The Management of the Diabetic Mellitus Patient During Cardiopulmonary Bypass

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Aorto-coronary artery bypass surgery is being employed with excellent results on an increasing number of patients with occlusive arteriosclerotic disease. Although it was previously thought that diabetic mellitus patients, whose arteriosclerosis is more diffuse and includes small vessel disease, could not benefit from this procedure; an increasing number are being operated on with comparable results. Since the perfusionist is the sole regulator of body metabolism during cardiopulmonary bypass, a review of the literature and a case report are presented.

Diabetes mellitus is a metabolic syndrome that is characterized by an inappropriate elevation of blood glucose. Glucose metabolism is necessary for the production of energy for all cellular functions. An abnormality of blood glucose levels is associated with alterations in lipid and protein metabolism for which a relative or absolute lack of insulin production is responsible.

Insulin is necessary to facilitate the transportation of glucose molecules across cell membranes. Cells that require insulin for metabolism include skeletal, myocardial and adipose tissue. Major cells that can accomplish glucose transfer without insulin include red blood cells, brain, kidney, nerve, liver and intestinal. Insulin, a protein, is produced in the pancreas by the beta cells of the Islets of Langerhans. The release of insulin is stimulated by oral and intravenous glucose and certain amino acids. Oral glucose provides the most significant stimulation for the release of insulin. Intravenous glucose causes the most rapid rise in plasma insulin levels, usually within three to five minutes. Amino acids enhance the ability of glucose to cause insulin secretion by the Islets of Langerhans.

There are four categories of diabetes mellitus: 1) Overt and clinical diabetes, in which fasting and random serum and urinary glucose levels are markedly elevated. 2) Chemical or asymptomatic diabetes is typified by normal fasting blood glucose levels and elevated post meal levels. 3) Latent or stress diabetes occurs in patients whose levels were previously elevated, such as during pregnancy, but have presently returned to normal. 4) Prediabetes applies to the time interval preceding a glucose intolerance in predisposed patients. It can usually only be applied to the offspring of two diabetic patients and is most often a retrospective diagnosis.

Patients are usually grouped according to types once they have been categorized. The four types of clinical diabetes mellitus are: 1) Genetic diabetes, which is subdivided into age of onset. This will be discussed in detail later. 2) Pan-
creatic diabetes occurs when destruction of the pancreatic islets has taken place. This destruction can be caused by chronic inflammation, carcinoma, or surgical removal of the pancreas. 3) Endocrinopathies, pregnancy, and stress are associated with endocrine diabetes. 4) Iatrogenic diabetes is initiated by certain drugs such as long term corticosteroid therapy. *(p525)*

Juvenile diabetes occurs during childhood and usually prior to puberty. The onset is abrupt and the disease is difficult to control. Patients are usually ketosis prone and have a virtual absence of plasma insulin. These patients must use injectable insulin.

Adult diabetes mellitus is the most common type of diabetes. They have a gradual onset usually past the age of thirty-five. They are seldom ketosis prone except in unusual stress or septic conditions. Their plasma insulin levels are diminished but not absent. Diet alone will control most adult diabetics. However, 20 to 30% of these patients will require injectable insulin. Oral hypoglycemic agents are used in the treatment of some of these patients.

Obesity is frequently associated with diabetes. Adult onset obesity is associated with hypertrophy of adipose cells. The hypertrophy in turn causes the cells to become less responsive to insulin. As less glucose can be disposed of, the resulting hyperglycemia stimulates an increased production of insulin. This may lead to pancreatic exhaustion, or at least, a relative insulin deficiency. *(p527)*

Normal fasting blood glucose levels are 70 to 110 milligrams per 100 milliliters of whole blood. Normal blood glucose levels after a 100 gram carbohydrate meal are less than 120 milligrams after one hour and less than 170 milligrams after two hours. Sugar should be absent from the urine at all times. *(p528)*

The treatment of clinical diabetes varies as to the category and the type of diabetes. Many adult diabetics can be treated by diet alone. Some adult patients, who are not ketosis prone and have been uncontrolled by diet, can be treated with oral hypoglycemic agents. Injectable insulin is indicated for use in juvenile onset patients and adult onset patients when oral agents have failed. Insulin is mandatory in diabetic ketoacidosis.

