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Hyperosmolar Hyperglycaemic State: A Life-Threatening Complication of Type 2 Diabetes Patients

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Abstract

Hyperosmolar hyperglycaemic state (HHS) is a life-threatening complication of type 2 diabetes (T2D), but it is preventable. There is no precise definition of HHS. It is characterized by severe hyperglycaemia with blood glucose levels greater than 600 mg/dl (33.3 mmol/l), a marked increase in serum osmolality greater than 320 mOsm/kg, and severe dehydration without significant ketoacidosis (<3 mmol/l). Early clinical diagnosis and prompt treatment, such as insulin therapy, restoration of electrolyte disturbances and management of concurrent illnesses may improve the outcome. Intravenous insulin and fluid replacement with careful monitoring are the main treatment policy of HHS. In this study an attempt has been taken to discuss various effects of HHS with prevention and treatment of this complication of diabetes.

Keywords: hyperglycemia, hyperosmolar, HHS management, fluid therapy, non-ketotic coma

1. Introduction

Hyperosmolar hyperglycaemic state (HHS) is a condition that occurs when the body makes insulin, but the insulin does not work properly. It is also previously known as hyperosmolar non-ketotic state (HONK) (Pasquel & Umpierrez, 2014). German physician August W. von Stosch (1783-1860) first described diabetic coma in 1828 that is later termed as the hyperosmolar hyperglycemic state. German pathologist Friedrich Theodor von Frerichs (1819-1885) and British physician and pathologist Julius Dreschfeld (1845-1907) first described the cases of HHS in the 1880s in patients with an “unusual diabetic coma” characterized by severe hyperglycaemia and glycosuria (Dreschfeld, 1886; Pasquel & Umpierrez, 2014). Usually, HHS is seen in elderly patients with T2D, but it is rarely seen among children and adolescents with type 1 diabetes (T1D) (Rosenbloom, 2010). Early diagnosis and proper treatment are vital and essential to reduce the high morbidity and mortality rates related to HHS (Chun, et al., 2022).

During HHS, the body becomes dangerously dehydrated due to very high blood glucose levels; and there is enough insulin production within the body to prevent ketosis. In this situation, blood glucose levels may be greater than 600 mg/dl (33.3 mmol/l) without ketoacidosis, an increase in serum osmolality (>320 mOsm/kg), arterial pH is greater than 7.3, bicarbonate (HCO_3–) is greater than 15 mEq/l, and body cannot use either glucose or fat for energy (Kitabchi et al., 2008; Innes, 2016; ADA, 2019). As a result, glucose moves into the urine, and causes increased urination. If it is not treated properly, lead to a life-threatening dehydration and patients may present with a fluid deficit of up to 7 liters (Chiasson et al., 2003). In severe HHS, there is little or no accumulation of ketoacids, plasma glucose levels frequently reach greater than 1,000 mg/dl (56 mmol/l), and plasma osmolality may be as high as 380 mOsm/kg (Rose, 2001). Although, the HHS is a life-threatening, it is preventable through the proper management. Less than 1% of all diabetes-related admissions are HHS, but death

among these is about 15-20% (Alghamdi et al., 2021).

2. Literature Review

The literature review is an introductory section of any research, which shows the works of previous researchers in the same field within the existing knowledge (Polit & Hungler, 2013). It helps the new researchers to understand the subject, and it serves as an indicator of the subject that has been carried out before. It also assists all researchers to improve research questions and to move forward energetically in the current research (Creswell, 2007). Kundavaram P. Abhilash discusses practical and concise guidelines for the diagnosis and management of HHS that can be applied in almost any kind of hospital setting (Abhilash, 2017). Sze May Ng and Julie Edge have observed that HHS is a life-threatening but preventable acute metabolic complication of diabetes. They have shown that the best clinical management of HHS in childhood involves careful correction of fluids and biochemical status of the patient and identification of precipitating causes whilst carefully monitoring for complications. They have tried to investigate how to make the diagnosis and also they have recommended treatment of this condition among children (Ng & Edge, 2017).

