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On Drugs and Therapeutics

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Glucose Control in the ICU

Once thought to be a beneficial response to critical illness, hyperglycemia is now recognized as independently associated with death and other adverse outcomes in various groups of critically ill patients. Whether normalization of blood glucose by insulin infusion is beneficial in such patients has been a subject of debate in the critical care community. Some new guidelines have been published.¹

CLINICAL STUDIES — Among 1548 patients (about 60% post-cardiac surgery) in a surgical intensive care unit (SICU) randomized to receive intensive insulin therapy (IIT) to achieve a target glucose of 80-110 mg/dL (4.4-6.1 mmol/L) or to standard therapy with a conventional target of 180-200 mg/dL (10.0-11.1 mmol/L), in-ICU-mortality was 4.6% with IIT and 8.0% with the conventional target, a 42% decrease.² A similar study in 1,200 subjects in a medical intensive care unit (MICU) showed no significant difference in mortality between patients on the intensive protocol compared to those receiving conventional glucose control (37.3% with IIT versus 40.0% in the control group).³ A combined analysis of these two studies found more hypoglycemic events in the IIT groups (11.3% vs. 1.8%), but with no serious consequences.⁴

Another study (n=523) confirmed the increased incidence of hypoglycemia with IIT – severe hypoglycemia (glucose \leq 40 mg/dL [\leq 2.2 mmol/L]) occurred in 28.6% of patients with IIT compared to 3.1% in conventionally treated patients – and found a 74% higher mortality (23.8% vs. 13.7%) in hypoglycemic patients, with no significant difference in mortality between IIT and conventionally treated patients.⁵

Among 537 patients in 18 ICUs with severe sepsis treated with IIT or conventionally, the rate of life-threatening hypoglycemia was significantly higher in the IIT group (5.3% versus 2.1%); there was no difference in mortality between the IIT and control groups, but the study was stopped early due to safety concerns.⁶

The Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation (NICE-SUGAR) trial included 6104 medical and surgical patients in 42 hospitals. The target range glucose for the control group was 144-180 mg/dL and for the IIT group was 81-108 mg/dL. The results showed no significant difference in 28-day mortality (22.3% vs. 20.8%, P=0.17), but at 90 days the mortality rate was significantly higher in the IIT group (27.5% vs. 24.9%, P=0.02).⁷

A systematic review and meta-analysis of 26 randomized controlled studies of IIT in the ICU setting found

Table 1. Some Studies of Insulin-Infusion Therapy in ICU Settings

Study (N)	Design and Setting	Glucose Target mg/dL (mmol/L)	Achieved Mean Glucose	Mortality
Van den Berghe 2001 ² N=1548	Randomized single center SICU	80-110 (4.4-6.1) 180-200 (10.0-11.1)	104 153	4.6% 8.0%*
Van den Berghe 2006 ³ N=1200	Randomized single center MICU	80-110 (4.4-6.1) 180-200 (10.0-11.1)	111 153	37.3% 40.0%
Arabi et al. ⁵ N=523	Randomized single center mixed ICU	80-110 (4.4-6.1) 180-200 (10.0-11.1)	115 171	13.5% 17.1%
WISEP ⁶ N=537	Randomized multicenter mixed ICUs	80-110 (4.4-6.1) 180-200 (10.0-11.1)	112 151	24.7% 26.0%
NICE-SUGAR ⁸ N=6104	Randomized multicenter mixed ICUs	81-108 (4.5-6.0) 144-180 (8.0-10.0)	115 144	27.5% 24.9%*

* Statistically significant difference

no significant mortality benefit with use of IIT in the ICU (RR 0.93; CI 0.83-1.04).⁸

CONCLUSION — Clinical studies indicate that intensive insulin therapy with tight glycemic control (80-110 mg/dL [4.4-6.1 mmol/L]) is generally not beneficial for ICU patients, and may be harmful. Medical Letter consultants believe, however, that less intensive glucose control (140-180 mg/dL [7.8-10 mmol/L]) may prove to be beneficial. Whether some subgroups of ICU patients, such as diabetic patients post-cardiac surgery, would benefit from tighter control of blood glucose remains to be established. □

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