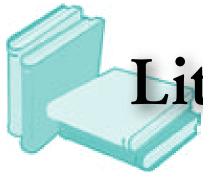

Literature Reviews

Intensive intraoperative insulin therapy versus conventional glucose management during cardiac surgery; a randomized trial.

Gandhi GY, Nuttall GA, Abel MD, Mullany CJ, Schaff HV, O'Brien PC, Johnson MG, Williams AR, Cutshall SM, Mundy LM , Rizza RA, McMahon MM. *Annals of Internal Medicine 146:233-243, 2007.*

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Abstract Excerpt

It is not known whether rigorous intraoperative glycemic control reduces death and morbidity in cardiac surgery patients. These investigators, via a prospective, randomized, open-label, controlled trial with blinded end point assessment, compared outcomes of intensive insulin therapy during cardiac surgery with those of conventional intraoperative glucose management. Study patients were adults with and without diabetes undergoing on-pump cardiac surgery. Primary outcome was a composite of death, sternal infections, prolonged ventilation, cardiac arrhythmias, stroke, and renal failure within thirty days after surgery. Secondary outcome measures were length of stay in the intensive care unit and hospital. Patients were randomly assigned to receive continuous insulin infusion to maintain intraoperative glucose levels between 80 mg/dL and 100 mg/dL (n=199) or conventional treatment (n=201). Patients in the conventional treatment group were not given insulin during surgery unless glucose levels were greater than 200 mg/dL. Both groups were treated with insulin infusion to maintain normoglycemia after surgery. Mean glucose concentrations were significantly lower at the end of surgery in the intensive treatment group (114 mg/dL) when compared to the conventional treatment group (157 mg/dL). 82 of 185 patients (44%) in the intensive treatment group and 86 of 186 patients (46%) in the conventional treatment group experienced an event. More deaths (4 versus 0) and strokes (8 versus 1) occurred in the intensive treatment group. Length of stay in the intensive care unit and in the hospital was similar for both groups. These investigators conclude that intensive insulin therapy during cardiac surgery does not reduce perioperative death or morbidity and the increased incidence of death and stroke in the intensive treatment group raises concern about routine implementation of this intervention.

Reviewer's Comments

Due to research published over the last few years indicating that intensive insulin therapy after surgery reduces morbidity and death in critically ill patients, strict glycemic control has become (perhaps) routine practice during the postoperative period following cardiac surgery. However, no consensus exists regarding optimal management of intraoperative hyperglycemia during cardiac surgery because of lack of evidence from randomized trials. Observational studies suggest an association between intraoperative hyperglycemia and adverse outcomes. However, if intraoperative hyperglycemia simply reflects severity of "stress", simple prevention of hyperglycemia may not be clinically beneficial and risks/costs of maintaining intraoperative normoglycemia may outweigh the potential benefits. Furthermore, simple, safe, and effective insulin infusion algorithms that achieve intraoperative normoglycemia are lacking. This clinical study represents the first randomized, controlled trial to asses the effect of strict intraoperative glycemic control during cardiac surgery on clinically significant outcomes when added to rigorous postoperative glycemic control. In contrast to previously published observational studies, these investigators showed that lowering glucose concentrations to near normal levels intraoperatively by insulin infusion did not beneficially affect outcome. On the other hand, increased incidence of death and stroke in the intensive treatment group raises concern about routine implementation of this intervention. Why were these interesting and unanticipated findings observed? The excellent companion Editorial (Ann Intern Med 146:307-308, 2007), written by a prolific clinical investigator in this area, Dr. Greet Van den Berghe, provides helpful perspective. Dr. Van den Berghe and associates, from Belgium, were among the first wave of investigators to document the clinical benefits of tight control during the immediate postoperative period. Dr. Van den Berghe postulates that postoperative tight glucose control (which all of the patients in this study were exposed to) has such a strong positive effect on outcome that any additional beneficial effect of tight control intraoperatively would be expected to be quite small. This study clearly shows that adding tight blood glucose control during cardiac surgery does not cause a large additional benefit compared with starting tight blood glucose control in the intensive care unit. Furthermore, the larger number of deaths and strokes in the intensive treatment group supports caution about adopting intraoperative tight glucose control. Dr. Van den Berghe appropriately states that much larger clinical trials are required to sort these issues out and, until then, "we should regard tight glucose control during cardiac surgery as experimental and confine its use to clinical trials."