature increase above 41 °C associated with a systemic inflammatory response, neurological dysfunction, and may cause multiple organ dysfunction syndrome (Bruchim et al. 2006). The imbalance between the heat generation and dissipation mechanisms lead to an exacerbated increase in the body temperature. Rapid and aggressive therapeutic interventions and patient monitoring are necessary to avoid serious secondary complications (Oglesbee et al. 2002; Flournoy et al. 2003b; Cardoso et al. 2010; Vitor et al. 2016). The objective of this literature review is to warn veterinarians about the risks of secondary heat disorders, address the main points of their pathophysiology, diagnosis and treatment, promoting a better understanding and a better clinical approach to the patient.

Heat stroke

Hyperthermia is defined as a body temperature increase above 39 °C. Depending on its aetiology, heat stroke can be classified as a "classical" or "exertional" type in human medicine. The classic form mainly occurs in sick or immunocompromised patients, very young or elderly individuals, affected by heat waves during the summer and high temperatures, confined or chained environments, or open places without thermal protection and access to water (Ruslander 1992). Moreover, in human medicine, exertional heat stroke is usually observed in young patients who collapse due to heat stress during exercise and those subjected to strenuous physical activity in hot climates (for example, military personnel and athletes) (Epstein and Roberts 2011; Bruchim et al. 2016).

Predisposing factors

Considering exogenous factors, heatstroke can occur due to lack of acclimatisation, water deprivation, high environmental humidity and poorly ventilated environments. The most common cause of heat stress is related to an animal's exposure to high temperatures, such as dogs left in cars on days with high temperatures and humidity. The use of some drugs (phenothiazines, diuretics, negative inot-

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ropies) that can lead to reduced heat dissipation through reduced cardiac output, lower circulating blood volume, development of myopathies and muscle rigidity can lead to the occurrence of tremors and/or a lower efficiency in heat dissipation and consequently create a greater predisposition to severe temperature increases (Flournoy et al. 2003b; Bruchim et al. 2006; Mann 2012).

Endogenous factors are those related to the animal itself, such as obesity, high body weight (giant breeds), brachycephalic dog breeds, animals used for work and concomitant diseases (Bruchim et al. 2006; Andress and Goodnight 2013). Obesity has been determined as a significant risk factor for the occurrence of disorders secondary to high temperature, since being overweight prevents adequate heat dissipation (Flournoy et al. 2003b). Very active animals are also susceptible to heat stress such as Golden Retrievers and Labrador Retrievers (Bruchim et al. 2017). In addition, Labrador Retrievers may be predisposed to an autosomal recessive inherited condition called exercise-induced collapse (EIC), characterised by episodic limb weakness, ataxia and collapse, which may explain some cases of hyperthermia in this breed (Minor et al. 2011). EIC is a mutation in the gene encoding the protein dynamin 1 (DNM1) that belongs to a family of catalytic enzymes involved in synaptic vesicle endocytosis and neurotransmission during sustained neural stimulation, such as during exercise. Another syndrome that can act as a predisposing factor is exercise-induced malignant hyperthermia in English Springer Spaniel dogs (Patterson et al. 2008).

Malignant hyperthermia, an autosomal dominant hereditary disease, is characterised as a pharmacokinetic reaction triggered by volatile anaesthetic agents (except nitrous oxide) and depolarising neuromuscular blockers (succinylcholine) due to a mutation in the gene for type 1 ryanodine receptor (RYR1) (Muniz et al. 2003). When these agents are administered to susceptible animals, they may experience tachypnoea, hyperthermia, hypercapnia, muscle rigidity, metabolic acidosis, cardiac arrhythmias and even death (Nelson et al. 1996; Brunson and Hogan 2004). Some dog breeds have been identified as more susceptible to malignant hyperthermia, such as Greyhounds, Border Collies, Cocker Spaniels, Doberman Pinschers, Pointers, and St. Bernards (Nelson 1991; Lanner et al. 2010).

