Chapter 20
Blood Sugar Control in Intensive Care Patients (NICE SUGAR)-2009

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Background

Hyperglycemia is common in acutely ill patients and is associated with increased mortality in some groups of patients. Based largely on a trial which demonstrated that an intensive intravenous insulin regimen to reach a target glycemic range of 80–110 mg/dL reduced mortality by 40% compared with a standard approach targeting blood glucose of 180–215 mg/dL in critically ill patients with recent surgery many professional organizations were recommending tight glucose control [1].

Objective

To test the hypothesis that intensive glucose control reduces mortality at 90 days in critically ill patients.

Intensive versus Conventional Glucose Control in Critically Ill Patients. (2009). *New England Journal of Medicine*, *360*(13), 1283–1297. doi: 10.1056/nejmoa0810625. https://www.nejm.org/doi/pdf/10.1056/NEJMoa0810625.

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Design and Methods

- The investigators conducted a parallel-group, randomized, controlled trial involving adult medical and surgical patients admitted to the ICUs of 42 hospitals.
- Adults who were expected to require treatment in the ICU on 3 or more consecutive days were randomly assigned within 24 h of admission to the ICU to undergo either intensive glucose control (target blood glucose range of 81–108 mg/dL) or conventional glucose control (target blood glucose of 180 mg or less per deciliter).
- Control of blood glucose was achieved with the use of an intravenous infusion of insulin in saline.
- In the conventional glucose control group, insulin was administered if the blood glucose level exceeded 180 mg/dL. Insulin administration was reduced and then discontinued if the blood glucose level dropped below 144 mg/dL.
- The trial intervention was discontinued once the patient was eating or was discharged from the ICU but was resumed if the patient was readmitted to the ICU within 90 days.
- The trial intervention was discontinued permanently at the time of death or 90 days after randomization, whichever occurred first.
- The primary outcome measure was death from any cause within 90 days after randomization.
- Secondary outcome measures were survival time during the first 90 days, cause-specific death and durations of mechanical ventilation, renal-replacement therapy, and stays in the ICU and hospital.
- Tertiary outcomes were death from any cause within 28 days after randomization, place of death (ICU, hospital ward, or other), incidence of new organ failure, positive blood culture, receipt of red-cell transfusion, and volume of the transfusion.
- The primary outcome was also examined in six predefined pairs of subgroups: operative patients and nonoperative patients, patients with and those without diabetes, patients with and those without trauma, patients with and those without severe sepsis, patients treated and those not treated with corticosteroids, and patients whose APACHE II (a scoring system ranging from 0 to 71 developed to grade the severity of illness in acutely ill patients) score was 25 or more and those whose score was less than 25.
- A blood glucose level of 40 mg/dL (2.2 mmol/L) or less was considered a serious adverse event.

Results

- Study data was used from 6030 patients.
- The mean blood glucose level was significantly lower in the intensive-control group than in the conventional-control group (115 ± 18 vs. 144 ± 23 mg/dL).

- More patients in the conventional-control group received steroids, 34.6% vs. 31.7%. The most common indication for corticosteroid administration in both groups was the treatment of septic shock.
- Ninety days after randomization, 27.5% of patients in the intensive-control group had died, as compared with 24.9% of patients in the conventional-control group.
- Intensive glucose control increased mortality among adults in the ICU: A blood glucose target of 180 mg or less per deciliter resulted in lower mortality than did a target of 81–108 mg/dL.
- Deaths from cardiovascular causes were more common in the intensive-control group than in the conventional-control group.
- A similar number of patients developed new single or multiple organ failures in both groups.
- There was no significant difference between the two groups in the numbers of days of mechanical ventilation and renal-replacement therapy or in the rates of positive blood cultures and red-cell transfusion. There was no significant difference in mortality in comparisons of operative vs. non-operative patients, patients with and those without diabetes, those with or without severe sepsis, patients with an APACHE II score of 25 or more and those with a score of less than 25.
- Severe hypoglycemia was significantly more common with intensive glucose control.

Importance

Based on previous trials, intensive glucose control had been widely recommended prior to this study [1]. This study suggested that a goal of obtaining normoglycemia may be harmful to patients in an acutely ill state.

Bottom Line

Prior to this study, many professional organizations recommended tight glucose control for acutely ill patients. The investigators in this study conducted a parallel-group, randomized, controlled trial involving adult medical and surgical patients admitted to the ICU. Patients were randomized to a intensive glucose control group with a target blood glucose level of 81–108 or a conventional-control group with a target glucose range of 180 or less. Results of the study showed that intensive glucose control increased mortality among adults in the ICU.

Updates

In 2012, the NICE-SUGAR investigators examined the associations between moderate and severe hypoglycemia (blood glucose of 41–70 and ≤40 respectively) and death among 6026 critically ill patients in intensive care units. The intensively treated group had 10- to 15-fold greater rates of hypoglycemia, and hypoglycemia was strongly associated with mortality [2].

The current recommended glycemic targets in the Standards of Care of the American Diabetes Association is that, "Insulin therapy should be initiated for treatment of persistent hyperglycemia starting at a threshold of 180 mg/dL…Once insulin therapy is started, a target glucose range of 140–180 mg/dL is recommended for the majority of critically ill and noncritically ill patients. More stringent goals, such as 110–140 mg/dL, may be appropriate for selected patients if they can be achieved without significant hypoglycemia" [3].

References

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