Iraj Shahramian and his coworkers have shown that HHS is a rare complication in children with DM that shows itself with a triad: hyperglycaemia, typically greater than 600 mg/dl; hyperosmolality, serum osmolality greater than 330 mOsm/l; and mild metabolic acidosis; pH greater than 7.2; which is a life-threatening emergency with a mortality rate of 10–50% (Shahramian et al., 2022). Haralampos J. Milionis and Moses S. Elisaf have provided an outline of the diagnostic approach of patients with manifestations of HHS and discuss the contemporary therapeutic recommendations. They have perceived that early clinical diagnosis and prompt treatment, consisting of fluid replacement, insulin therapy, and restoration of electrolyte disturbances and management of concurrent illnesses may improve the outcome (Milionis & Elisaf, 2005). Francisco J. Pasquel and Guillermo E. Umpierrez have provided a historic review of the clinical presentation, diagnosis, and treatment of HHS. They have reviewed that mortality in HHS is between 10 and 20%, which is about 10 times higher than the mortality rate in patients with DKA (Pasquel & Umpierrez, 2014).

Guillermo E. Umpierrez and Abbas E. Kitabchi have shown that DKA and HHS are two acute complications of diabetes that can result in increased morbidity and mortality if not efficiently and effectively treated. According to their investigation, mortality rates are 2–5% for DKA and 15% for HHS, and usually mortality happens for the precipitating causes, such as urinary tract infections and pneumonia (Umpierrez, & Kitabchi, 2002). Adrian Scott has found that HHS is a medical emergency that higher mortality and potential for complication by myocardial infarction, stroke, seizures, cerebral oedema and central pontine myelinolysis (Scott, 2015). Sang Hoon Chun and his coworkers have studied on a HHS affected 17-year-old boy who presented with polydipsia, polyuria, and a drowsy mental status with T1D (Chun et al., 2022).

Sanjeevani R Zadkar has discussed that in HHS, levels of insulin in circulation reduce significantly, but stress hormones, such as cortisol, catecholamines, glucagon, and growth hormone increase along with greater degree of dehydration. He also explains that basic hematological, biochemical, and radiological investigations are important to find and rule out precipitating factors and complications. He advised that aggressive corrections of the fluid and electrolyte imbalance along with the maintaining levels of insulin are very important components of the treatment (Zadkar, 2019). Haradhan Kumar Mohajan and Devajit Mohajan have discussed the aspects of DM in a series of papers (Mohajan & Mohajan, 2023a-s). Lindsay K. Buchert has shown that both DKA and HHS are emergencies characterized by hyperglycemia, dehydration, and electrolyte abnormalities that are associated with high mortality (Buchert, 2021).

3. Research Methodology of the Study

Research is a logical and systematic search for new useful information on a specific topic, which investigates to find solutions of scientific and social problems through the systematic analysis (Rajasekar et. al., 2013). In any research, methodology is the organized and meaningful procedural works that follow scientific methods efficiently (Kothari, 2008). It provides the research design and analysis procedures to perform a good research (Hallberg, 2006). Research methodology provides the principles to the researchers for organizing, planning, designing and conducting a good research. Therefore, it is the science and philosophy behind all researches (Legesse, 2014). To rationalize the selection of a research methodology, a researcher must understand its philosophical origins and unique characteristics (Rieger, 2019).

Ethical approval is essential to uphold the possible benefits, and minimize harm to participants, science, and society (NASW, 2021). We have tried to maintain the reliability and validity throughout in our study (Mohajan, 2017). We have started our research through the discussion of signs and symptoms of HHS. Then we gave tried to compare the DKA and HHS through the study of symptoms and treatment of both diseases. Finally, we have stressed on the treatment of HHS. In this study we have stressed on the secondary data sources. The valuable information of our research is collected from the published and unpublished data sources. We have used various

research resources, such as journal articles, books written by famous authors, internet, websites, etc. to furnish our research fruitfully (Mohajan & Mohajan, 2023a, b).

4. Objective of the Study

The vital objective of this study is to discuss the hyperosmolar hyperglycaemic state (HHS) of diabetes mellitus. Other trivial objectives of the study are as follows:

- to indicate signs and symptoms of HHS,
- to show the differences of DKA and HHS, and
- to stress on the treatment of HHS.

