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Pihl, Tina Holberg

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Gc-globulin as a diagnostic and prognostic marker in horses - A PhD project

Tina Holberg Pihl1, Stine Jacobsen1, Gunnar Houen2, Pia Haubro Andersen1.

1Large Animal Surgery, Dep. of Large Animal Sciences, Faculty of Life Sciences, University of Copenhagen, 2Department of Research and Development, Statens Serum Institut, Copenhagen

Resumé
Gc-globulin is a serum protein, which is significantly reduced shortly after tissue injury in humans and laboratory rodents. A low serum concentration of Gc-globulin can therefore be used as a diagnostic and prognostic marker in patients with trauma, sepsis and liver failure. This Ph.D. project will investigate Gc-globulin in horses and evaluate the concentration in horses with acute abdominal pain.

Introduction
Group specific (Gc) globulin also known as vitamin D-binding protein is part of the extracellular actin-scavenging system that removes actin from the circulation (Lind et al, 1996). Actin is an intracellular structural protein, which is released to blood in patients with tissue injury and cell death. Circulating actin forms filaments, which cause microthrombosis and endothelial injury. These effects of circulating actin are extremely harmful, and high levels of free actin are potentially lethal (Haddad et al, 1990; Enuklhevel et al, 2000). Gc-globulin binds to actin and removes it from the circulation via the reticulosephalial system (Figure 1).

Plasma concentrations of Gc-globulin decrease shortly after conditions causing tissue injury and cell death, for example physical trauma (Figure 2) (Dahi et al, 2001), sepsis (Lee et al., 1989), experimentally induced endotoxemia (Watt et al., 1989) or liver failure (Schad et al, 2007). In humans, decreases in Gc-globulin levels are observed within 60 minutes after trauma (Dahi et al, 1998).

Studies in humans and laboratory rodents have shown that very low concentration of plasma Gc-globulin are related to an increased risk of developing shock and lethal complications of trauma (Figure 3) (Dahl et al, 1999). Gc-globulin is thus a prognostic marker in intensive care medicine. It has been suggested that treatment with Gc-globulin to patients with severe tissue injury may prevent the development of shock and thereby increase survival chances (Vasconcellos & Lind, 1993). The in vivo toxicity of Gc-globulin infusion is currently being investigated in horses and other species.

Gc-globulin has been demonstrated in horse plasma and its structure closely resembles that of human Gc-globulin (Robinson & Burtrick, 1992). Gc-globulin concentrations in horses under clinical conditions have never previously been investigated.

Ph.d. project
The Ph.D. project focuses on Gc-globulin as a prognostic marker in horses with acute abdominal pain.

Acute abdominal pain (colic) is a high frequency in horses and is one of the most frequent reasons for a horse to die or be euthanized (Hilger et al, 2001; Tinkler et al, 1997). Impactions and intestinal strangulations are the most common causes of colic. When an intestine is strangulated ischemia of the intestine will develop and the horses needs acute surgery to survive. Many horses do not survive the surgery because they develop shock or sepsis.

Goal
To assess the usefulness of acute phase proteins (Serum Amyloid A (SAA), haptoglobin, fibrinogen, intestinal fatty acid binding protein (I-FABP), and Gc-globulin) for predicting the need for surgery and the prognosis of horses with acute abdominal pain.

Hypothesis
Low Gc-globulin concentration and high SAA, haptoglobin, fibrinogen and I-FABP in plasma and peritoneal fluid correlates with the extent of intestinal ischemia, the need for surgery and survival rate of the horse.

Methods
2. Assessment of Gc-globulin concentration in plasma and peritoneal fluid in healthy horses.
3. Comparison of the acute phase protein concentrations and the need for surgery and survival rate by collection of blood and peritoneal samples of 100 horses with acute abdominal pain referred to the University Hospital for Large Animals (K.U-LIFE).
4. Assessment of acute phase protein concentrations and kinetics in plasma and peritoneal fluid in horses with induced intestinal ischemia under general anaesthesia.

References