



Different algorithms for glycemic control will yield different results

Emily L. Drennan, MD · Evan G. Pivalizza, MD

Received: 19 September 2011 / Accepted: 4 November 2011 / Published online: 16 November 2011
© Canadian Anesthesiologists' Society 2011

To the Editor,

We read with interest Abdelmalak *et al.*'s recent randomized controlled trial of insulin infusion algorithms.¹ As stated in the title, “validation” of the algorithm is successful as reported. However, further statistical comparisons reported between the groups (Table 2) lose significance once the significant differences between the two treatment algorithms are appreciated.

The conventional group is noteworthy in that so few patients (15%) were treated with insulin compared with those treated in the intensive group (90%). While the targets of glycemic control differed between the two groups, it is unclear how the conventional group could be expected to achieve glycemic control with such infrequent use of insulin.

If an appropriate comparison is to be made between the two groups, treatment initiation should be equivalent. In the target group, insulin was started at a glucose level exactly that of the upper target limit (6.1 mmol·L⁻¹). However, in the conventional group, insulin was introduced at a glucose level of 11.9 mmol·L⁻¹, which is 7.5% above the upper target limit (11.1 mmol·L⁻¹). Given the anticipated delay to achieve target range after start of insulin, the conventional group was disadvantaged from the outset, and assigning statistical significance to the % time in the relative target range favours the intensive group (Table 2). Furthermore, the desired target range prejudices the conventional treatment group further as that of the intensive group is significantly narrower (27–37% of outer limits vs 10–11%, respectively), again favouring the intensive

group since % time *within* target is a reported measure. In Table 2, assigned statistical significance to differences in time within a glucose range of 4.4–6.1 mmol·L⁻¹ or even > 6.1 mmol·L⁻¹ will obviously favour the intensive group, since the conventional group never received insulin at a glucose < 8.3 mmol·L⁻¹.

We appreciate the authors' publication of a detailed safe and effective insulin strategy. However, although statistical differences in glucose measures were found between the two groups, we caution that these are to be expected given the inherent inequalities assigned to the non-insulin conventional group management.

Future prospective evaluations could include the same initial glucose trigger followed by divergent insulin algorithms. If separate triggers are chosen, insulin must be initiated at an equivalent point within the trigger range, and ranges should be mathematically comparable.

Conflicts of interest None declared.

References

1. Abdelmalak B, Maheshwari A, Kovaci B, *et al.* Validation of the DeLiT Trial intravenous insulin infusion algorithm for intraoperative glucose control in noncardiac surgery: a randomized controlled trial. *Can J Anesth* 2011; 58: 606–16.

Reply

Drennan and Pivalizza misinterpret our validation of an insulin infusion protocol.¹ Our analysis was conducted in the context of a randomized trial that compared the effects of tight glucose control and routine glucose management on a composite of major complications.² Validation of our

E. L. Drennan, MD · E. G. Pivalizza, MD (✉)
University of Texas Medical School–Houston, Houston,
TX, USA
e-mail: evan.g.pivalizza@uth.tmc.edu

tight control algorithm was based on good glucose control in patients assigned to tight control and the absence of hypoglycemic episodes that have bedevilled other glucose control trials.^{3,4} We succeeded in that regard, as the median plasma glucose concentration in our tight control group was 6 [interquartile range: 5.6-6.7] mmol·L⁻¹ and none experienced severe hypoglycemia (i.e., glucose < 2.2 mmol·L⁻¹). Our insulin algorithm was thus validated by good results in patients assigned to tight control and not by comparison to patients assigned to routine glucose control.

Drennan and Pivalizza state that “it is unclear how the conventional group could be expected to achieve glyceic control with such infrequent insulin use.” Precisely. Since the targets were very different, we had no expectation that the routine group would have similar glucose concentrations. In fact, our underlying trial would have failed if glucose control results were comparable in the two treatment groups. That so few patients in the routine glucose group were given insulin simply reflects the fact that few of those patients reached the intervention threshold.

Competing interests None declared.

References

1. *Abdelmalak B, Maheshwari A, Kovaci B, et al.* Validation of the DeLiT Trial intravenous insulin infusion algorithm for intraoperative glucose control in noncardiac surgery: a randomized controlled trial. *Can J Anesth* 2011; 58: 606-16.
2. *Abdelmalak B, Maheshwari A, Mascha E, et al.* Design and Organization of the Dexamethasone, Light Anesthesia, Tight Glucose Control (DeLiT) Trial: a factorial trial evaluating the effects of corticosteroids, glucose control, depth-of-anesthesia on perioperative inflammation, morbidity from major non-cardiac surgery. *BMC Anesthesiol* 2010; 10: 11.
3. *Preiser JC, Devos P, Ruiz-Santana S, et al.* A prospective randomised multi-centre controlled trial on tight glucose control by intensive insulin therapy in adult intensive care units: the Glucontrol study. *Intensive Care Med* 2009; 35: 1738-48.
4. *Brunkhorst FM, Engel C, Bloos F, et al.* Intensive insulin therapy and pentastarch resuscitation in severe sepsis. *N Engl J Med* 2008; 358: 125-39.

Basem Abdelmalak MD
Daniel I. Sessler MD
Cleveland Clinic, Cleveland, OH, USA