Implementing a continuous insulin infusion protocol on a cardiac surgical service
A PA's perspective

The author describes how one rural hospital used aggressive glucose control with continuous IV insulin to reduce complications and death among surgical patients, whether they had diabetes or not.

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Among patients undergoing cardiac surgery, 25% to 29% have diabetes, making it the fourth most common comorbid condition in this group.[1,2] In some cardiac surgery practices, almost half of all patients have diabetes.[1] Moreover, hyperglycemia occurs in the majority of critically ill patients even without a history of diabetes.[3]

Patients with diabetes are 2.5 to 4 times more likely to develop deep sternal wound infections (DSWIs) than are those without diabetes.[4] These chest wound infections of the sternum or mediastinal tissue, including mediastinitis, are among the most devastating complications of cardiac surgery involving midline sternotomy. DSWIs contribute to higher morbidity and mortality, lengthen hospital stays, and dramatically increase hospital costs.[4]

Several studies have shown that aggressive glucose control provided through the use of a continuous intravenous insulin (CII) protocol dramatically reduces morbidity and mortality for both diabetic and nondiabetic patients in medical and surgical ICUs. At Geisinger Medical Center, Danville, Pa, the author's institution, such a protocol was implemented. Within 1 year, sternal wound infection rates and mortality rates in patients undergoing coronary artery bypass graft (CABG) surgery were both reduced dramatically.

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Background

Between 2000 and 2003, the DSWI rate at Geisinger Medical Center was 1.7% to 2%. Superficial infection rates during that time were 1.7% to 3.3%. (Superficial sternal wound infections [SSWIs] involve the skin and/or subcutaneous tissues but not the sternal bone hardware that reapproximates the sternotomy at the time of sternal closure.) During these years, the certified registered nurse anesthetists in the OR and the nurses in the cardiac care unit (CCU) would provide insulin to patients simply by titrating infusions per a set range glucose level parameter. There were wide variations in care. Ability to achieve the goal glucose level was essentially based on nurses' comfort level and experience with IV insulin titration. In an effort to control hyperglycemic states in cardiac surgery patients and reduce the number of DSWIs, Geisinger instituted a CII protocol. The goal was to implement a standard that would control glucose levels in a timely fashion and would be readily accepted by the CCU nursing staff.

Prior studies

A substantial volume of data for both medical and surgical patients shows that in-hospital hyperglycemia is associated with adverse outcomes and that CII can reduce morbidity and mortality in hyperglycemic patients. One researcher performed a meta-analysis of 15 studies and found that among patients admitted for acute MI, those with hyperglycemia (blood glucose higher than 100 mg/dL), with or without a history of diabetes, had an increase in in-hospital mortality and heart failure.[5] Similar results were reported in a prospective study of 336 patients,[6] in which a multivariate analysis revealed an independent association between glucose levels on admission and mortality. The 1-year mortality rate was 19.3% in patients whose admission glucose levels were less than 100 mg/dL and rose to 44% when glucose levels were higher than 199 mg/dL. The mortality rate for diabetic patients in this study was higher than that for those without diabetes (40% versus 16%).[6]

DIGAMI study The benefits of insulin therapy were proven in the Diabetes Mellitus and Insulin Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study, which saw mortality after acute MI reduced by 30% with the infusion of a glucose-insulin solution designed to achieve serum glucose levels less than 200 mg/dL.[7] In this study, 620 patients with acute MI and hyperglycemia (both diabetic and nondiabetic patients) were assigned to an insulin infusion group or a control group. Patients in the infusion group received IV insulin for 24 hours, followed by SC insulin multiple times a day for 3 months or longer. Patients in the control group received the standard therapy of only SC insulin. At the study's conclusion, with a mean follow-up of 3.4 years, the infusion group maintained a 25% mortality benefit and solidified the importance of early and aggressive glucose control even in patients without a history of diabetes.[7]

Perioperative glycemic control A group of researchers studied diabetic patients who underwent CABG to determine if tight perioperative glycemic control with a modified glucose-insulin-potassium (GIK) solution would optimize myocardial metabolism and thus improve survival and other outcomes, such as ischemic events and wound complications.[8] The researchers separated patients into a GIK group and a non-GIK group. The GIK subjects received a perioperative infusion of D5W, regular insulin, and potassium chloride (KCl) infused at 30 mL/h. The non-GIK subjects received a perioperative infusion of D5W at 30 mL/h. All infusions continued for 12 hours postoperatively. The results of this study were impressive. The GIK group needed less postoperative cardiac pacing and less inotropic support, gained less weight, needed less ventilator support, and had lower incidences of postoperative atrial fibrillation, pneumonia, and wound infections. The result was an overall shorter length of stay. After 2 years of follow-up, the GIK group had fewer recurrent wound infections of the sternotomy and leg incisions and fewer episodes of recurrent ischemia; they also maintained a lower angina class.[8]

Length of stay was reduced one day for each 50-mg/dL lowering of the average 3-day postoperative blood glucose level.