Prolonged muscle tremors and seizures are also an important factor in raising the body temperature (Bruchim et al. 2017). The presence of a continuous generalised seizure for more than 5 min can characterise it as status epilepticus, responsible for important neurological and physiological changes depending on its duration. During its initial phase, an increase in the metabolism and oxygen consumption is observed. The release of catecholamines enhances the sympathomimetic effects in the body causing an increased heart rate, blood pressure, salivation, vomiting and increased body temperature secondary to the exacerbated muscle activity (Berendt 2004; Giral 2007). Moreover, a severe temperature elevation can itself lead to major brain damage, making this a cycle of major physiological damage (Aminoff and Simon 1980).

The anatomical conformation of brachycephalic breeds predisposes them to inadequate airflow in the upper respiratory system, making breathing mechanisms difficult which can also be observed in animals with upper respiratory tract disease, such as, laryngeal paralysis and tracheal collapse (Flournoy et al. 2003b). Evaporation through the respiratory tract is the main form of heat loss in dogs (Drobatz 2015). In brachycephalic breeds, this mechanism may be compromised due to the presence of primary morpho-functional alterations, such as, nostril stenosis, soft palate thickening, tracheal hypoplasia and excessive nasopharyngeal turbinates that characterise the brachycephalic syndrome (Canola et al. 2018). These changes lead to airway narrowing and increased resistance to air passage. Under thermal stress, there is an increase in amount of breathing, an increase in the negative intrathoracic pressure and greater deformity of the soft tissues of the anterior respiratory tract, consequently leading to a continuous cycle of airway obstruction and a greater respiratory effort, making brachycephalic dogs more susceptible to thermal stress (Trappler and Moore 2011; Davis et al. 2017).

Pathophysiology of heat stroke

The body has efficient thermoregulatory mechanisms responsible for maintaining the balance between heat production and dissipation. The thermoregulatory centre located in the preoptic region of the hypothalamus acts in the conversion of signals and activation of the neurohormonal system, activating body cooling mechanisms (convection, radiation, conduction and evaporation). As the

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body temperature rises, the evaporation mechanism becomes the main thermal control mechanism by activating the respiratory centre, increasing the respiratory rate and minute volume (Flournoy et al. 2003b; Trappler and Moore 2011; Romanucci and Salda 2013). This mechanism allows for large volumes of air to be in contact with the evaporative surface areas and regulates the cooling in the respiratory system.

Mammals have developed several mechanisms to deal with stress and maintain homeostasis, such as temporary changes in the gene expression to survive in different environments, as well as changing the cell structure and functions to deal with adverse conditions. One of these mechanisms includes heat shock proteins, whose function is to increase the ability of enzymes to function during extreme heat, acting as "molecular guardians" that induce a state of cellular tolerance and assist in the maintenance of intracellular function and structural protein integrity (Bouchama and Knochel 2002). They can exert their protective effect through preventing the disaggregation of denatured proteins and assisting the refolding of denatured proteins into their native configuration; attenuating the loss of the epithelial barrier integrity and preventing endotoxin leakage across the intestine wall; attenuating arterial hypotension to reduce cerebral ischaemia and neural damage; and interfering with oxidative stress and blocking the apoptotic cell-signalling pathways (Yang and Lin 1999; Yan et al. 2006).

Acclimatisation is a physiological process that allows the organism to adapt to extreme environmental and climatic changes (Horowitz 2002), through a continuous and repetitive process of the thermoregulatory system, requiring a long period of development, taking between 10 and 20 days in animals and up to 60 days for complete acclimatisation (Johnson et al. 2006). For this process to occur, some systems must be activated, such as increased cardiac work, activation of the renin-angiotensin-aldosterone system, sodium reabsorption and plasma volume expansion, as well as an increase in the glomerular filtration rate and an increase in the plasma volume and resistance to the occurrence of rhabdomyolysis (Bouchama and Knochel 2002). The characteristics of the acclimatisation process include a reduced core temperature and heart rate, an increased cardiovascular reserve and an increased evaporative cooling capacity (Horowitz 1998).

