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Case Report

Successful Treatment of Severe Hyperthermia in Captive White-Tailed Deer (*Odocoileus virginianus*)

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ABSTRACT

Hyperthermia is a common, serious issue when capturing wildlife and has the potential to cause irreversible damage and death if severe, especially among cervids. During a disease surveillance program in white-tailed deer, 72 animals were chemically immobilized for sample collection. Most of the deer became hyperthermic (body temperatures >2°C above physiological norm) and of those, three became severely hyperthermic (>4.2+°C above physiological norm). Since the deer were sedated for regulatory purposes, reversal of the immobilant was not an option to restore natural thermoregulation. Rather, flunixin meglumine was administered to each animal in conjunction with cold water enemas and/or copious external application of water. Body temperatures rapidly cooled and stabilized within normal physiological ranges after the treatment. Once the samples were collected, each deer was returned to their pens and given the immobilizing agents' antidotes. All deer survived and appeared healthy 30 days post-capture indicating the protocol used for hyperthermia treatment was effective.

Keywords: White-tailed deer; *Odocoileus virginianus*; Hyperthermia; Capture; Treatment; Flunixin meglumine.

INTRODUCTION

Hyperthermia is a major concern when capturing and immobilizing wildlife because of the potential neurological effects and associated morbidity and mortality. When body temperature increases, so does metabolic oxygen demand of the animal, which can lead to hypoxemia if ventilation does not sufficiently increase [1]. When mammals become severely hyperthermic, the blood-brain barrier can break down, causing subsequent cephalic edema [2]. Heat-damaged cells also begin leaking potassium and damaged proteins into the interstitial space which can overwork the liver, clog glomeruli in the kidneys, and cause hyperkalemia resulting in irreversible damage [3]. Body temperatures greater than 2°C (3.6°F) above normal body temperatures are considered hyperthermic [4]. Normal body temperature in ruminants, including white-tailed deer (*Odocoileus virginianus*), is approximately 38.5°C (101.4°F); 40.6°C (105°F) is considered the threshold for hyperthermia in cervids [5]. Factors frequently cited as contributors to hyperthermia when capturing wildlife include, but are not limited to:

Drug combination-certain immobilizing drugs can inhibit or alter thermoregulation and cause respiratory depression, which increases the potential for hypoxia and exacerbates thermoregulation issues in animals that rely on panting as ungulates do [4]. These drugs include potent opioids such as fentanyl, thiafentanil, sufentanil, and etorphine and alpha-2 agonists such as xylazine and medetomidine [4,6,7]. These drugs can also cause increases in metabolism and muscle contractions in the excitatory phase of immobilization due to their adrenergic agonism, which contributes to increases in body temperature [6]. Some tranquilizers can also affect thermoregulatory abilities of immobilized animals by reducing the responsiveness of the hypothalamus to body temperature changes [6].

High ambient temperatures-the effect of ambient temperature on capture-induced hyperthermia is relatively insignificant at mild temperatures (<24°C/<75°F) [1]. However, as ambient

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temperatures increase, capture induced hyperthermia and capture myopathy occurs more frequently [4,6,8-10]. Kock and Burroughs [6] suggest avoiding wildlife capture events at temperatures greater than 25°C (77°F), although hyperthermia can also occur at cooler ambient temperatures.

Method of capture-there is a plethora of techniques for capturing and immobilizing wildlife; the methods that induce the most stress, physical exertion, and physiological changes have the highest potential to cause capture related hyperthermia [4,11]. Kock et al. [11] demonstrated that chemical immobilization most dramatically increased body temperature followed by drive net capture, net gunning, and drop netting, respectively. Rocket netting is also relatively stressful and causes greater increases in body temperature of wildlife than clover trapping [8]. Clover traps and drop nets most likely have the smallest temperature increases due to the lack of pre-capture exertion and relatively low stress compared to other capture methods.

Physical exertion-when muscle fibers contract and energy is expended, heat is produced. If a wildlife capture event induces a large amount of physical exertion, long chases, or prolonged struggling (as explained in methods of capture), body temperatures will increase [8,12].

Exertional rhabdomyolysis (capture myopathy)-the link between hyperthermia and capture myopathy is incompletely understood. However, anecdotal evidence suggests that capture myopathy exacerbates hyperthermia and vice versa [4,10,13]. Capture myopathy is a non-infectious disease induced by prolonged psychological and physiological stress and extended periods physical exertion that results in muscle necrosis and occasionally organ failure [4,10]. Death can result from capture myopathy within hours of a capture event and as far out as a month, however the exact pathogenesis is incompletely understood [4,13]. Muscle lysis is commonly associated with capture-induced myopathy and is most likely a result of sympathetically induced overexertion during extreme stress, which increases body temperature and subsequently causes further harm to the organs and muscles [10]. There is no cure for capture myopathy and often, the damages that result from of severe hyperthermia and capture myopathy are irreversible.