IN THIS ARTICLE

Key Points

- ➤ Hyperglycemia has notable detrimental effects on clinical outcomes in critically ill patients, including those recovering from cardiac surgery.
- ➤ Continuous intravenous insulin (CII) infusion improves glucose levels and reduces morbidity and mortality in hyperglycemic hospitalized patients.
- ➤ Geisinger Medical Center safely implemented an insulin protocol that achieved positive results within 1 year.

Competencies

Medical knowledge	◆◆◆◆◆
Interpersonal & communication skills	◆◆◆◆
Patient care	◆◆◆◆◆
Professionalism	◆
Practice-based learning and improvement	◆◆◆◆◆
Systems-based practice	◆◆◆◆◆

For an explanation of competencies ratings, see the table of contents.

Furnary and colleagues found that hyperglycemic patients undergoing cardiac surgery suffer increased mortality and higher sternal wound and overall infection rates.[4] In Van den Berghe and colleagues' study, hyperglycemic patients treated with intensive insulin therapy had decreases in overall mortality, risk of sepsis, acute renal failure, need for blood transfusions, and illness-related neuropathy.[9] The mortality for the intensive therapy group was 4.6%, versus 8% in the control group. In this landmark study, the conventional group was treated with a CII when the blood glucose level was greater than 200 mg/dL. The intensive CII group was treated to achieve a blood glucose level of less than 110 mg/dL. All patients were in an ICU setting and were studied for 1 year in follow-up.

A post-hoc analysis of Van den Berghe's findings suggested a gradual decrease in risk of ICU and in-hospital death with decreasing glucose levels without an identifiable threshold below which no further risk reduction occurred.[10] There is also a hospital cost benefit to glycemic control. Furnary showed that in cardiac surgery patients, length of stay was reduced by one day for each 50-mg/dL lowering of the average 3-day postoperative blood glucose level. Even factoring in the additional cost of IV insulin therapy and the nursing staff labor involved, a net savings of more than $680 per patient was achieved through the reduction in infectious complications through the use of the insulin protocol.[4]

Recommendations from professional organizations

Medical and surgical groups have weighed in heavily on CII therapy. In 2004, the American College of Cardiology and the American Heart Association, in conjunction with the American Association of Thoracic Surgery and the Society of Thoracic Surgeons, revised the *Guideline Update for Coronary Artery Bypass Graft Surgery: Summary Article*. Under the recommendation of "Reducing the Risk of Perioperative Infection," the task force stated that the risk for DSWIs is reduced by aggressive control of perioperative hyperglycemia with CII.[11]

The American Association of Clinical Endocrinologists (AACE) has acknowledged that hospitals struggle with proper glucose management and lack a standard of care. For ICU patients, the AACE recommends 110 mg/dL as the upper limit for glucose levels. For patients not in critical care units, the intended target glucose levels are 110 mg/dL preprandial and 180 mg/dL maximal.[12] Patients should receive IV insulin therapy when they are critically ill, insulin deficient, and on prolonged NPO status, in the perioperative period (including after organ transplantation), receiving total parenteral nutrition therapy, recovering from a stroke, in labor and after delivery, or suffering from other illnesses requiring prompt glucose control.[2,11]