However, in the presence of predisposing factors, lack of acclimatisation and severe elevation of body temperature (> 41 °C), the thermoregulatory mechanisms become inefficient, resulting in a complex series of events leading to compromised microcirculatory blood flow, vascular and tissue injury. Nevertheless, cytotoxicity and the development of systemic inflammatory response syndrome (SIRS) can culminate in multiple organ dysfunction, mainly central nervous system damage (Flournoy et al. 2003b; Cardoso et al. 2010; Davis et al. 2017).

Cardiovascular changes during heat stroke may initially resemble the distributive shock seen in sepsis (Romanucci and Salda 2013). Activation of peripheral and hypothalamic receptors are required for body temperature regulation. Peripheral vasodilation generated by sympathetic activity and splanchnic vasoconstriction are responsible for the increased cardiac output and elevated peripheral circulation (Epstein and Roberts 2011) as a protective attempt to transfer the central circulation to the periphery, which may progress to compromised splanchnic circulation, reduced circulating plasma volume and circulatory shock (Romanucci and Salda 2013; Nybo et al. 2014). Myocardial injuries occur due to the reduced tissue perfusion, acidosis and electrolyte imbalance, as well as being associated with an increased venous pressure and pulmonary oedemas, while subendocardial petechial haemorrhages and localised areas of myocardial necrosis are common necropsy findings (Bruchim et al. 2009).

Due to considerable increases in the pulmonary vascular resistance and direct thermal damage to the pulmonary endothelium, there is considerable risk of developing cor pulmonale or acute respiratory distress syndrome (ARDS). Significant lung injury during hospitalisation in humans can lead to the development of disseminated intravascular coagulation, non-cardiogenic pulmonary oedema or ARDS (Curley and Irwin 1996).

In humans, heat stress is related to cerebral hypoperfusion, direct vascular damage, cerebral and cerebellar oedema, neuronal necrosis, haemorrhage and multifocal vascular thrombosis with tissue infarction. Elevated temperatures are responsible for permanent or transient (Laitano et al. 2019) brain injuries and neurological and cognitive sequelae can be marked soon after the event or persist and become permanent (Walter and Carraretto 2016). Encephalopathy is the main manifestation

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of an abrupt and severe occurrence, which may explain why the disease was labelled as a type of stroke in human medicine (Knochel et al. 1961). However, in veterinary medicine, this definition must be used with reservations, since, based on a retrospective study, not all dogs showed signs of neurological dysfunction on hospital admission (Bruchim et al. 2006), and this may be due to the intrinsic thermal resistance of the brain of these animals (cooling system consisting of a network of blood vessels that branch from the carotid artery) (Oglesbee et al. 2002). The mechanisms of injuries to the central nervous system are not well understood, but studies in rodents have shown that, in cases of classic heatstroke, there is an increase in the intracranial pressure with a secondary ischaemia and reduced cerebral blood flow (Lin et al. 1995). In patients with heat stroke, the most visible histological changes observed in the central nervous system (CNS) are neuronal degeneration in the cerebellum and cerebral cortex, congestion, oedema and microhaemorrhages (Shibolet et al. 1967).

The gastrointestinal tract involvement may occur due to splanchnic vasoconstriction and redistribution of blood flow to the periphery (Pires et al. 2017). The severity of the hyperthermia is directly related to the hypoperfusion of the gastrointestinal tract, the injury itself and the increased membrane permeability. Structural and functional changes facilitate bacterial and endotoxin translocation into the bloodstream, which are normally harmless when contained in the intestine (Bruchim et al. 2017). In dogs suffering from heat stroke, the bacterial translocation process is not evident, but due to the presence of haemorrhagic diarrhoea and haematemesis in these patients, it is important to highlight it as a predisposing factor to systemic inflammatory response syndrome (SIRS) and multiple organ dysfunction syndrome (MODS) (Bruchim et al. 2017).

Acute renal failure occurs due to a decreased renal perfusion secondary to hypovolemic shock, dehydration, endotoxemia, myoglobulinemia secondary to rhabdomyolysis, the release of cytokines and vasoactive mediators and micro-thrombosis associated with disseminated intravascular coagulation (DIC) (Segev et al. 2015a). Renal damage ranges from mild proteinuria, glomerular ischaemia, and urinary sediment abnormalities to acute tubular necrosis (Leon and Bouchama 2015).

