Clinical Commentary

Glucostasis in equine patients

J. H. van der Kolk

Department of Equine Science, Medicine Section, Faculty of Veterinary Medicine, Utrecht University, Yalelaan 114, 3508 TD, Utrecht, The Netherlands.

Total volvulus of the ascending colon without doubt must be regarded as one of the most stressful events in a horse’s life and the condition is rapidly fatal without intervention. Knowles and Mair (2009) present clinical data on an unusual case of total volvulus of the ascending colon associated with multiple mesenteric abnormalities in a yearling Friesian colt.

Meckel’s diverticulum is the most common congenital anomaly of the human gastrointestinal tract, affecting 1–2% of the general population. Although a diverticulum of the small intestine was noted in 1598 by Fabricius Hildanus, the diverticulum is named after Johann Friedrich Meckel, who described its anatomy and embryology in 1809 (Geier et al. 2007). In comparison, it has been stated that mesodiverticular bands, which are remnants of the vitelline duct, are the most common congenital abnormalities of the intestine encountered during exploratory laparotomy in horses with colic (Edwards 2004) although Meckel’s diverticulum has also been reported in horses (Grant and Tennant 1973; Hooper 1989; Edwards 2004). However, the reported incidence of congenital abnormalities of the gastrointestinal tract of horses is very low (Edwards 2004).

To differentiate between enteritis and strangulation as the cause of colic remains a challenge especially in nonadult horses. Although the clinical examination in the case reported failed to identify a definitive cause of the colic, surgery was fully justified on the basis of the continuous pain unresponsive to analgesic drugs. Remarkably, the possibility of an inflammatory component in the current case is not well appreciated in the discussion given the granulocytosis upon admission, the signs of acute inflammation on the serosal surface of the colon detected at post mortem examination and last but not least mucosal inflammation in the caecum found on histology. It underscores assessment of the rectal temperature as a cardinal parameter during clinical examination. The (secondary) involvement of bacterial pathogens such as Salmonella and Clostridium spp. can not be excluded in the reported case.

Transabdominal ultrasonography revealed small volumes of peritoneal fluid. Although abdominocentesis was not performed as it was considered unlikely to have altered the decision of whether to proceed with an exploratory laparotomy, there were certainly indications for it in order to evaluate possible inflammatory involvement (leucocyte count, leucocyte differentiation, protein content, the presence of bacteria with the option of culturing) and associated prognosis. On the other hand, abdominocentesis is also of interest regarding the prognosis in intestinal strangulation such as volvulus of the ascending colon. For example, colours of the peritoneal fluid other than yellow are associated with a poorer prognosis. In addition, peritoneal fluid lactate concentration may aid in early detection of intestinal ischaemia secondary to a strangulating obstruction. Horses with large colon ischaemia secondary to a strangulating obstruction had a higher peritoneal lactate concentration than those with nonstrangulating obstruction (8.09 ± 5.20 [n = 8] vs. 2.07 ± 2.37 [n = 60] mmol/l). Plasma lactate concentrations exceeded peritoneal fluid lactate (i.e. peritoneal:plasma lactate ratio <1.0) less frequently as peritoneal fluid lactate values increased (Latson et al. 2005).

Stress activates the hypothalamo-pituitary-adrenal (HPA) axis, generating a cascade of hormonal messages from the hypothalamus to the pituitary which culminates in an increase in plasma cortisol concentration (Alexander et al. 1996). As preceded by the elevated plasma cortisol concentration, the plasma glucose concentration increases following acute stress either due to increased gluconeogenesis and/or decreased insulin sensitivity. Indeed, 21% of horses presenting with acute abdominal disease had ‘extreme hyperglycaemia’, defined as blood glucose concentrations above 10 mmol/l at admission with horses that did not survive to hospital discharge having a higher mean blood glucose concentration at admission (Hollis et al. 2007). This finding raises the question of who is afraid of hyperglycaemia in horses? First of all within the stress concept ‘extreme hyperglycaemia’ in horses suffering from colic reflects the severity of the disorder and indicates the urgency to eliminate its cause usually by surgical intervention. In addition, the excess of glucose will be eliminated via the urine associated with (transient) diuresis.