When immobilizing wildlife, constant body temperature monitoring is important, and thresholds should be established before the capture so proper treatment can take place when body temperatures rise to unacceptable levels. Treatment for hyperthermia and capture myopathy are essentially palliative and restorative with a focus on keeping the animal calm and comfortable while restoring physiological norm. The case report that follows describes an apparently effective treatment protocol for the control of capture-induced hyperthermia in three white-tailed deer on the Texas-Mexico Border.

CASE REPORT

On the 14th and 15th of May 2019 near Zepata, Texas, 72 captive white-tailed deer (*Odocoileus virginianus*) were captured for regulatory ante-mortem Chronic Wasting Disease (CWD) surveillance. The capture event took place between the hours of 7:00 pm (5/14) and 4:00 am (5/15) using chemical immobilization *via* remote delivered dart. Weather conditions during the capture were partly cloudy, no precipitation, muggy (humidity greater than 70%), and temperatures in the range of 22.2°C to 31.6°C (72°F to 89°F) [14]. The deer surveyed consisted of bucks and does, all intact adults (>16 months), which were darted from the ground in their respective breeding pens using a Dan-Inject. 22 blank powered rifle, modified to accept Pnue-Dart darts. The bucks and does were darted with 2.0mL and 1.5mL of BAM® (Wildlife Pharmaceuticals, Inc. Windsor CO) respectively; a premixed immobilization cocktail of butorphanol at 27.3 mg/mL (a mild opioid), azaperone at 9.1 mg/mL (a neuroleptic tranquilizer), and medetomidine at 10.9 mg/mL (an alpha-2 agonist). Animals were immobilized in groups of three to seven (regardless of sex and age), loaded on a flat-bed trailer and transported approximately 400 m to the sampling station.

Because these deer were being sampled for CWD surveillance to meet regulatory requirements, Texas Parks and Wildlife Department staff assisted by checking official unique identification numbers, tattoos, and owner ear tags to verify that 100% of the age-eligible deer were tested. Tonsil biopsies were taken from every animal. Animals were immobilized for longer than ideal periods of time, sometimes upwards of 50 minutes, due to the nature of the surveillance program.

Immediately upon arriving at the surveillance station, body temperature and respiration rate were evaluated and monitored approximately every 10 minutes until returned to pens. Body temperature was monitored using an AmerisourceBergen® thermometer inserted in the rectum. Regardless of body temperature, animals were intermittently sprayed with water. All 72 of the deer that arrived to the survey station received flunixin meglumine (Bayer Corporation Whippany NJ); if the rectal temperature was less than 40.56°C (105°F), 1.5 mL of flunixin meglumine at 50 mg/mL was administered *via* intramuscular injection in the rump, if the rectal temperature was greater than 40.56° (105°F), the same dose was administered *via* intravenous injection in the jugular vein. If rectal temperatures were over 41.67°C (107°F), a single cold-water enema was given in conjunction with the dose of flunixin meglumine as explained previously.

After samples were collected from the last deer in their respective immobilization group, all of the deer received a subcutaneous injection in the shoulder of Excede® (Zooetis Parsippany NJ) at 200 mg/mL and dosed at 1 mL per 33 pounds and the group was transported back to their pen and reversed simultaneously with a dose 2 mL of Atipamezole with a concentration of 25 mg/mL (alpha-2 antagonist) per 1 mL of BAM® and 0.5 mL of Naltrexone with a concentration of 50 mg/mL (opioid antagonist). Over 50% of deer had elevated temperatures (40.5°C+ or 105°F+) and required treatment to decrease body temperature; some required very aggressive treatments.

Three white-tailed deer does arrive to the CWD sampling station with severe hyperthermia. The deer were all from different immobilization groups and were the only individuals in their respective group with such extreme temperatures. The

body temperature of each of the three individuals were 42.78°C (109.0°F), 43.00°C (109.4°F), and 43.28°C (109.9°F). These animals were the first of their groups to be handled by the sampling team due to the severity of their body temperature. Reversal of the immobilizing agents was not an option due to the regulatory requirements that needed to be fulfilled. They were immediately given an intravenous dose of 1.5 mL of flunixin meglumine in the jugular vein followed by two cold-water enemas and continuous external dousing with water on the axillary region, groin, and head. The enemas were 16.9 fl oz refrigerated water bottles given one immediately after the other. The tail was held down tight against the anus for several minutes (2-4 minutes) to ensure that most of the water given stayed in the animal rather than leaking out. Body temperatures could no longer be read with a rectal thermometer because the results would be skewed from the introduction of cold water to *via* the rectum. However, all three deer body temperatures decreased subjectively (head and thoracic palpation) within 2-3 minutes.