Reduced blood perfusion due to peripheral vasodilation leads to liver dysfunction. The pathophysiological process of a liver injury may be related to several factors such as hepatitis secondary to hypoperfusion and micro-thrombosis (Leon and Bouchama 2015). This organ is responsible for the synthesis of most coagulation factors and maintenance of homeostasis, therefore, severe liver damage can favour the hypo-coagulation process and the occurrence of bleeding (Romanucci and Salda 2013; Blois 2017). The endothelial thermal injury occurs with the release of thromboplastin and factor XII which are responsible for the activation of the coagulation cascade and complement system, culminating in the development of the systemic inflammatory response syndrome (SIRS), microthrombosis, disseminated intravascular coagulation and haemorrhages (Bhavani et al. 2015; Blois 2017).

An increased intracellular calcium concentration in response to the metabolic heat production and decreased adenosine triphosphate (ATP) levels due to muscle cell apoptosis can lead to rhabdomyolysis, which usually occurs due to excessive and strenuous exercise, with greater risk and severity in dehydrated patients. If not treated quickly, the myoglobin release can lead to an exacerbated production of uric acid, causing acute kidney injury due to its precipitation in the renal tubules as well as leading to the development of coagulopathies and even death (Leon and Bouchama 2015).

Clinical signs

Clinical signs vary according to the severity of the heat disorder. Changes in the breathing pattern (panting), an elevation in the body temperature, prostration, emesis and diarrhoea may be common in mild to moderate conditions, and may rapidly progress to ataxia, seizures and cardiorespiratory collapse in more severe cases. Other signs, such as muscle tremors, oedema and blood dyscrasias, may also be observed. Clinical signs of organ failure can manifest after 3 to 5 days of heat stroke; therefore, patients must be kept under observation during this period (Mazzaferro 2017).

In the cardiovascular evaluation, a weak or irregular pulse, ventricular tachycardia, premature ventricular complexes (VPCs) and arterial hypotension can be observed. Signs of neurological dysfunction in dogs range from syncope, disorientation, stupor, cortical blindness, ataxia, seizures or coma (Flournoy et al. 2003b). Patients in shock may pres-

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ent with seizures as reported in studies where about 35% of patients had seizure activity during or before presentation, and, within this population, 47% had an obtuse mental state and 24% a comatose state (Bruchim et al. 2006).

Diagnosis

The diagnosis is mainly based on neurological dysfunction, hyperthermia and a history of exposure to high temperatures and physical activities (Leon and Bouchama 2015). Patients may present with an advancing state of shock. Other signs that can be observed on physical examination are dry and hyperaemic mucous membranes, reduced capillary filling time secondary to peripheral vasodilation. Signs related to blood dyscrasias, such as petechiae, melena or haematochezia, may also be present. In more severe cases, in the event of neurological dysfunction, patients may experience ataxia, reduced central reflexes, a reduced level of consciousness, seizures and coma (Hall et al. 2021).

Hyperthermic patients need complete laboratory work, including haematological and biochemical profiles, coagulation tests, blood gases, lactate and urinalysis. The haematocrit and total solids values may be elevated due to dehydration and haemoconcentration, however, gastrointestinal losses, vasculitis or renal losses can lead to a reduction in the values of the total solids and anaemia. In the presence of disseminated intravascular coagulation, thrombocytopenia, increased coagulation times and increased fibrin degradation products may be observed (Blois 2017).

