Starvation and maluntrition clinical nutrition and health

Health & Medicine, Nursing

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Metabolic Adaptations during Starvation The Cuban poet Pedro Luis Boitel had been on a hunger strike for 53 days. He died of starvation. When somebody is starving, several metabolic adaptations and changes occur to preserve functioning of vital organs. An understanding of various metabolic pathways related to functioning of the body during various phases of starvation is essential to understand the survival crux of the Cuban poet for 53 days. During the early fasting stage, i. e., several hours after a meal, the glucose levels in the blood of Boitel would have started to drop (Berg, 2002). This leads to decrease in insulin secretion and increase in glucagon secretion. Glucagon then mobilizes stores of glycogen. Glycogen is mobilized mainly from liver. Other storage sites for glycogen are muscles and skin. Boitel would have initially sustained on blood glucose levels maintained through these mechanisms. Glucagon stimulates breakdown of glycogen and causes inhibition of glycogen synthesis by triggering the cascade of cyclic AMP. This ultimately leads to phosphorylation and activation of the enzyme phosphorylase. Glucagon then causes inhibition of the enzyme glycogen synthetase. This prevents synthesis of glycogen and its storage into muscle and liver. Glucagon also causes inhibition of the synthesis of fatty acids by diminishing pyruvate production and by decreasing the activity of acetyl CoA carboxylase (Berg, 2002). This, it does by keeping it in unphosphorylated state. All this is aimed to mobilize glycogen and decrease conversion of glucose in the blood to glycogen so that the glucose levels in the blood are maintained in adequate ranges for functioning of vital organs like brain and heart which, at this stage are still dependent on glucose alone for energy.

Glycogen releases glucose-6-phosphate and this is hydrolyzed to release large amounts of glucose. Liver is the main source of glycogen in this context in a starvation patient like Boitel. Since insulin levels are low, glucose cannot enter into the fat tissue and muscle (Berg, 2002). Thus, decreased insulin levels and increased glucagon levels help maintain blood sugar levels during early starvation. Also, another important aspect is; both the liver and muscle use fatty acids are source of energy to preserve glucose levels. All these mechanisms would have amounted to decrease in the glycogen stores of the liver of Boitel. Though gluconeogenesis continues, it only helps restore the glucose that was converted by peripheral tissues to lactate and alanine. The brain however, oxidizes glucose completely, the end-products being H2O and CO2 (Berg, 2002) (Refer to Fig. 1). Fig. 1: Choice of fuel during starvation (Berg, 2002) Gradual increase in the concentrations of citrate and acetyl CoA causes decrease in glycolysis in a starving patient like Boitel after about a week of starving. Alanine, lactate and pyruvate are eventually shifted to the liver to get converted to glucose. Triacylglycerols can get cleaved and glycerol derived from this is used for synthesis of glucose (Cahill and Veech, 2003). For about a week to ten days after initiation of fasting, Boitel’s body would have metabolically adapted the above mechanisms for functioning of vital organs and survival. In prolonged starvation, as in case of Boitel who starved for 53 days, further depletion of carbon skeletons for glucose production decreases, leading to proteolysis for the purpose of gluconeogenesis. In such a situation, proteins that are degraded are not replenished, instead; they are used as sources of carbon for synthesis of glucose. Secretions of pancreas and also intestinal epithelium proteins are

initial protein sources. They actually turn over rapidly. Later muscle proteins are used. After about 3-4 days of starvation, large amounts of 3-hydroxybutyrate and acetoacetate, known as ketone bodies are produced in the liver. Synthesis of these ketone bodies increases dramatically from the liver as the duration of starvation increases like in the Cuban poet and these are released into the blood. Brain uses these ketone bodies, especially acetoacetate for energy in place of glucose, because glucose stores are also diminished and brain has to survive. Ultimately, as availability of glucose further decreases, even heart uses ketone bodies for energy. After several weeks of beginning of starvation, brain begins to use ketone bodies as a major source of fuel (McCue, 2010). Ketone bodies are actually equivalent to fatty acids and they can pass the blood brain barrier easily. As more and more fatty acids get converted to ketone bodies and brain begins to use ketone bodies, the need for glucose diminishes and thus much less muscle is degraded when compared to initial days of starvation. During early days of starvation in Boitel, about 75g per day of muscle would have broken down. However, after some days, only about 25 grams of muscle would have broken down. Ultimately, the survival time of the starving person like Boitel is dependent on the depot size of triacylglycerol (Zechner et al, 2009). “ Tissues that cannot use ketone bodies for energy respond to these small molecules by activating chaperone-mediated autophagy” (Finn and Dice, 2006, p. 1) These are the important metabolic adaptations of the body during various stages of starvation Boitel would have undergone. During early stages of fasting, the body tries to preserve the glucose content in the blood by decreasing insulin production and increasing glucagon production.

Insulin allows glucose to enter the liver and muscles and get converted to glycogen, thus decreasing the glucose levels in the blood. Decrease in insulin secretion thus helps in maintaining blood glucose levels. Increase in glucagon causes gluconeogenesis and release of glucose from liver initially and from muscle in later stages. However, after few days, like about 3 days, even the existing glucose stores get exhausted and this is when protein degradation comes into picture. Protein degradation yields ketone bodies which are used as source of energy by brain, skeletal muscles and to some extent by heart. Exhaustion of even these would have ultimately led to the death of the Cuban poet due to heart failure. References Berg, J. M., Tymoczko, J. L., Stryer, L. (2002). Biochemistry. 5th edition. NewYork: W H Freeman. Cahill, G. F. and Veech, R. L. (2003) Ketoacids? Good Medicine? Trans Am Clin Clim Assoc, 114, 149-163. Finn, P. F., and Dice, J. F. (2006). Proteolytic and lipolytic responses to starvation. Nutrition, 22(7-8), 830-44. McCue, M. D. (2010) Starvation physiology: reviewing the different strategies animals use to survive a common challenge, Comp Biochem Physiol, 156, 1-18. Zechner, R., Kienesberger, P. C., Haemmerle, G., Zimmermann, R. and Lass, A. (2009) Adipose triglyceride lipase and the lipolytic catabolism of cellular fat stores, J Lipid Res, 50, 3-21