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Diabetes, Hyperglycemia, and Infections☆

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Postoperative infection is not only a major source of morbidity and mortality in patients undergoing surgery, but also an important cause of increased hospital stay and resource utilization. Diabetes has been shown in multiple studies to increase the risk of post-surgical infection. More recently, hyperglycemia has been investigated as an independent risk factor for postoperative infection. This paper will review the effects of intra-operative, postoperative, and long-term glycemic control on postoperative infection rates. The mechanisms by which surgery causes hyperglycemia will be reviewed, as well as the immunologic and humeral effects of hyperglycemia.

Key words: diabetes; hyperglycemia; surgical infection; anesthesia; infectious complications.

Postoperative infections are a devastating complication for patients undergoing surgery. They are the second most common cause of nosocomial infection and account for approximately 17% of all hospital-acquired infections.[1] These infections lead to longer hospital and intensive care unit stays, substantially increased mortality, and contribute significantly to healthcare costs.[2] For centuries, scientists have searched for infectious risk factors, as well as for means of infection modification and prevention.

It has been well established that patients with Diabetes Mellitus (DM) are at increased risk for both surgical and nosocomial infections.[3–5] Infection rates have been quoted to be two to five times more prevalent in diabetics than in the nondiabetic population.[6] A large, albeit retrospective cohort study, showed that nearly half of all diabetics have at least one yearly hospitalization or physician claim for an infection.[7] The relative risk for diabetic infectious disease-related hospitalization was 2.17. Further, death attributed to infection was significantly higher in diabetics. A large,

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12-month prospective study revealed that patients with DM had increased risk for lower respiratory tract, urinary tract, skin, and mucous membrane infections.[8] One still-unanswered question, however, is whether this increased risk is due to hyperglycemia itself, or other associated features found in the diabetic disease state such as microvascular changes or immunologic dysfunction. A large number of studies have looked to answer this question. If perioperative hyperglycemia is an independent risk factor for post-surgical infection, anesthesiologists and surgeons may be empowered to significantly affect infectious outcomes without changing the more difficult-to-control variables of diabetic status or long-term glycemic control.

Due to the consistency among studies and compelling evidence that diabetes leads to increased infection risk, major focus has been placed on whether hyperglycemia, as an independent risk factor, is associated with increased infection. Even in nondiabetics, hyperglycemia is associated with an increased risk of morbidity and mortality.[9] The overwhelming majority of studies examining hyperglycemia and surgical infection have focused on the cardiac population, likely because 16–28% of patients undergoing cardiac surgery are diabetic.[10–12] Furthermore, deep sternal wound infections, though rare, remain a devastating and often lethal complication following cardiothoracic surgery, with mortality as high as 14%.[13,14] Increased hospitalization, resource utilization, and morbidity are only a few of the consequences of sternal wound infections.

A landmark study, published in 2001, by van der Berghe and coworkers, cast light on the significance of postoperative hyperglycemia.[15] This study included ICU patients, the majority of which had undergone cardiac surgery. They showed that treating hyperglycemia aggressively with a target blood glucose level between 80–110 g/dL in the surgical intensive care unit significantly reduced morbidity and mortality, both in the intensive care unit and during hospital stay. Patients treated aggressively achieved not only lower glucose levels with increased in-hospital survival and decreased infections, but also experienced long-term effects of increased one-year survival. One-year mortality was decreased from 8.0% to 4.6%. The effect was greatest in patients with multi-organ failure in the face of sepsis. The results of this trial instigated a flurry of studies and aroused interest in the deleterious effects of hyperglycemia, with focus on the cardiac surgical population.

POSTOPERATIVE HYPERGLYCEMIA IN THE CARDIAC SURGERY PATIENT

In a retrospective study, Zerr and colleagues at the Portland Diabetic Project established that increased mean glucose levels for the first two days following cardiac surgery is an independent risk factor for deep sternal wound infection in diabetics.[16] This group found that a continuous intravenous insulin protocol was superior to standard subcutaneous insulin for glycemic control. Improved glycemic control decreased deep sternal wound infections from 2.4% to 1.5%. The same group conducted a prospective study of 2,467 diabetic patients undergoing cardiac surgery.[17] They looked at both the efficacy of subcutaneous insulin injections versus continuous intravenous insulin infusions in maintaining glucose less than 200 mg/dL, as well as deep sternal wound infection rates between these two groups. Their results indicated that, indeed, postoperative hyperglycemia was associated with deep sternal wound infection in diabetics. Furthermore, a continuous insulin infusion, which they also found to be superior to subcutaneous insulin in reaching target glucose levels, resulted in a 66% reduction in deep sternal wound infection. They concluded that hyperglycemia in the postoperative setting may be