Elevated serum urea and creatinine values are related to the presence of renal or prerenal azotaemia, and creatinine concentrations > 132.60 µmol/l correlate with a worse prognosis. The commonly found results suggestive of heat stress are due to rhabdomyolysis and muscle damage, including increased creatinine kinase (CK), aspartate transaminase (AST) and alanine transaminase (ALT) activity (Blois 2017; Mazzaferro 2017). Owing to tissue hypoperfusion, an increase in the serum muscle enzyme levels is marked, especially CK with a mean value of 283.90 µkat/l, reaching up to 5 761.50 µkat/l (Bruchim et al. 2016). The specific gravity of urine must also be evaluated in order to measure the ability to concentrate the urine and sediments should be examined for the presence of casts that may indicate renal tubular damage. Myoglobinuria can occasionally be noted on urinalysis and is indicative of rhabdomyolysis (Mazzaferro 2017). Approximately 68% of dogs with thermal injuries may have nucleated red cells, and their relative or absolute numbers are related to a higher risk of kidney damage, DIC and death (Blois 2017).

Although acute kidney injury invariably occurs in dogs with heatstroke, it is often subclinical at presentation, so it is extremely important to use techniques that promote early glomerular and tubular damage. The use of renal biomarkers may be useful in the early identification of renal injury. Novel urinary biomarkers for kidney injury include neutrophil gelatinase-associated lipocalin (NGAL), C-reactive protein (CRP) and retinol-binding protein (RBP) and protein to creatinine ratio (UPC). In a prospective study by Segev and collaborators, the presence of the biomarkers between healthy and heat stroke dogs were compared. Considerably high values of different biomarkers were observed in dogs that suffered heat stroke, allowing identification of an acute kidney injury even in its initial course (Segev et al. 2015b).

Treatment

FLUID THERAPY

Heat stroke is characterised by a state of distributive shock and may present a deficit in the absolute or relative volume and, for this reason, fluid therapy should be instituted immediately, whose objective is to reanimate the circulating volume, and improve the peripheral and visceral perfusion (Flournoy et al. 2003a). The volume of the fluid lost by the thermal stress must be replaced during the first 24 hours. The calculated water deficit can be replaced (50% of the total volume) in first 3 h to 6 h and the remainder in the following 9 h, thus, avoiding the rapid administration of large volumes over a short period of time (Hongjun et al. 2015; Blois 2017). In patients showing signs of hypotension and hypoperfusion, the use of balanced crystalloid solutions can be used for initial resuscitation in an initial bolus ranging from 10 ml/kg to 20 ml/kg (Hemmelgarn and Gannon 2013). The infusion of fixed fluid rates of 90 ml/kg/h in dogs or 60 ml/kg/h in cats are contraindicated as excessive fluid volumes can cause hypoxemia, pulmonary and cerebral oedemas and cardiac ar-

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rest (Rabelo 2012). The administration of crystalloids (e.g., balanced electrolyte solutions), should be based on goals for re-establishing cardiovascular stability and electrolyte balance, with a continuous reassessment of the circulatory and perfusion parameters (heart rate, pulse quality, capillary filling time, mucosal colour and blood pressure) (Flournoy et al. 2003a; Leon 2006). Based on the haematological examination and the patient's needs, the use of blood and blood products may be considered. The use of fresh frozen plasma, whole blood or platelet-rich plasma can be considered in cases of coagulopathies, as well as the use of red blood cells or a whole blood transfusion in anaemic patients (Tocci 2010).

COOLING

Cooling the patient suffering from hyperthermia is essential and can be performed by increasing the temperature gradient between the skin and the environment (for conduction cooling), increasing the water vapour pressure gradient between the skin and the environment (for evaporative cooling) as well as by increasing the velocity of the air adjacent to the skin (for convection cooling) (Bouchama and Knochel 2002). Applying fluids at room temperature over the surface of the body (Haskins 2007) using airflow sources (ventilators) increases the efficiency of the heat dissipation mechanism. Areas with little to no hair should be used to apply damp towels, and regions with a thick layer of hair should be avoided, as once wet, they can act as a thermal insulator, preventing heat loss (Flournoy et al. 2003a). Alcohol should not be used to soak the whole body due to risk of intoxication. It could be considered soaking the paw pad, but its effectiveness has not been investigated.

