

Linking hypothermia and hyperglycemia

One of the adverse events associated with hypothermic therapy is a decrease in insulin sensitivity and insulin secretion, which can lead to hyperglycemia—a condition combated through intensive I.V. insulin therapy and frequent monitoring.

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nduced hypothermia (IH) principle (defined as a core temperature of below 94° F [35° C]) is an evidence-based intervention strategy that can improve the neurologic outcome of unconscious patients after traumatic brain injury, stroke, or sudden cardiac arrest.¹ Although IH has been shown to be neurologically protective, it's becoming clear that many factors figure into whether beneficial effects are seen with hypothermic therapy.²

Caregivers should have some knowledge regarding the evidence supporting hypothermia's clinical applications and of the physiologic consequences and adverse events that may develop when a patient is treated with hypothermia. These sequelae can be serious and, if not properly managed, may negate some or all of the potential benefits associated with hypothermic therapy.

Fortunately, many of these adverse events may be prevented or modified by high-quality intensive care treatment. Care should include careful monitoring of fluid balance and tight control of metabolic aspects such as glucose and electrolyte levels—the many physiologic changes taking place when a patient is cooled.

One of the adverse events associated with hypothermic therapy is a decrease in insulin sensitivity and insulin secretion, which can lead to hyperglycemia.³ Hyperglycemia may be associated with increased mortality, while strict regulation of glucose levels has been found to decrease mortality and length of stay in the ICU.⁴ The amount of I.V. insulin required to maintain glucose levels within the normal range (80 to 110 mg/dL) is likely to increase during the induction of hypothermia, and healthcare professionals employing hypothermic therapy should be aware of this phenomenon. Hyperglycemia should be combated through intensive I.V. insulin therapy and frequent monitoring.

Understanding the physiologic response that occurs during hypothermia explains the hyperglycemia phenomenon often observed during IH.

Description

Holy Cross Hospital (HCH), a 571bed hospital in Broward County, Fla., has been named one of the 100 Top Cardiovascular Hospitals in the nation. HCH implemented an IH program for postcardiac arrest victims in 2007. On initial implementation, patients who were to receive IH therapy were placed on an I.V. insulin infusion protocol for management of hyperglycemia. The dosing of the insulin infusion was predetermined through a standard-ized, paper-based protocol.

These protocols for glycemic control are complex, requiring frequent bedside glucose monitoring and repeated intricate calculations to titrate insulin doses. Also, research has shown that standardized, nurse-managed, paper-based I.V. insulin protocols don't always produce optimal results.⁵

On implementation of the paperbased I.V. insulin protocol, patients were hyperglycemic, and an upward titration of the protocol occurred hourly. The frequency of checks was hourly and based on the result, changes were made to the I.V. insulin infusion administration rate. The patients' glucose levels remained high despite the use of insulin drip rates as high as 20 units/hour of I.V. regular insulin being infused. Paper protocols as a result were maximized during hypothermia and yet still didn't effectively control the patients' blood glucose levels. Over time, however, the circulating blood glucose levels would drop and nurses were quickly titrating patients off the insulin drips with inadequate control, resulting in less than optimal outcomes such as inadequate blood glucose control



(hyperglycemia followed by hypoglycemia).

At the beginning of 2009, HCH implemented a computer-guided software system designed to customize I.V. insulin dosing to the individual patient, especially those requiring quick control of their blood glucose levels. The system was easy to use and once initiated

Figure 1: Percent distribution for the 13 IH patients' blood glucose readings using the system (345 readings)







Figure 3: Case study: Insulin drip over time

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only required a current blood glucose measurement to calculate the patient's next I.V. insulin dose.

Patients receiving IH therapy were placed on the system, which uses four data points to formulate each patient's specific physiologic insulin dosing curve. When the caregiver enters the patient's current glucose level, the tool calculates the patient's next I.V. insulin dose.

