

Case Report: COPD - A Cause for Hypoglycemia in Elderly People

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I. Introduction

Hypoglycemia is a common complication associated with treatment of diabetes. Often mild, in its more severe forms, hypoglycemia can cause seizures, coma, and even death. ^[1] Hypoglycemia is a condition characterized by abnormally low blood glucose (blood sugar) levels, usually less than 70 mg/dl. The spectrum of symptoms depends on duration and severity of hypoglycemia and varied from autonomic activation to behavioral changes to altered cognitive function to seizures or coma. The short and long term complications include neurologic damage, trauma, cardiovascular events and death. Severe untreated hypoglycemia can cause a significant economic and personal burden, therefore identification and prevention of hypoglycemia can reduce diabetes burden by prevention of hypoglycemia complications. ^[2]

The brain depends on a continual supply of glucose and is vulnerable to any glucose deprivation. Unable to synthesize or store this primary source of energy, the brain is one of the first organs affected by lowered blood glucose levels. Once plasma glucose concentrations fall below the physiological range at a glycemic threshold of ~ 70 mg/dl, a sequence of responses is activated that includes release of neuroendocrine hormones (also called counter regulatory or anti-insulin hormones), stimulation of the autonomic nervous system (ANS), and production of neurogenic and neuroglycopenic symptoms to protect the brain and limit systematic effects of hypoglycemia.

The normal physiological counter regulatory response to hypoglycemia consists of suppression of insulin release and secretion of glucagon and pancreatic polypeptide from the pancreas, epinephrine from the adrenal medullae, norepinephrine from sympathetic postganglionic nerve terminals and adrenal medulla, cortisol from the adrenal cortex, and growth hormone from the anterior pituitary gland. In humans, inhibition of insulin secretion is the initial defense against falling glucose and occurs at a plasma glucose concentration of ~ 80 mg/dl.

Glucagon and epinephrine are the primary fast-acting hormones in the defense against acute hypoglycemia. Glucagon acts to increase endogenous glucose production and does so via increases in hepatic glycogenolysis and gluconeogenesis, providing three carbon glucose substrates (lactate, pyruvate, alanine, and glycerol). Epinephrine can also acutely increase endogenous glucose production. Epinephrine has effects similar to glucagon on hepatic glucose production but can also stimulate net renal glucose production. Additionally, epinephrine has an important physiological function in reducing insulin-stimulated glucose uptake.

During the prolonged hypoglycemia that is usually observed in clinical practice, it is the reduced glucose uptake in peripheral tissues that contributes most to the preservation of circulating glucose levels and hence the defense against hypoglycemia. Activation of the sympathetic nervous system (via both circulating catecholamines and direct innervation) results in increased lipolysis in adipocytes. The increased release of free fatty acids (FFAs) results in significant glucose sparing (because tissues can oxidize FFAs instead of glucose). In fact, the contribution of FFAs has been estimated to be 25% of the total defense against hypoglycemia. ^[3]

Hypoglycemia can be caused by various factors, including regulatory, enzymatic, or substrate defects. In patients with diabetes mellitus, iatrogenic hypoglycemia can be caused by absolute or relative insulin excess and compromised glucose counter regulation, with the majority of cases involving interplay of these factors. ^[4]

Chronic obstructive pulmonary disease (COPD) defines a group of chronic inflammatory pulmonary disorders characterized by partially reversible airflow limitation. The notion that COPD is primarily a lung disease has been challenged, and the broader definition of COPD as a systemic inflammatory syndrome has been proposed. Evidence for this approach has been provided by strong associations with increased rates of cardiovascular diseases, anemia, musculoskeletal disease and malignant conditions seen in COPD patients.

Moreover, it is predicted that COPD will be the third leading cause of death worldwide by 2020, which will impose an even greater burden on the healthcare system globally. If the mortality from co-morbid conditions associated with COPD is taken into count, then this disease poses an even greater impact on health outcomes. The common risk factors for COPD are air pollution, aging, respiratory infections, bronchial asthma (BA), low socioeconomic status. ^[5]

II. Case Report

A 75 year old male patient, who is a watchman by occupation, was admitted to the hospital in an unconscious state, with hypoglycemia for evaluation. On examination patient blood pressure was found to be 120/80mmhg and pulse rate was 80/min. and his past medical history as told by his family was that patient is alcoholic; a toddy drinker since 50 years and also a beedi smoker the patient's appetite is decreased. And he has no history of hypertension, jaundice, seizures, Coronary Artery Disease but for COPD. A finger stick point of care test indicated that the concentration of glucose in his blood was 30 mg/dl. The patient is advised for CBP. And reports revealed, White Blood Cells (WBC): 13.2 cubic.mm (4-10) neutrophils: 11.84/uL (1.8-7), lymphocytes: 0.40/L (1-4), MCH (mean corpuscular haemoglobin): 34.6pg (27-32), platelets: 23/L (1.50-5.00). The patient was given 25% Dextrose after which the patient regained consciousness. And was on following medications for one day and referred to a psychiatrist and was discharged the following day. 5% Dextrose with thiamine. (lifeline), Inj. Neurobion plus ,1 amp, given intramuscularly , twice a day, Tab. Librium , 15mg , twice a day, Nebulization Duolin, three times a day.