Peripheral vasoconstriction must be prevented by avoiding the use of ice packs and immersing the patient in cold water baths, decreasing the risk of reduced blood circulation in the central viscera. In addition, the application of ice packs inhibits radiation cooling, causing intense cutaneous vasoconstriction, preventing vascularisation and blood stasis in the peripheral capillaries, which can cause DIC. Nevertheless, the use of ice to promote cooling can cause discomfort to the patient due to direct contact with the skin, in addition to leading to increased heat production in the presence of shivers (Weiner and Khogali 1980; Flournoy et al. 2003a).

Figure 1. Active cooling using an ice pack in the neck region (Source: Personal archive)

Based on the concept that the brain temperature can be controlled through cerebral blood flow, cooling techniques can be used by cooling with ice packs (only in this case, can it be considered) in the head and neck regions (Dennis et al. 2003; Palmer et al. 2001) (Figure 1). The cooling of the patient must occur gradually and must be stopped once the body temperature reaches 39.5 °C due to the risk of the progression of hypothermia (Hemmelgarn and Gannon 2013).

The use of enemas and gastric lavage despite being described in the literature are not recommended due to the high risk of aspiration and pneumonia, and increased intestinal permeability (Bouchama et al. 2007). Antipyretic and non-steroidal anti-inflammatory drugs (NSAIDs) are contraindicated in the management of hospitalised patients, since the mechanism of action of the former has no action in reducing the temperature of hyperthermic patients, acting only in the thermoregulatory centre to control fever. The use of NSAIDs can compromise renal perfusion and the occurrence of gastrointestinal ulcers (Mazzaferro 2017).

AIRWAYS AND OXYGENATION

Due to the increase in the body temperature, there is discomfort and an increase in the respiratory rate, consequently increasing the oxygen demand. Oxygen should be provided through masks, nasal tubes, incubators or endotracheal intubation (Mann 2012). Comatose patients should be intubated immediately and oxygen supplementation along with intermittent positive pressure ventilation should be started until the animal can breathe spontaneously (Hemmelgarn and Gannon 2013) (Figure 2). Brachycephalic dogs are highly predisposed to partial or complete upper respiratory

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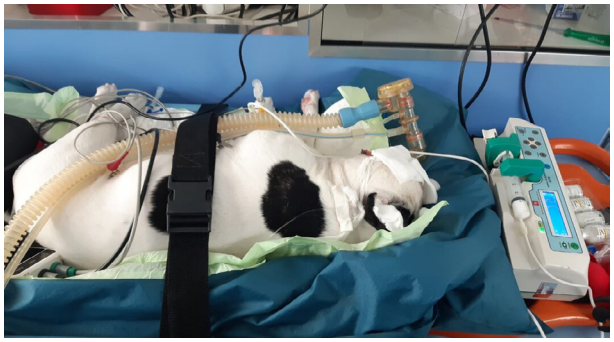

Figure 2. Transport in a mobile intensive care unit after a patient has suffered from respiratory failure. Maintenance of invasive ventilation with controlled positive pressure under sedation, using continuous infusion of propofol (Source: Personal archive)

tract obstruction secondary to their anatomical conformation. The process of an increased body temperature and increased respiratory rate can lead to an airway oedema, a reduced gas exchange and an increased respiratory effort. In these patients, endotracheal intubation and mechanical ventilatory support are indicated. The presence of continuous inspiratory effort predisposes the animal to inflammation of the soft tissues in the anterior airway, and pharmacological assistance with the use of glucocorticoids (dexamethasone) in anti-inflammatory doses (0.15 mg/kg) may be necessary to reduce the local oedema and inflammation (Fawcett et al. 2018; Mendes Junior et al. 2021).

The development of complications secondary to an upper respiratory tract obstruction is common, and pneumonia, non-cardiogenic pulmonary oedema, and acute respiratory distress syndrome may occur. Monitoring the pulmonary function through pulse oximetry, arterial blood gases and imaging tests is important in establishing an early diagnosis and the adequate support necessary (Pease et al. 2009).

