A Commentary: Effects on Glargine Insulin on Glycemic Control in Patients with Diabetes Mellitus Type II Undergoing Off-pump Coronary Artery Bypass Graft

The association between perioperative hyperglycemia and adverse outcomes after cardiac surgery is well established.[1] At present, in most of the cardiac centers, perioperative blood glucose is managed by continuous intravenous insulin infusion (CIII). However, CIII is fraught with the risks of fluctuations of blood glucose levels and risks of hypoglycemia.

Insulin glargine (IG) is a long-acting analogue of human insulin available for clinical use for more than a decade. Evidence from clinical trials suggests that IG has a lower risk of hypoglycemia. Unlike traditional insulin preparations that are absorbed rapidly from the abdomen than from the arm or leg, the site of administration does not influence IG's unique absorption kinetics, even when the insulin is injected into a working limb.[2] The main role of basal insulin secretion is to limit hepatic glucose production and lipolysis in the fasting state, particularly overnight, without impairing glucose availability for brain function. IG was specifically designed to provide basal insulin requirement.[3] IG lowered plasma glucose by a relatively hepatospecific action with greater suppression of endogenous glucose production compared with little or no increase in glucose disposal.[4]

Before the study by Gandhi *et al*.,[5] there had been only one study reported in literature by Forouzzannia *et al*.[6] which compared the effects of continuous insulin infusion with or without subcutaneous (s.c.) IG on glycemic control in diabetic patients undergoing coronary artery bypass grafts (CABG). Although they mentioned that good control of intraoperative blood glucose entails maintaining blood glucose level below 200 mg/dl, they kept a target of blood glucose level between 120 and 180 mg/dl.[6] Lazar HL (2012) compared aggressive glycemic control (90–120 mg/dl) against moderate control (120–180 mg/dl) in 82 patients undergoing CABG surgeries. In this report, there was no difference in the incidence of adverse effects between groups.[7] Furthermore, hypoglycemic events were more frequent in the aggressive group. This report supports the conclusion of NICE-SUGAR[8] trial and suggests that moderate control (120–180 mg/dl) may provide an appropriate balance between preventing adverse outcomes associated with perioperative hyperglycemia and avoiding dangerous hypoglycemia. Although there is still no consensus as to the best intraoperative blood glucose levels to be maintained, in general, the literature suggests maintaining blood glucose levels between 150 and 180 mg/dl.[9] Moreover, a study discovered that intraoperative hyperglycemia (blood glucose level >200 mg/dl) as well as relative normoglycemia (blood glucose level <140 mg/dl) was found to be associated significant morbidity and mortality.[10] Further, it found that blood glucose levels ranging from 140 to 170 mg/dl were associated with lowest risk of adverse outcomes.[10] Hence, probably, to minimize risk of hypoglycemia, we may be little more liberal with the intraoperative blood sugar target range.

Forouzzannia *et al*. administered 15 U of IG in all patients irrespective of body weight, which is likely to be <0.3 U/kg (they have mentioned body mass index (BMI) of about 26 kg/m^2 and not the weight).[6] Wang *et al*. examined the pharmacokinetic and pharmacodynamic dose-response effects of single (s.c.) injections of IG in obese type 2 diabetic individuals and observed that over a dose range of 0.5–2.0 units/kg, circulating plasma insulin levels increased modestly despite large (s.c.) IG doses.[4] Silinskie KM *et al*. compared the efficacy and safety of dosing IG by weight versus percentage of total daily insulin (TDI) in cardiac surgery patients transitioning from continuous insulin infusion to (s.c.) insulin. Patients received either 50% of their TDI requirement or 0.5 units/kg of glargine as a one-time dose, 2 h before stopping the continuous insulin infusion.[11] The percentage of blood glucose measurements in target range (80–140 mg/dl) was similar between the weight-based group and the percentage-based group. In this small cohort, dosing IG by weight at the dose of 0.5 U/kg proved to be safe.[11] We ought to remember that IG is supposed to deliver the basal insulin requirements and not the entire insulin requirement. We are of the opinion that for patients with normal BMI or till 30 kg/m^2, IG dose of 0.3 U/kg and those who are overweight a dose of 0.5 U/kg may suffice for the basal insulin requirement.

