

Glycemic control in Intensive Care Unit

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The ideal glycemic control in Intensive Care Units (ICUs) whether medical, surgical, or cardiac is controversial. It has been subject to many discussions and the final word has not been said. In early 2001, Van den Berghe *et al.*^[1,2] studied patients and found that an intensive glycemic control was important to reduce the mortality and morbidity both in medical and surgical ICU; however, more recent studies have not been able to substantiate the results. The NICE-SUGAR^[3] showed very contrary results that a very tight control might actually be detrimental to the outcome of patients in the medical ICU. Other studies such as ACCORD^[4] though not in ICU setting also showed that very tight blood glucose may actually not be beneficial in the outcome of cardiac patients. There were speculations as to whether this was due to drug interactions, weight gain, or hypoglycemia. The strong message that it gave was that very tight control in high-risk individuals was not of benefit.

When we discuss glycemic control, we are talking control, glycemic variability, and incidence of hypoglycemia. How tight should the control be, the challenges faced in our country and how to address it are some of the questions that need to be answered. Let's start with medical ICU. Most hospitals have an ICU; however, the problems faced are very different. In most hospitals, doctor to patient and staff nurses to patient ratio are sadly low; this is due to paucity of medical and paramedical professions. This is superadded by the fact that many different specialties such as anesthetists, physicians, and critical care specialists are in charge of the ICU; so there is no uniformity. Most importantly, I feel that there is no written protocol, which can be easily followed. Patients in medical ICU^[5] are critical and are not capable of reporting signs of hypoglycemia or the symptoms are masked because of sympathetic under activity, at other times, the symptoms of the medical condition may mimic hypoglycemia. The cost of frequent testing is another problem faced. In this scenario, to set targets of very low glucose levels are sometimes not

possible, feasible, or advisable. The variables affecting the plasma glucose values are the oxygen therapy, pH, anemia, and hypotension and few drugs such as acetaminophen and mannitol.^[6] This may actually show different values in point of care glucometers.

In the surgical ICU, the scenario is quite different, as the patients are not sick and are there in ICU only postoperatively for a few hours or days. They are conscious and the blood glucose can be maintained at ideal conditions. The studies in surgical ICU patients have shown that a good control in them does improve outcomes.

In coronary care unit (CCU),^[7,8] the patients admitted are those who have had an unstable angina, myocardial infarction, or who have undergone coronary artery bypass grafting (CABG). The data on these subjects are influenced to a large extent not only in the trials done in CCU patients but also by the ADVANCE^[9] and ACCORD trial. The physician/endocrinologist may be very aggressive with the management of blood glucose pushing the patient into frequent hypoglycemia. This leads to less than ideal treatment as some doses are not given, or a sliding scale is followed. The GLUCO-CABG^[10] study targeted blood glucose in the CCU to 100–140 mg/dl and showed that this did not significantly reduce perioperative complications compared with target glucose of 141 and 180 mg/dl. However, an aggressive approach helped patients with no history of diabetes. A more recent study has shown that patients without diabetes did worse when the blood glucose was not well controlled and had longer periods of hospital stay; however, patients with diabetes on insulin before the admission did better when the blood glucose was in the hyperglycemic range of 180–240 mg/dl.^[11] The studies also show that the outcomes followed a U-curve with outcomes worst in the very low glucose levels and the very high levels.

A recent study has found a relationship between glycemic gap^[12] and outcomes. This was calculated with the A1c-derived average glucose and the initial glucose values. A glycemic gap of >80 was found to be significantly associated with mortality in patients who were not known

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diabetic. The findings have suggested that the patients with preexisting diabetes fare worse than those with newly diagnosed diabetes. Thus, it is also important to stratify patients on this also before control. The other important thing to take note is that whether the patient was on insulin before or not. Those on insulin fare worse than those who were not on insulin for the glycemic control.

It is important that every hospital should see what works for them. A protocol should be followed which is feasible. This has to be done in concurrence with the ICU in charge and the physicians. The ideal is of course to have an insulin infusion. We in our hospital usually have an insulin infusion with 50 units of insulin with 50 ml of normal saline, and this will give an insulin dose of around 1 unit per ml, and this is given depending on the requirement. The fluids to maintain hydration are decided in consultation with the treating physician or ICU in charge. The fluids will depend on the central venous pressure and parenteral nutrition.

There are many protocols in the use for glycemic control in patients in ICU, studies with intravenous insulin followed by subcutaneous protocols have been used, and they have been of benefit. The major advantage of this is of course the cost-effectiveness, as this will not require very frequent testing.^[13]

The American Diabetes Association guideline^[14] is to do a glycosylated hemoglobin for all patients with diabetes. Treatment is started if blood glucose is more than 180 mg/dl, to maintain blood glucose between 140 and 180 mg/dl. Noncritically ill patients can however be maintained at 110–140 mg/dl also. The insulin regimen should be basal, nutritional, and correction bolus. Sliding scale of insulin should be discouraged. There should also be a hypoglycemia protocol like there is a hyperglycemic protocol. These protocols need to be revisited and changed as per the requirement. The protocol that is most beneficial appears to be one that is formulated with the local medical team. Every hospital has to audit their protocols to understand what works for the hospital. A retrospective audit of insulin infusion management^[15] involving a locally developed dynamic insulin infusion guideline in a tertiary ICU showed a U-shaped relation in the non-diabetes mellitus (DM) cohort with an increased ICU mortality in the lowest and highest glucose quintiles. No clear pattern is found in the DM cohort.^[16] It is also important to identify the diabetic status, as to newly diagnosed diabetic, known diabetic, and how the control of diabetes is and a glycosylated hemoglobin should be done for all patients on admission.^[17] The data does suggest that the glucose control should be very personalized to each individual and blood glucose values should be fixed differently for nondiabetics,

newly diagnosed diabetics, diabetics on insulin, and based on the underlying condition.^[18]

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