ANXIETY AND SEDATION CONTROL

Anxiety and agitation reduction are also important as part of the treatment and the association of analgesics and sedatives can be a good choice. Butorphanol is an opioid with a good sedative effect and it can be used alone or in combination at a dose of 0.2 mg/kg to 0.4 mg/kg (Hemmelgarn and Gannon 2013). Acepromazine at a dose of 0.01 mg/kg to 0.02 mg/kg combined or not with an alpha-2 agonist is also effective in reducing stress and promoting tranquillity with easy reversal if necessary. In animals that need to be intubated, propofol may be indicated for anaesthetic induction (Hemmelgarn and Gannon 2013; Fawcett et al. 2018) (Figure 3).

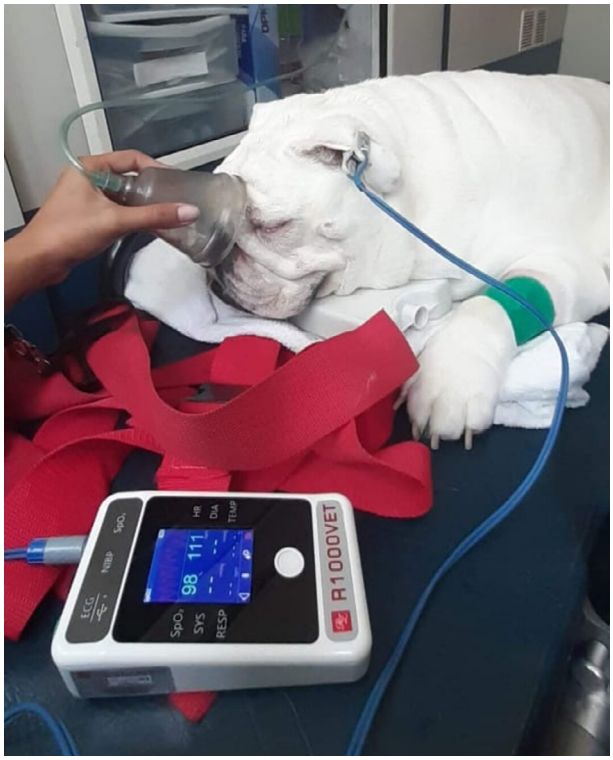

Figure 3. Patient slightly sedated using acepromazine after onset of agitation and respiratory distress secondary to hyperthermia (Source: Personal archive)

ANTIBIOTIC THERAPY

The intestinal mucosa has the function of promoting a protective barrier between the intestine and the sterile circulatory system. Its structure is fragile and susceptible to injury under physical and physiological stresses, leading to the breakdown of this barrier and increased permeability, promoting the translocation of bacteria and toxins in the circulation (Lim 2018). Normally, these microorganisms and toxins present in the circulation are efficiently transported and eliminated by the hepatic portal system. However, in the presence of excessive stress with a large release of endotoxins, as well as when there is a reduction in the hepatocellular function and immunosuppression, the development of systemic inflammatory response syndrome (SIRS) and sepsis are observed (Unterer et al.2015; Krentz and Allen 2017).

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The use of antimicrobials is controversial due to the potential for bacterial resistance and changes in the intestinal microbiota. Though its use may be indicated in the presence of signs of intestinal hypoperfusion, immunosuppression and liver dysfunction. The use of broad-spectrum antimicrobials is recommended, effective against most gram-negative, gram-positive and anaerobic bacteria, with continuous treatment until cardiovascular stabilisation, regulation of the enteral feeding and cessation of gastrointestinal signs (Unterer et al. 2015; Fawcett et al. 2018).

GASTROINTESTINAL TRACT PROTECTION

Vomiting and diarrhoea are commonly present and the patient must receive necessary support for the treatment and protection of the gastrointestinal tract mucosa. The use of proton pump inhibitors and H_2 blockers reduce the risk of mucosal damage due to stress, as well as the use of sucralfate may be indicated for the prevention of gastric ulcers. After stabilisation of the patient, nutritional support should be started with preference for enteral feeding, unless, it is impossible to use this route (Monning and Prittie 2011).