In the study by Forouzzannia *et al*., patients undergoing both on-pump and off-pump CABGs were included.[6] However, the number of patients who underwent on-pump procedures was significantly more in the group who received only CIII (P = 0.031)! Hence, strictly speaking, the groups were not comparable. Moreover, significantly more patients in CIII group needed inotropic agents (P = 0.039)! On-pump CABGs are often associated with mild-to-moderate hypothermia and use of inotropes. Higher percentage of blood glucose levels above 200 mg/dl in CIII reported in the study could be attributed to hypothermia and/or use of inotropes. In the study by Gandhi *et al*., all patients underwent off-pump CABG, and they reported better perioperative glycemic control with significant reduction in postoperative morbidity.[5] Data regarding use of inotropes,

an important piece of information, whenever we are dealing with blood glucose level, if presented, would have enhanced our understanding in a more clear manner.

To conclude, although the idea of (s.c.) IG seems novel, we ought to remember that this has been tried only in a small study. How the attributes of IG differ intraoperatively in CABG patients needs to be studied further and the dose of IG needs to be standardized before we embrace IG wholeheartedly for intraoperative control of blood glucose in patients undergoing CABG.

Soumya Sankar Nath, Pravin Kumar Das

Department of Anaesthesiology and Critical Care, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, Uttar Pradesh, India

Address for correspondence: *Dr. Soumya Sankar Nath, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow - 226 010, Uttar Pradesh, India. E-mail: soumyanath@rediffmail.com*

References

1. Reddy P, Duggar B, Butterworth J. Blood glucose management in the patient undergoing cardiac surgery: A review. World J Cardiol 2014;6:1209-17.
2. Powers CA, D'Alessio D. Endocrine pancreas and pharmacotherapy of diabetes mellitus and hypoglycemia. In: Bruntan L, Chamber B, Knollman B, editors. Goodman Gilman's The Pharmacological Basis of Therapeutics. 12th ed. New York: McGraw Hill Books; 2011. p. 1237-73.
3. Hilgenfeld R, Seipke G, Berchtold H, Owens DR. The evolution of insulin glargine and its continuing contribution to diabetes care. Drugs 2014;74:911-27.
4. Wang Z, Hedrington MS, Gogitidze Joy N, Briscoe VJ, Richardson MA, Younk L, *et al.* Dose-response effects of insulin Glargine in type 2 diabetes. Diabetes Care 2010;33:1555-60.
5. Gandhi H, Sarvaia A, Malhotra A, Acharya H, Shah K, Rajavat J. Effects of glargine insulin on glycemic control in patients with diabetes mellitus type II undergoing off pump coronary artery bypass graft. Ann Card Anaesth 2018;21:167-72.
6. Forouzzannia SK, Mohammadi SM, Mirhosseini SJ, Abdollahi MH, Mostaghion SH, Hosseini H, *et al*. Comparing effects of continuous insulin infusion with or without subcutaneous glargine insulin on glycemic control in diabetic patients undergoing coronary artery bypass graft. Iran J Diabet Obes 2009;1:5-10.
7. Lazar HL. Glycemic control during coronary artery bypass graft surgery. ISRN Cardiol 2012;2012:292490.
8. NICE-SUGAR Study Investigators, Finfer S, Chittock DR, Su SY, Blair D, Foster D, *et al.* Intensive versus conventional glucose control in critically ill patients. N Engl J Med 2009;360:1283-97.
9. Sudhakaran S, Surani SR. Guidelines for perioperative management of the diabetic patient. Surg Res Pract 2015;2015:284063.
10. Duncan AE, Abd-Elsayed A, Maheshwari A, Xu M, Soltesz E, Koch CG, *et al.* Role of intraoperative and postoperative blood glucose concentrations in predicting outcomes after cardiac surgery. Anesthesiology 2010;112:860-71.
11. Silinskie KM, Kirshner R, Hite MS. Converting continuous insulin infusion to subcutaneous insulin glargine after cardiac surgery using percentage-based versus weight-based dosing: A pilot trial. Ann Pharmacother 2013;47:20-8.

Access this article online	
Quick Response Code:	Website: www.annals.in
	DOI: 10.4103/aca.ACA_213_17

How to cite this article: Nath SS, Das PK. A Commentary: effects on glargine insulin on glycemic control in patients with diabetes mellitus type II undergoing off-pump coronary artery bypass graft. Ann Card Anaesth 2018;21:173-4.