Intensive insulin therapy reduced the incidence of neurologic complications in critically ill patients

Van den Berghe G, Schoonheydt K, Becx P, Bruyninckx F, Wouters PJ. **Insulin therapy protects the central and peripheral nervous system of intensive care patients.** Neurology. 2005;64:1348–53.

Clinical impact ratings: Hospitalists ★★★★★☆☆ Critical Care ★★★★★★☆ Neurology ★★★★★★☆

QUESTION

In critically ill patients, does intensive insulin therapy improve neurologic outcomes, including critical illness polyneuropathy (CIP)?

METHODS

Design: Preplanned subgroup analyses of a randomized controlled trial of 1548 mechanically ventilated, critically ill patients.

Allocation: Unclear allocation concealment.*

Blinding: Blinded (outcome assessors).*

Follow-up period: Up to 12 months after discharge.

Setting: Surgical intensive care unit (ICU) of a hospital in Leuven, Belgium.

Patients: A stratified subgroup of 63 patients with isolated brain injury at baseline (mean age 57 y, 63% men) and a subgroup of 405 patients who were in the ICU for ≥ 7 days (mean age 61 y, 68% men).

Intervention: Intensive insulin therapy to maintain strict glycemic control between 4.4 and 6.1 mmol/L (80 and 110 mg/dL) (n = 33 and n = 181 for separate subgroups, respectively) or usual care, in which insulin therapy was recommended only when blood glucose levels were > 12 mmol/L (220 mg/dL), with the goal of maintaining levels between 10.0 and 11.1 mmol/L (180 and 200 mg/dL) (n = 30 and n = 224).

Outcomes: Mortality and duration of ventilation; prolonged ventilation subgroup: CIP; isolated brain injury subgroup: intracranial pressure.

Patient follow-up: 100%.

MAIN RESULTS

Among the 405 patients who had prolonged ICU stays, those in the intensive insulin group had reduced risks for ICU mortality, CIP, and ventilation > 14 days (Table). In the subgroup analysis of 63 patients with isolated brain injury, the intensive-insulin and usual-care groups did not differ for ICU mortality (18% vs 23%, P = 0.6), hospital mortality (36% vs 30%, P = 0.6), or mortality at 6 (48% vs 30%, P = 0.3) or 12 months (51% vs 30%, P = 0.2). The intensive insulin group had a shorter duration of ventilation (median 7 vs 15 d, P < 0.001) and lower intracranial pressure (peak 16 vs 19 mm Hg, P < 0.001; mean 11 vs 13 mm Hg, P = 0.003).

CONCLUSION

In critically ill patients with prolonged ventilation or with isolated brain injury, intensive insulin therapy reduced the probabilities of further prolonged ventilation and some neurologic complications.

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*See Glossary.

Intensive insulin therapy vs usual care in 405 critically ill, mechanically ventilated patients with ≥ 7-day ICU stay†

Outcomes at 12 mo	Intensive insulin	Usual care	RRR (95% CI)	NNT (CI)
ICU mortality	12%	21%	43% (9 to 64)	12 (7 to 67)
CIP	25%	49%	49% (33 to 62)	5 (3 to 7)
Ventilation > 14 d	32%	42%	24% (1 to 42)	10 (6 to 235)

†CIP = critical illness polyneuropathy; ICU = intensive care unit. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

Publication of the results of the trial by Van den Berghe and colleagues in 2001 (1) prompted important changes in our view of glucose management for critically ill patients. In a surgical ICU population, intensive insulin therapy ("tight control") decreased mortality, bloodstream infections, acute renal failure, need for transfusions, and CIP. These effects were most apparent in patients who remained in the ICU for > 5 days, most of whom were general surgical patients. Many ICUs have adopted intensive insulin therapy based on these data, and other studies of various populations of critically ill patients are in progress.

The current study by Van den Berghe and colleagues is a prespecified subgroup analysis of patients who had acute central nervous system diseases, primarily those with intracerebral or subarachnoid hemorrhage or those who had undergone intracranial surgery. In this group, tight control was associated with a decrease in CIP and a shorter duration of mechanical ventilation. This therapy also led to lower intracranial pressure and substantially lower vasopressor requirements to maintain cerebral perfusion pressure. ICU mortality was 18% in patients who received tight control and 23% in those who received usual care; this nonsignificant trend was reversed at 12 months of follow-up.

Most of the above argues in favor of using continuous insulin infusions to maintain tight control over blood glucose in patients with these critical neurologic illnesses, although debate on the mechanism of this effect continues (2–4).

Any new therapeutic idea needs to be carefully evaluated to understand its limitations. Implementing tight control began slowly because of concerns over the possibility of causing hypoglycemia. The anecdotal experience of many centers is that hypoglycemia may actually be less common than feared, because of the frequent measurement of blood glucose. Emerging evidence of a possible interaction of tight control with disturbances of metabolism in areas of ischemic or traumatic damage deserves careful evaluation (5). On balance, however, tight control is one of the most promising advances in contemporary neurocritical care.

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