The reduction of feed intake and gluconeogenesis during hyperketonemia in dairy cows indicates a signal of abundant energy availability

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High milk production and simultaneously inadequate feed intake during early lactation causes a negative energy balance and hence the mobilisation of adipose tissue. Because milk production requires huge amounts of glucose for lactose synthesis gluconeogensis runs at a maximum level mainly in the hepatic mitochondria. Gluconeogenesis requires oxaloacetate as a substrate. However, oxaloacetate is also required for fatty acid oxidation in the citric acid cycle. Due to a lack of oxaloacetate acetyl-CoA is increasingly used for the synthesis of ketone bodies in the hepatic mitochondria. Ketone bodies, mainly beta-hydroxybutyrate (BHBA), can be used as an alternative energy source by many organs including the immune system. However, if the plasma concentration of BHBA becomes too high (>1.5 mM) an impairment of the immune system is a consequence, together with an increased susceptibility of infectious diseases and further metabolic disorders. It has been shown that a high concentration of BHBA, also passing through the blood-brain barrier, reduces appetite and feed intake via reduced expression of Agouti-related protein (AGRP), an important inhibitor of anorexigenic signalling in the brain. Peripherally, elevated BHBA (demonstrated by infused BHBA) caused a reduction of glucagon secretion and hence a reduced gluconeogenesis and decreased plasma glucose concentration. It was also shown that an LPS-induced mastitis caused an increased metabolisation of BHBA, obviously used as a fuel for various inflammatory or anti-inflammatory reactions. Simultaneously, the characteristic increase of glucagon as a stimulator of gluconeogenesis during inflammation was reduced in animals with elevated BHBA. It appears that elevated BHBA in parallel with reduced glucose concentrations induce a priority usage of ketone bodies for energetic purposes which may explain the paradox reaction of reduced feed intake. Gluconeogenesis is reduced through elevated ketone body concentration, possibly to save oxaloacetate for the degradation of acetyl-CoA , and to use the ketone bodies as an energy source, also for the immune system. However, the observed reactions do obviously not consider the enormous specific need of glucose by the mammary gland as a consequence of breeding for high milk production in dairy cows.

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