All 72 of the deer surveyed responded quickly and positively to the treatment and survived more than 30 days and appear healthy; all the deer tested negative for CWD. The repercussions of the physiological damage associated with capture-induced stress and hyperthermia typically occur within a month [10,13]. Therefore, it is reasonable to assume that any detrimental effects of the capture event would have occurred within 30 days and that any morbidity or mortality thereafter was most likely unrelated.

DISCUSSION

Hyperthermia can occur for many reasons, but the thermoregulatory center of the brain, the hypothalamus, is always involved. Prostaglandins are released during cellular damage, which cross the blood brain barrier and bind to the hypothalamus. This triggers a fever-like immunological response and allows the body temperature to rise. When stress and injury occur during capture, prostaglandins are released, potentially exacerbating capture induced hyperthermia.

Flunixin meglumine is a Nonsteroidal Anti-Inflammatory Drug (NSAID) associated with the inhibition of prostaglandin synthesis. A study in dairy cattle conducted by Soto et al. [15] indicated that inhibition of prostaglandin synthesis with flunixin meglumine did not actually reduce body temperatures. Furthermore, a similar study in broiler chickens found that there was no statistical difference in blood concentration of prostaglandin when treated with flunixin meglumine [16]. They did, however, find that treatment with flunixin meglumine significantly increased survival of post hyperthermia in broilers compared to those that did not receive treatment. Little is known about the exact physiological pathways in which flunixin meglumine reduces body temperatures, but anecdotal evidence supports its use in treating hyperthermia and increasing survival. Texas Parks and Wildlife Department found that the use of flunixin meglumine during pronghorn capture in the Texas Panhandle for relocation to the Trans-Pecos Region of Texas not only reduced body temperatures, but also resulted in a better survival rate than in the pronghorn released without the treatment (Bob Dittmar DVM, personal communication). Texas Parks and Wildlife routinely administers flunixin meglumine to bighorn sheep during capture events in the Black Gap WMA in western Texas for effective body temperature reduction (Bob Dittmar DVM, personal communication).

[A proposed mechanism for hyperthermia-mitigating effects of flunixin meglumine in wildlife capture events follows.] Capture events are typically associated with some degree of physical exertion, trauma, and tissue damage [17]. Evidence suggests that both damage to tissue and stress from capturing can independently drive a febrile response by increasing thermogenesis and decreasing heat loss.

The stress response is associated with tachycardia, increased metabolic rate, and increased muscle tone which serve to increase heat production while adrenergic vasoconstriction serves to reduce heat loss to the environment [18]. Additionally, adrenergic agonism at the hypothalamus stimulates non-shivering thermogenesis by brown adipose tissue [19]. It is hypothesized by the authors that both handling-induced stress and direct adrenergic agonism by medetomidine would stimulate these mechanisms of heat production and inhibit of heat loss *via* decreased dermal circulation. Though physiological changes resulting from stress and/or chemicals contribute to hyperthermia, it is likely that tissue damage and subsequent prostaglandins also play a major role.

Prior to capture, animals often experience a period of heavy exertion, and sometimes trauma while trying to avoid capture [20]. Regardless of the nature of damage, damaged cells lyse their products and agonize Toll-like receptors of immune cells, which then produce pro-inflammatory cytokines including Interleukin-1 beta and Interleukin-6 [21-31]. These inflammatory signals interact with the hypothalamus and induce prostaglandin synthesis-specifically prostaglandin E2 (PG-E2) [24,25]. PG-E2 then signals the hypothalamus to induce purposeful thermogenesis through increased muscle tension, non-shivering thermogenesis by brown adipose tissue, dermal and peripheral vasoconstriction, and increased metabolic rate [26-28]. Flunixin meglumine stops the activation of PG-E2 by inhibiting the enzyme cyclooxygenase-2 [29-31]. With decreased PG-E2 levels, the thermogenic stimuli at the hsypothalamus may decrease and subsequent heat production decreases while heat loss is allowed through dermal vasodilation. After flunixin meglumine has taken effect, other measures of cooling such as water enemas and physical wetting of the animal may be enhanced due to peripheral vasodilation at the gastrointestinal tract and skin, respectively.

Body temperatures of >41°C (>106°F) are considered by most veterinarians to be a medical emergency and are often associated with both immediate and delayed fatality [4]. Furthermore, the experience of the senior author is that animals with body temperatures greater than 42.2°C (108°F), prior to the use of flunixin meglumine, seldom survived (Walt Cook DVM PhD, personal communication).

CONCLUSION

This case report serves as further anecdotal evidence of: 1) the efficacy of flunixin meglumine for temperature reduction in wild ruminants, most likely due to the immunologically-induced febrile response, and 2) an effective protocol for the treatment of severe hyperthermia in captive white-tailed deer capture events. The recommendations for the treatment of severe hyperthermia in white-tailed deer, which can most likely be extrapolated to other exotic and wild hoof-stock, is administration of flunixin meglumine, external cooling through direct water application, and delivery of cold water *via* rectal enema.

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