III. Discussion

In the presented case patient even had a co morbid condition of chronic obstructive pulmonary disease (COPD). Analysis study of incidence of the hypoglycemia in COPD patients according to Food and Drug Administration reports state that On Aug, 19, 2013: 29,113 people who have chronic obstructive pulmonary disease 53 (0.18%) of them have Hypoglycemia of them 49.44% in males and 50.56% in females. And also its incidence is 91.55% in 66 above aged population. The mechanism of occurrence of hypoglycemia in COPD patients is still unknown. Alcoholism is a worldwide disaster that affects almost all organs of body in some manner. Its causes are complex. Alcohol has been shown to impair the hormonal counter regulatory responses to low blood glucose levels.

The chronic state of inflammation in COPD patients is believed to shift the metabolism of the patients toward net protein catabolism, in turn increasing the resting energy expenditure. As a result, the fat-free mass of such patients is depleted, which is accompanied by an increase in systemic markers of inflammation. Other studies have also shown a link between systemic inflammation and skeletal muscle loss in COPD, even when weight loss is not apparent. Circulating Tumor necrosis factor (TNF- α) levels have been found to be elevated in cachectic COPD patients with chronic hypoxemia, a potential stimulus for activation of the pro inflammatory cytokine system in such patients. TNF- α , a central inflammatory mediator in the process of muscle wasting, promotes cachexia by reducing peripheral insulin action. Muscle loss and decreased fat oxidative capacity, along with low physical activity, lead to further muscle loss and fat gain. Fat gain in turn elevates circulating TNF- α , escalating insulin resistance and muscle loss.^[6]

The hypoglycemic effect of alcohol, probably caused by inhibition of gluconeogenesis in the liver, is well known.^[7] Alcohol is metabolized mainly in the liver in two stages and catalyzed by alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH), with Nicotinamide adenine dinucleotide (NAD⁺) as a hydrogen acceptor. As can be seen from the pathway shown in Figure, the presence of alcohol within the cell makes a heavy demand on a limited supply of NAD⁺, (a niacin-derived coenzyme) and consequently the NAD⁺/NADH (Nicotinamide adenine dinucleotide reduced form) ratio falls. In particular, the oxidation of lactate to pyruvate will become much slower than the reverse reaction, which accounts for the observed accumulation of lactate leading to reduction in capacity of liver to deliver glucose to blood. Other redox reactions depending on NAD⁺ that occur in the tricarboxylic acid cycle also similarly become slower in the presence of alcohol. The maximum rate of oxidation of acetate may not be more than 25% of the normal. Therefore acetate is diverted into the fatty acid synthetase system accounting for the fatty liver condition commonly found in alcoholics^[8] Hypoglycemia (a low blood glucose level) observed is the result of the failure of a metabolic pathway called gluconeogenesis i.e., production of glucose from non-carbohydrate sources like lactate, glycerol and amino acids. All these precursors require NAD⁺ for the synthesis of glucose and since NAD⁺ is in short supply, gluconeogenesis is greatly reduced.^[9] Lactate when present in an abnormally high concentration in the blood competes in the renal mechanism for the excretion of uric acid. Therefore the kidney is unable to fully excrete this end product of nucleic acid metabolism and its accumulation leads to the symptoms of the disease gout.^[10] Chronic malnutrition decreases the availability of triglyceride in adipose tissue, which results in deficient glycerol available to be converted to glucose and fewer fatty acids to support energy metabolism.

Treating hypoglycemia is important. Delay may lead to seizures, coma or even death especially in diabetic patient.^[11]

Management of hypoglycemia includes two priorities: 1) immediately restoring glucose levels in a patient who presents with severe hypoglycemia, and 2) taking steps to help stabilize long-term glucose control and prevent additional episodes of hypoglycemia.

Immediate treatment of hypoglycemia involves the administration of glucose.^[12] This will completely alleviate the hypoglycemia; however, it will not correct damage to the Central nervous system or embryonic

tissue. Another option, in some cases, is to administer glucagon. However, this is ineffective in people who have been fasting or have experienced prolonged hypoglycemia. This is because glucagon stimulates glycogenolysis to restore blood glucose levels, but in fasting or prolonged hypoglycemic patients, liver glycogen stores have already been used up.

IV. Conclusion

Hypoglycemic condition is commonly being seen in severe alcoholics. And there is immediate necessity for the individualized treatment based on patient characteristics. COPD also has an effect on blood glucose levels and causes hypoglycemia, yet further research should be done to elucidate how this factor can affect the basic pathophysiologic processes.

References

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Abbreviations

Chronic obstructive pulmonary disease (COPD)
Alcohol dehydrogenase (ADH)
Aldehyde dehydrogenase (ALDH)
Nicotinamide adenine dinucleotide (NAD+)
Tumor necrosis factor (TNF)