

STEROIDS IN SHOCK.... FRIEND OR FOE???

Elke Rudloff, DVM, DACVECC
Animal Emergency Center

Most of us have been taught to treat hypovolemic or traumatic shock with a high-dose corticosteroid injection (e.g. 30 mg/kg methylprednisone IV). When the question is asked “why”, the usual answer is “to stabilize cell membranes”. What does this answer mean? If we take a closer look at the literature, can we actually justify the clinical use of high dose corticosteroids in the treatment of shock? This handout is meant to inform you of the evidence and the current recommendations that exist for the use of corticosteroids in the treatment of shock. Lets start with a review of shock pathophysiology....

Shock is the clinical manifestation of inadequate oxygen delivery to the tissues. Poor perfusion can occur from hypovolemic (intravascular water loss or hemorrhage), cardiogenic (heart muscle failure, dysrhythmias), and/or distributive (severe vasodilation: sepsis, systemic inflammation, medication, trauma) events. When there is a lack of oxygen delivery to the tissues, there is a reduction in the production of adenosine triphosphate (ATP).

Energy is released with the breakdown of ATP. This energy is essential for basic cellular functions such as manufacturing of RNA and DNA, keeping cytosolic electrolytes balanced, and maintaining the repair of cellular, nuclear, and lysosomal membranes. A lack of ATP results in events that are catastrophic to the cell, to include buildup of cytosolic sodium and calcium, cellular swelling, and disruption of the cellular membrane. When cellular dysfunction/death occurs on a grand scale, organ dysfunction can occur potentially causing death.

When the cellular membrane loses its integrity, fatty acid metabolism through the enzymatic action of phospholipase A-2 initiates the arachidonic acid cascade and the production of pro-inflammatory mediators (leukotrienes, thromboxane, and prostaglandins). Release of pro-inflammatory cytokines (TNF- α , IL-1, IL-8) from the white blood cells initiates a systemic inflammatory response syndrome. In addition to the trauma from hypoxia, when dysfunctional cells are reperfused with oxygen during resuscitation, there can be additional injury from radical oxygen species that have accumulated. These events can produce multiple organ dysfunction/failure.

In the lab, corticosteroids have a number of inhibitory effects on many of the metabolic enzyme pathways that are necessary for mediator production during shock. For example, corticosteroids inhibit phospholipase A-2 and cyclooxygenase. Corticosteroids will also reduce chemotaxis and adhesion of inflammatory cells as well as the release of radical oxygen species. Most of the studies infused methylprednisolone *prior* to the event tested. However, can we translate these laboratory findings to positive statistical clinical benefits that outweigh negative side effects?

Raflo, et al (Am J Surg. 1975 Sep;130(3):321-7) were one of the first researchers to investigate the use of massive doses (60 mg/kg IV) of methylprednisolone given to laboratory dogs *prior* to severe, lethal, hemorrhagic shock. No significant differences were seen in cardiac output, mean arterial blood pressure, superior mesenteric artery flow, and survival between treated and sham groups. No clinical studies have been performed to test the theory that high dose

corticosteroids are of benefit in treating shock during resuscitation. So what is the harm anyway??

Many of us have witnessed the negative effects of high dose corticosteroids in our patients. Hemorrhage from GI ulceration is likely the worst of the side effects in dogs, and most deadly. In addition, increased hospital acquired infection, mortality, renal and hepatic dysfunction, and hyperglycemia are recognized as significant complications associated with critically ill people treated with high dose corticosteroids.

Nevertheless, if we dissect the issue of using corticosteroids in critically ill people (where most of the clinical studies are occurring), we can find some interesting and potentially life-saving information that can benefit our veterinary patients. First of all, there is a recognized syndrome of relative adrenal insufficiency that can be documented in critically ill people. Also, in people suffering septic shock having persistent hypotension unresponsive to vasopressors, there is a proven benefit with the use of low doses (physiologic) of hydrocortisone (equivalent to 0.03 mg/kg methylprednisolone IV q 8 hours) for 5 days. Blood pressure was shown to improve, and the vasopressors could be more rapidly weaned. In addition, there was an increased survival rate. There continues to be no evidence for or against the use of corticosteroids during hypovolemic, non-septic shock, in humans or animals.

What about in the dog presenting with gastric dilatation volvulus (GDV)? This is a great clinical example of shock and reperfusion injury where corticosteroids can be administered prior to reperfusion. Unfortunately there is no evidence to support the use of corticosteroids in this situation. In fact, a retrospective review of dogs with GDV treated with and without corticosteroids at the Animal Emergency Center found that there was no clinical benefit to the use of corticosteroids prior to decompression.

The conclusions we can make after researching the literature regarding the use of corticosteroids in the patient with shock are as follows:

- Consider low dose corticosteroid supplementation in animals with septic shock requiring vasopressor therapy
- Supplement low dose corticosteroids in any animal with suspected or confirmed hypoadrenocorticism
- Continue supplementation of corticosteroids in any patient receiving chronic corticosteroid treatment

Oh, and by the way, did you know that corticosteroids are NOT recommended for the treatment of head or spinal injury?????????