Nurses at HCH noted that the tool controlled the IH patient's glucose quickly while maintaining a steady rate of I.V. insulin infusion. The frequency of checks on initiation was every half hour for the first one or two blood glucose readings but once under control, the readings quickly changed to hourly and then every 2 hours as the patient's condition stabilized. Patients typically remained on insulin during hypothermia therapy and as rewarming occurred, they gradually came off the insulin drip. These patients only receive normal saline solution as a maintenance drip with no added glucose provided. There were no incidences of hypoglycemia observed in any of the patients during the IH treatment. (See Figure 1.)

Case study

An 86-year-old male collapses in the garden following a cardiac arrest. The HCH emergency nurses begin immediate assessment to determine neurologic and cardiac response status. The induced hypothermia team responds to a "code white" and transfers the patient to critical care within 60 minutes upon his arrival to the hospital. CCU nurses continue lowering the patient's core body temperature to 89.6° F (32° C). Twenty-four hours from the time the iced saline is infused, the nurse begins to



warm the patient 32.9° F (0.5° C) per hour. Nurses closely monitor vital signs, blood glucose, and other lab readings such as urine output, and watch for symptoms of hyperthermia. The patient's blood glucose level was high upon arrival to the CCU, with readings above 250 mg/dL. The patient's insulin drip rate was titrated using new technology, with glucose levels gradually declining to below 150 mg/dL-an hour post initiation of cooling. The patient stayed within the desired blood glucose range (90-150 mg/dL) until rewarming was initiated. (See Figures 2 and 3.)

A closer look at cellular respiration

The Krebs cycle is the first of two stages of a process called cellular respiration, in which glucose is transformed into a usable form of chemical energy called adenosine triphosphate (ATP). Although cellular respiration is a relatively complicated process, involving dozens of steps, its chemical equation is quite simple. It begins with the raw materials of glucose and oxygen that yield carbon dioxide and water (both waste products) and free energy, some of which is captured and stored in a usable form as ATP. Cells obtain glucose from the blood, through the walls of nearby capillaries. These capillaries carry not only glucose, but also oxygen and many other important nutrients.

Once inside the cell, glucose is absorbed by organelles called mitochondria. These important structures play host to the two stages of cellular respiration: the Krebs cycle and the electron transport chain. Combined, these chemical conversions and the raw material glucose that feeds them produce the energy that drives nearly every cellular

process in your body. ATP is essential for the energy-requiring processes of brain cells, including cell membrane integrity, through the active transport of sodium, potassium, and calcium ions.⁶ Hypothermia leads to a lowering of the metabolic rate and includes changes in energy metabolism and decreases in ATP demand. Brain metabolism shifts from glucose to a lipid metabolism when brain temperatures are lower than 93.2° F (34° C). Glucose isn't efficiently utilized under hypothermic conditions.³

Insulin-resistant hyperglycemia, with a glucose level greater than 230 mg/dL, progressively leads to a metabolic shift from hemoglobin 2,3-diphosphoglycerate (2,3-DPG) and failure of oxygen unloading in the cerebral tissue.³

Hemoglobin is an intracellular protein responsible for transporting oxygen in the blood. Under certain conditions oxygen binds to hemoglobin and is released into the body tissues. Each hemoglobin molecule has a limited capacity for holding oxygen molecules. The oxyhemoglobin dissociation curve describes the relation between the partial pressure of oxygen and the oxygen saturation. The effectiveness of hemoglobin-oxygen binding can be affected by several factors, including hypothermia. Hypothermia causes a leftward shift of this curve.⁷

2,3-DPG is a highly anionic organic phosphate present in human red blood cells; it's essential in enabling hemoglobin to unload oxygen in tissue capillaries.⁸ Reduced levels of 2,3-DPG and hypothermia result in a leftward shift of the curve and increased affinity of oxygen binding to hemoglobin. With the decrease in the oxygen in the plasma, due to the leftward shift of the curve, glucose is unable to bind with oxygen as described in the Krebs cycle and, therefore, circulating glucose levels are high.

A system that works

Because hypothermia results in decreased insulin secretion and insulin resistance, it's especially important to manage patients' blood glucose levels, which we did with the aide of a computer-guided glucose management software system.

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