Methods

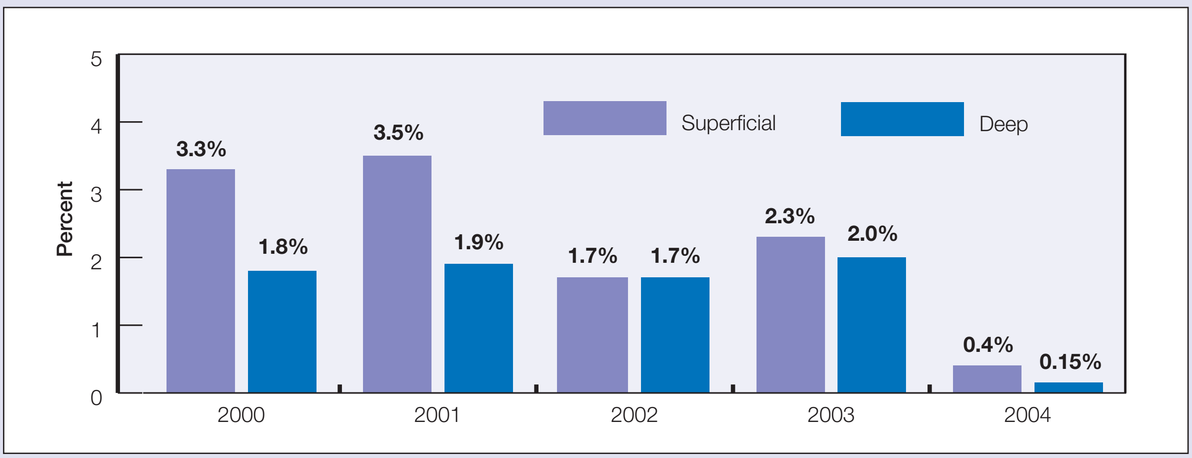
Geisinger Medical Center, a 437-bed HMO teaching hospital in rural Pennsylvania, undertook an initiative to institute a safe, effective, nurse-driven CII protocol for patients undergoing cardiothoracic surgery procedures. The CCU is an open 18-bed unit that is fully staffed by PAs around the clock, with close coverage from the attending cardiothoracic surgeons.

First protocol After an in-depth orientation and education session on the importance of a CII protocol was presented to the departments of anesthesia and cardiothoracic surgery and to the nursing staff in the CCU, Geisinger staff members tried their first CII protocol starting in the fall of 2003. That initial protocol did not control the patient's blood glucose in a timely fashion, and the nurses in the CCU found it difficult to use.

Second protocol While easier to use, the second protocol tried did not consistently reduce blood glucose levels to within the goal range of 100 mg/dL to 150 mg/dL. Even though the second CII protocol was easier to use, the CCU nurses noted that it was not effective at achieving a lower glucose level and were quick to dismiss it. It was obvious that after this experience, the CCU nurses were discouraged about the lack of tight glucose control in their postoperative patients using this second protocol.

FIGURE 1

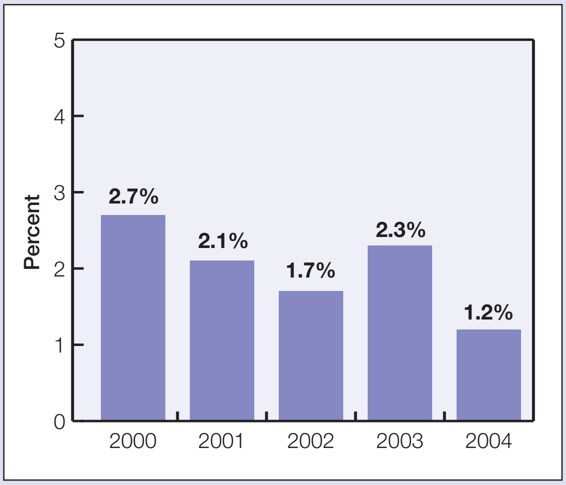
Sterile wound infection rates in patients undergoing cardiac surgery



Data from Society of Thoracic Surgery database, 2000 to 2004, Geisinger Medical Center, Danville, Pa.

FIGURE 2

Mortality rates for patients undergoing coronary artery bypass grafting



Data from Society of Thoracic Surgery database, 2000 to 2004, Geisinger Medical Center, Danville, Pa.

Third protocol In January 2004, a third protocol was tried, and the CCU nursing staff accepted it for its ease of use. It rapidly controlled hyperglycemia. In the spring of 2004, this third CII protocol was presented to and approved by pharmacy and therapeutics for routine use in the CCU.

This approved and accepted CII protocol, which has been studied on both medical and surgical ICU patients[13,14] originated in the endocrinology section of the department of internal medicine at Yale University School of Medicine, New Haven, Conn. It was designed to focus on three main data elements to adjust insulin infusions: 1) current blood glucose value, 2) previous blood glucose value, and 3) current insulin infusion rate.

Results

After the CII protocol was instituted in January 2004, the SSWI rate decreased to 0.4% and the DSWI rate was only 0.15% (see Figure 1). During that year, the patients on the cardiac surgery service had an average starting glucose level of 189 mg/dL, and the mean glucose level while on the protocol dropped to 132 mg/dL. The average time to obtain the goal blood glucose level of 100 mg/dL to 140 mg/dL was 5.2 hours. Under the protocol, the number of hypoglycemic episodes (defined as a blood glucose level less than 60 mg/dL) was less than 1% of all glucose readings. All hypoglycemic episodes were asymptomatic and were quickly treated per protocol directions.