5. Signs and Symptoms of HHS

Symptoms of HHS are dehydration, increased thirst (polydipsia), increased volume of urination (polyuria), increased hunger (polyphagia), weight loss, nausea, vomiting, and abdominal pain, weakness, low blood pressure with standing, leg cramps, altered level of consciousness, neurologic signs, such as blurred vision, headaches, focal seizures, myoclonic jerking, reversible paralysis, intravascular coagulopathy, mesenteric artery occlusion, rhabdomyolysis, motor abnormalities including flaccidity, depressed reflexes, tremors or fasciculations, hyperviscosity and increased risk of blood clot formation (Stoner, 2005; Henry et al., 2016; Frank & Solomon, 2016).

HHS patients have visible signs, such as a constellation of sunken eyes, slurred speech, inability to concentrate or confusion, and longitudinal furrows on the tongue (Gross et al. 1992; Wolfsdorf et al., 2014). HHS presents some clinical manifestations, such as polydipsia and polyuria in the early stages progressing to oliguria, fitting, stroke, trauma, coma, heart attacks, and death if untreated (Rosenbloom, 2010).

6. Comparison Between DKA and HHS

DKA is the most frequently regarded as hyperglycaemic crisis, but HHS occurs less frequently. However, HHS has much higher mortality rates as high as 20% than DKA that has only 4% (McNaughton et al., 2011). DKA presents in hours, but HHS comes on over many days and the extreme dehydration and metabolic disturbances may be extreme than that are in DKA. The DKA is more common in T1D; whereas, HHS is expected to be more common in obese adults with T2D (Mohn et al., 2021). DKA presents a triad of hyperglycaemia, ketonaemia and acidosis. On the other hand, HHS has severe hyperglycaemia, high serum osmolality, and severe dehydration without significant ketoacidosis (Ng & Edge, 2017). The amount of fluid deficit is much higher in HHS, but glucose levels are usually very high than DKA (Abhilash, 2017). About 33% of patients with severe hypertonicity, ketosis, and acidosis crises show a mixed picture of DKA and HHS, may be due to β-cell exhaustion as a result of temporary glucotoxicity (Wachtel et al., 1991; Scott, 2015).

7. Treatment of HHS

DKA and HHS are two common diabetic emergencies that can be managed with optimal fluid and blood glucose management along with optimization of electrolyte imbalances, infection and sepsis, hypoglycaemia during treatment, and renal failure (Abhilash, 2017). Additionally, HHS needs to reduce osmolality by 3–8 mOsm/kg/h. Also a full history, physical examination, and review of drug therapy are needed to normalize HHS. Further, it is necessary to prevent arterial or venous thrombosis, foot ulceration, and other potential complications (Scott, 2015).

HHS is a medical emergency and prompt treatment of HHS is necessary for the recovery. Common triggers of HHS are inadequate insulin therapy and illness, such as infection, cerebrovascular disease and myocardial infarction. Treatment procedures of HHS are rapid restoration of fluid deficit and electrolyte abnormalities (e.g., significant depletion of potassium, phosphate and magnesium), intravenous insulin, and correction of hyperglycaemia and hyperosmolality depending upon the degree of free water and sodium deficit (Ng & Edge, 2017). Initial treatment of HHS are intravenous fluids to manage dehydration, intravenous insulin in those with significant ketones, low molecular weight heparin to decrease the risk of blood clotting, and antibiotics among those in whom there are concerns of infection. HHS patients need to use intravenous 0.9% sodium chloride solution as the principal fluid to restore circulating volume and reverse dehydration that cause a fall in blood glucose. It typically takes a few days for the person to return to baseline (Scott, 2015).

8. Conclusions

HHS is a life-threatening complication that results severe dehydration and hyperglycaemia in patients with T2D. It is also characterized by high blood sugar, very high serum osmolality, and without significant ketoacidosis. The procedures of treatment are for restoring volume and osmolarity, for controlling blood glucose, and for adjusting the electrolyte inequalities. A high degree of awareness is necessary during the treatment of HHS. Many sides of HHS emergency are preventable. Accurate fluid management is essential to prevent the

complications and reduce mortality. Mortality and morbidity in HHS is only partly related to age and comorbidities. Therefore, awareness, early diagnosis, and aggressive proper treatment play crucial role in preventing the morbidity and mortality from HHS. Early identification and treatment of HHS can reduce length of stay in hospital and healthcare costs. Improved education, improved care coordination, and effective communication must be provided to healthcare givers, such as among nurses, general practitioners and physicians to ensure the prevention and treatment of HHS.

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