On the other hand, many studies have shown an association between (short-term) hyperglycaemia and adverse outcome of a critical illness, both in adult and
paediatric human patients in intensive care units (Vlasselaers et al. 2009). Furthermore, targeting of blood glucose concentrations to age-adjusted normal fasting concentrations improved short-term outcome of human patients in a paediatric intensive care unit (Vlasselaers et al. 2009). In comparison, derangements of blood glucose concentration are common in critically ill foals (Hollis et al. 2008).

To address the question of whether targeting blood glucose concentrations with insulin to an age-adjusted normal (fasting?) concentration improves outcome of critically ill equine patients randomised controlled intervention studies are needed in order to assess a causal relationship. Long-term hyperglycaemia is detrimental in man and some animal species predominantly due to a direct (nonenzymatic) chemical reaction of sugars with proteins referred to as glycation. The free carbonyl group present in noncycised sugars is able to form a Schiff base with the amino group of lysine residues on various proteins. Migration of the double bond formed, in the Amadori reaction, leads to a stable product that accumulates spontaneously when proteins interact with glucose. Increased glucose concentrations in diabetic patients might enhance the rate of accumulation of such glycated proteins. Besides, the formation and accumulation of the carbohydrate sorbitol within (neuronal) cells might play a role in its detrimental effects. Fortunately, detrimental pathological effects associated with long-term hyperglycaemia in horses have not been substantiated yet despite research into biochemical indices of vascular function, glucose metabolism and oxidative stress in horses with Cushing's disease (Keen et al. 2004). Remarkably, in the equine species the plasma concentration of fructosamine (glycation between glucose and albumin) is relatively low even in diabetes (Reijerkerk and van der Kolk 2003).

With reference to long-term hyperglycaemia the metabolic syndrome should be mentioned. The metabolic syndrome is a common metabolic disorder that results from the increasing prevalence of obesity and its pathophysiology seems to be largely attributable to insulin resistance in man (Eckel et al. 2005). The concept of the metabolic syndrome has existed for at least 80 years in man and its constellation of metabolic abnormalities includes glucose intolerance (type 2 diabetes, impaired glucose tolerance, or impaired fasting glycaemia), insulin resistance, central obesity, dyslipidaemia and hypertension (Eckel et al. 2005). Substantial evidence shows that insulin resistance plays an important part in risk-factor clustering, and probably contributes in some way to many of the untoward outcomes attributed to the metabolic syndrome. On the other hand, a diagnosis of the metabolic syndrome has negligible association with risk of cardiovascular disease and as a consequence the diagnosis of the metabolic syndrome has no apparent clinical value in man (Kahn 2008). It has been stated that more research is needed to understand the cause of risk-factor clustering and the pathogenesis of insulin resistance and that both actions would better serve the health of those people at risk of diabetes and cardiovascular disease than seeking a diagnosis of the metabolic syndrome (Kahn 2008).

Glucose tolerance has also been studied in the equine species for a long time (Link 1940; Johnson 2002). However, the analogy between the detrimental effects of both short- and long-term hyperglycaemia in man and horses remains unsubstantiated and care should be taken when comparing the 2 conditions. Interestingly, a subset of obese human individuals seems to be protected against obesity-related metabolic complications. These individuals are described as metabolically healthy but obese, or as having uncomplicated obesity, or metabolically benign obesity (Karellis 2008). Up to 30% of obese people seem to be metabolically healthy (Karellis et al. 2004).

As stated by the authors, there are anecdotal reports of a high incidence of genetic abnormalities amongst Friesian Horses including retained placenta (Sevinga et al. 2002), dwarfism (Back et al. 2008), dissecting aortic aneurism (van der Linde-Sipman et al. 1985) and oesophageal dysfunction (Broekman and Kuiper 2002). The current case report illustrates the need to monitor and address (potentially) genetic disorders in breeds with restricted gene pools.

References