Insulin was discovered in 1921 by F.G. Banting and C.H. Best. Today the pharmacological sources are beef and pork pancreas. There are essentially three types of insulin which are classified according to the longevity of their action. Crystalline insulin is a short-acting and rapid onset type of insulin. This insulin is best for emergencies such as diabetic ketoacidosis. The second type is known as intermediate insulin. This type is longer acting and not as rapid in its onset. The third type, long acting insulins, have generally had disappointing results for clinical diabetes mellitus. *(p533)*

The diabetic patient undergoing cardiopulmonary bypass is subject to many metabolic changes. All patients develop a mild hyperglycemia due to stress prior to and during the induction of anesthesia. This may be due to an increased catecholamine production, which may inhibit insulin secretion. The administration of dextrose containing fluids, therefore, should be discouraged prior to and during anesthetic induction in the diabetic mellitus patient.

The institution of cardiopulmonary bypass results in hyperglycemia which cannot totally be controlled by insulin administration. Dextrose containing primes in-
crease the blood glucose level, which continues to remain elevated throughout the first postoperative day of surgery.\textsuperscript{9} Patients with a normal body weight have smaller increases in insulin levels after perfusion than markedly obese patients. After cardiopulmonary bypass obese patients will maintain a higher blood glucose level.\textsuperscript{10} It should also be noted that blood glucose levels will rise significantly even in patients who have had a non-dextrose containing prime during cardiopulmonary bypass. Since elevation of blood glucose has been shown to be a powerful stimulant of pancreatic secretion, these findings may suggest a decreased hormonal response after cardiopulmonary bypass.\textsuperscript{9} Dextrose, therefore, is not utilized in the extracorporeal prime at this institution in order to avoid contributing to hyperglycemia. Consequently, it is important to monitor blood glucose levels prior to, during, and after cardiopulmonary bypass.

Moderate hypothermia during cardiopulmonary bypass has an inhibiting effect on insulin response to exogenous glucose. Insulin levels are significantly higher in normothermia than in hypothermia. Abnormally low plasma insulin concentrations were observed after glucose administration to hypothermic dogs.\textsuperscript{11} This effect persisted even upon return to normothermic levels in another group of dogs.\textsuperscript{12} In general it is believed that hypothermia during cardiopulmonary bypass restricts insulin secretion by increasing catecholamine production. There is conflicting evidence as to the role of catecholamines in the diabetic mellitus patient undergoing cardiopulmonary bypass. Blackard, Nelson and Labat have presented evidence that catecholamine secretion is reduced during hypothermia.\textsuperscript{11} However, Replogle and Stremmel feel that circulating catecholamine levels are increased. They feel that any increase in circulating epinephrine and norepinephrine during cardiopulmonary bypass would restrict insulin secretion regardless of any glucose load.\textsuperscript{8, 11} Reduced insulin levels may also be caused by a decreased metabolic and energy requirement induced by cooling and/or decreased blood flow through the Islets of Langerhans.

There are several other factors that can affect insulin production during cardiopulmonary bypass. Compensated heart disease has been associated with a decrease in insulin secretion.\textsuperscript{8} Mandlebaum and associates have noted that the process of oxygenation of blood during cardiopulmonary bypass is associated with a decrease in plasma insulin levels. Insulin secretion is inhibited by hypocalcemia and excessively high levels of blood glucose, which can occur during cardiopulmonary bypass.\textsuperscript{8}

When the glucose level in the blood rises to 300 milligrams or more, much of the excess glucose is excreted by the kidneys.\textsuperscript{13} This process can easily be monitored by utilizing ACETEST* tablets and TESTAPE* strips on urine specimens. This will give an early indication of rising glucose levels in the blood.

Blood glucose levels above 1000 milligrams per 100 milliliters of whole blood can be found in some diabetic patients in certain metabolic conditions. In this instance, glucose will not diffuse easily across the cell membrane. The resulting increased osmotic pressure in the extracellular space causes water to move out of the cell resulting in dehydration of the intracellular space. This condition is known as hyperosmolar, hyperglycemic, nonketotic coma and is usually associated with a very high mortality rate.\textsuperscript{7}(p535), \textsuperscript{13}(p923), \textsuperscript{14}

Excessive glucose lost in the urine will also cause a diuresis due to the osmotic effect of glucose in the tubules. A corresponding loss of electrolytes may occur. It is

*AMES, Division of Miles Laboratory, Elkhart, Indiana
therefore important to monitor serum sodium and potassium since abnormal levels may cause cardiac arrhythmias. They can also be used as an early indication of diabetic ketoacidosis and osmotic shifts.