RENAL SUPPORT

Acute kidney injury (AKI) induced by the process of hyperthermia or sepsis that has vasodilation and ischaemia as a mechanism, is marked by a reduction in the renal function, therefore, monitoring the urinary output should be performed (Flournoy et al. 2003a). After initial resuscitation, urinary output should be evaluated and ideally maintained between 1–2 ml/kg/h (Keir and Kellum 2015; Mazzaferro 2017). In cases of persistent oliguria (< 1 ml/kg/h) or anuria with adequate hydration and a mean arterial pressure, the use of furosemide may be considered to restore the urinary output (Monning and Prittie 2011).

CENTRAL NERVOUS SYSTEM SUPPORT

Constantly monitoring the patient's neurological status is essential during the treatment of hyperthermia, and should be aimed at the contributors responsible for the encephalopathy (hyperthermia, dehydration and hypoperfusion), and the use of drugs for the rapid and efficient reversal should be promoted. In the case of increased intracranial pressure, the use of mannitol or a 7.5% hypertonic saline solution can be instituted, where the latter is superior because it reduces the risk of dehydration due to osmotic diuresis. In cases of seizures, the use of diazepam is recommended (Flournoy et al. 2003b; Hemmelgarn and Gannon 2013).

Prognosis

The prognosis for this syndrome is reserved due to several variables involved. It has a high mortality rate, reaching values between 50% to 64% and, in most cases, patients die within the first 24 h of treatment. On the other hand, animals hospitalised for more than 72 h have a higher survival rate (Drobatz and Mancintire 1996; Bruchim et al. 2006). Factors that lead to the high mortality rate include obesity, prolonged time (4 min to 90 min) between the thermal insult and presentation on admission, hypoglycaemia (2.611 1 mmol/l), azotaemia (creatinine >132.60 μmol/l) 24 h after presentation, development of DIC, acute kidney injury, and neurological injury. In addition, prothrombin time > 18 s and activated partial thromboplastin time above 30 s can also be considered as the greatest risk factors for death (Bruchim et al. 2006; Aroch et al. 2009). In a prospective study, it was observed that the presence of elevated prothrombin times and activated partial thromboplastin and a reduction in the concentration of fibrinogen in the first 24 h after presentation were associated with the patient survival, being, therefore, good prognostic tools (Bruchim et al. 2017).

Comparing the surviving and non-surviving patients, elevations in the glucose, total protein, albumin and cholesterol concentrations and significantly higher concentrations of creatinine and total bilirubin in the latter can also be seen, in addition to the occurrence of ventricular arrhythmias (Drobatz and Mancintire 1996). Due to the high rate of systemic complications and fatality in cases of heat stroke, treatment is challenging, complex and expensive, while the prognosis is uncertain. Some risk factors can be used as diagnostic and prognostic tools, but others are not very useful in this process (Aroch et al. 2009).

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Prevention

Considering the mechanisms involved in heat stroke, the prevention of its occurrence must start with the education and awareness of the owners. Some critical points can be considered in the educational process, such as, providing an abundant supply of clean and fresh water to the animals; performing physical exercises only during the coldest hours of the day and in shaded places; taking care when exercising very obese animals as they have difficulty dissipating heat; providing shelter with good ventilation and shade for the animals; using sun protection on light-skinned animals; not leaving animals in cars during sunny and very hot days; in cases of hyperthermia, avoiding the use of ice water or ice to cool the animals, and guide the owners correctly on first aid prior to arrival at the hospital (Mann 2012).

The detection of signs of heat stress in work dogs, such as, excessively breathless animals looking for shaded places and reluctance to work are important before the heat stress becomes a pathological condition is of utmost importance. The animals must be kept at the adequate body conditions with regular visits to the veterinarian, respecting the animals' work cycle, with a maximum time of 15 m of work in the open air at temperatures above 30 °C, avoiding longer hours in the heat during the day and places with little shade; the resting periods of the animals between work cycles must be at least 40 min; maintain adequate hydration of the animals by providing a necessary amount of water for their maintenance (40–60 ml/kg/day). It is also important to monitor the body temperature of these animals since some of them continue to work even with a continuous increase in the temperature until they collapse (Gordon 2017).

Conflict of interest

The authors declare no conflict of interest.

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