The mortality rates for patients undergoing CABG averaged 2.2% per year for the years 2000 to 2003. For 2004, the mortality rate for these patients declined to 1.2%, showing a 54% reduction after the CII protocol was instituted (see Figure 2).

At Geisinger Medical Center, we were able to show that effective glycemic control can be safely and efficiently introduced into a hospital through teamwork and the cooperation of the departments of anesthesia, cardiothoracic surgery, pharmacy, and nursing. After 1 year under the protocol, we demonstrated a dramatic reduction in both SSWI and DSWI rates in all cardiac surgery patients as well as a reduction in CABG mortality rates.

Discussion

A large volume of evidence indicates that hyperglycemia impedes the normal physiologic response to infection. Periods of elevated serum glucose levels are associated with accelerated nonenzymatic glycosylation of body proteins causing inactivation. Glycosylation of the C3 component of complement occurs at its opsonic binding site and renders it impotent, unable to bind to the surface of invading bacteria.[15] Hennessy and colleagues demonstrated that glycosylation of newly synthesized collagen in hyperglycemic states was associated with increased collagenase activity and decreased wound collagen content.[16] Fortunately, wound healing improves dramatically with glucose control.[16]

Leukocyte function is impaired during hyperglycemia. Several studies found abnormalities in granulocyte adherence, impaired phagocytosis, delayed chemotaxis, and a decline in bacteriocidal capacity.[17-21] These leukocyte deficiencies and phagocytic impairments are reversed with adequate plasma glucose control.[22,23]

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Stressors

Under the stress of critical illness, there are a disruption in glucose counter-regulatory hormones and alterations in carbohydrate metabolism, including increased peripheral glucose demands, enhanced hepatic glucose production, insulin resistance, and relative insulin deficiency.[3] Adding to the stress, vasopressors and enteral nutrition are commonly used in patients undergoing cardiac surgery, predisposing them to hyperglycemia.[24] Hyperglycemia

The successful implementation of a CII protocol started with the education of all departments involved.

causes an increase in the beta-oxidation of free fatty acids in the myocardium.[1] In the ischemic diabetic myocardium, increased catecholamine levels, decreased insulin levels, increased cortisol levels, and increased glucagon levels cause a further decline in insulin sensitivity.[1]

In a postoperative, recently ischemic, and now hyperglycemic patient, free fatty acids accumulate in the myocardium and may exert a negative inotropic effect. The increasing free fatty acids may potentiate any ongoing ischemic injury, increase myocardial oxygen demand, and inhibit glucose oxidation. These processes will increase lactate levels in the blood, which will also act as a negative inotrope.[1]

Benefits of insulin therapy

Insulin suppresses fatty acids as well as inflammatory cytokines and inflammatory growth factors. In addition, insulin improves cell membrane stability, myocardial contractility, and endothelial function.[25]

Hyperglycemia causes increased numbers of proinflammatory cytokines such as interleukin-6 and tumor necrosis factor.[8] An elevated inflammatory response then takes place, leading to capillary leak syndrome, resulting in increased pulmonary water accumulation and altered autonomic tone. The increase in lung intravascular volume results in longer periods of ventilatory support. Alterations in autonomic tone may lead to systemic hypotension and render pharmacologic inotropic support less effective in the postoperative patient. The benefits of insulin therapy also include alterations in coronary coagulation achieved by decreasing serum levels of plasminogen activator inhibitor-1, thus preventing coronary thrombosis.[8] The negative effects that hyperglycemia has on the body's ability to respond to infection, on cellular permeability, and on myocardial cellular function can be eliminated with aggressive insulin therapy.

Conclusion

The successful implementation of a CII protocol at Geisinger Medical Center started with the education and orientation of all departments involved. The author offered extensive teaching of the science behind tight glycemic control, followed by orientation in the particular steps of the protocol for the departments of anesthesia, cardiac surgery, nursing, and pharmacy. In addition, the author emphasized to all departments that it was essential to initiate insulin protocols while the patient is at greatest risk of stress-induced hyperglycemia. Such situations would be during an MI, at the start of surgery, and during trauma resuscitation. The author shared the successful implementation of our insulin protocol on the cardiothoracic surgery service with medical and other surgical services.

Within 1 year, we were able to demonstrate the positive effects of CII. Geisinger's goal is now to ensure that all surgical patients receive appropriate management of hyperglycemia during their surgery and in the postoperative recovery period. □

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