Diabetes mellitus complicated by ketoacidosis and hyperkalemia can be fatal. Acidosis in the diabetic mellitus patient can result from the presence of acetoacetic acid combining with bicarbonate ions from the extracellular fluids. Renal regulation of this metabolic state begins by secreting excess hydrogen ions in order to increase sodium bicarbonate levels in the extracellular fluid. This should assist in raising the pH. Also, when large amounts of hydrogen ions are being excreted, a decrease in potassium ion excretion occurs resulting in hyperkalemia. (p437)

Administration of sodium bicarbonate can assist the kidneys in the correction of this acidosis. This will decrease hydrogen ion secretion and allow potassium ion secretion. Another treatment for hyperkalemia is to give glucose in combination with insulin. Glucose is known to drive potassium into the cell resulting in a decrease of potassium ion concentration in the extracellular space. (p917), 16 Peritoneal dialysis may also be some assistance in removing potassium from the body. However, its effect may not be seen for several hours. 17

Hyponatremia can be a direct result of an increase of keto acid excretion in the diabetic patient. Approximately 50% of the keto acids that are excreted will combine with sodium from the extracellular space. This loss of sodium ions contributes to the already present ketoacidosis leading to a more profound metabolic acidosis. 13 (p924)

Dehydration, elevated blood glucose levels and hyponatremia will result in changes of serum osmolality. The normal range of serum osmolality is between 280 and 310 milliosmols per liter. 7 (p532)

Diabetic mellitus patients are more susceptible to infection due to their decreased blood supply to the tissues. This is usually caused by their extensive small vessel disease. Therefore the usual sterile precautions used in setting up the extracorporeal circuit apply.

CASE REPORT

P. V. was a 52 year old caucasian female with a twelve year history of significant mitral valvular disease. Her past history included treatment for lupus erthematous with Prednisone. In July 1976 she was admitted with a diagnosis of acute pulmonary edema and diabetes mellitus secondary to steroid therapy. She underwent cardiopulmonary bypass for mitral valve replacement on 25 August 1976.

The patient weighed forty-one kilograms with a body surface area of 1.32 square meters. Laboratory data included: BUN, 13; Potassium, 3.2; and a glucose of 320 milligrams. She was on regular insulin therapy at this time.

A Harvey 800* oxygenator was primed with 1500 milliliters of Polyonic 148**, 250 milliliters of packed red cells, 500 milligrams of calcium chloride and 1000 units of Sodium Heparin. This prime was chosen to avoid contributing to any hyperglycemia that would develop. Hypothermia to 28 degrees Centigrade was utilized.

*William Harvey Research Inc., Santa Ana, California
**Cutter Laboratories, Berkely, California
During cardiopulmonary bypass there was a progression of her hyperglycemia (see Table One). This was due to a suppression of circulating plasma insulin. Midway through the procedure, after the patient had been warmed to 35 degrees Centigrade, an attempt was made to lower the glucose levels by administering fifteen units of U100 regular insulin. When this failed another fifteen units were given.

In addition to her hyperglycemia, a severe metabolic acidosis and the presence of hyperkalemia were developing. The acidosis was probably due to an accumulation of ketone bodies and was more likely a ketoacidosis. Sodium Bicarbonate was given in an effort to reverse the situation and place the patient in a normal metabolic state. An increase in blood flow rate was also utilized.

The metabolic acidosis and an over administration of potassium chloride resulted in the hyperkalemia. Reversing the metabolic state probably increased potassium ion excretion through the kidneys and lowered the potassium concentration in the extracellular fluid. It is important to carefully monitor serum potassium levels and to limit the administration of potassium chloride.

The urine output was also monitored. As the serum osmolality rose, there was an increase in urine production due to an increase in osmotic pressure in the tubules.

The patient was unable to be weaned from cardiopulmonary bypass due to poor left ventricular function. Death did not appear to be related to her hyperglycemic state.

SUMMARY

Management of the diabetic mellitus patient during cardiopulmonary bypass requires the careful monitoring of certain parameters and careful use of glucose containing intravenous fluids. In addition to arterial and venous blood gases, the perfusionist should also monitor blood for blood glucose levels, serum osmolality, hematocrit, sodium and potassium levels. This institution obtains specimens for these tests prior to bypass, every half hour during bypass and after bypass. Urinary glucose levels are also tested at the same intervals. Anesthesia may use small amounts of dextrose to counteract any insulin given to the patient the morning of surgery. Glucose containing solutions are not administered during cardiopulmonary bypass.

Since the perfusionist is the sole regulator of body metabolism during cardiopulmonary bypass, he or she should be cognizant of all potential complications that could result from perfusion of the diabetic mellitus patient. Understanding the background and the physiology of this disease can be helpful in the management of these patients.

### Table 1

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<th>Units given</th>
<th>Insulin</th>
<th>Sodium</th>
<th>Potassium</th>
<th>Glucose</th>
<th>pH</th>
<th>Osmolality</th>
<th>Urine</th>
<th>Acetest</th>
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