The Critical Role of Carbohydrate Administration in Safe, Effective TGC

Rationale: Tight glycemic control (TGC) remains controversial, and safe, effective TGC elusive. Two TGC trials are analysed for root causes of differences in glycemic outcome and variability.

Methods: A retrospective analysis using records from 211 Glucontrol-A,B TGC patients (Liege, Belgium) and 393 SPRINT TGC patients (New Zealand). Glycemic targets are: Glucontrol-A and SPRINT: 4.4–6.1 mmol/L; Glucontrol-B: 7.8–10.0 mmol/L. Cohorts were matched by APACHE II and percentage males (p>0.35). Cohort and per-patient comparisons (median [IQR]) are shown for: a) blood glucose (BG) outcome; b) carbohydrate administration (all sources); c) insulin rate. Uniquely, SPRINT doses insulin based on carbohydrate given and BG; Glucontrol-A,B on BG alone.

Results: Cohort BG was: SPRINT: 5.7 [5.0–6.6], Glucontrol-A: 6.3 [5.3–7.6], Glucontrol-B: 8.2 [6.9–9.4] mmol/L. Insulin dosing was: 3.0 [1.0–3.0], 1.5 [0.5–3.0] and 0.7 [0.0–1.7] U/hr, respectively. Nutrition from carbohydrate (all sources) was: 435.5 [259.2–539.1], 311 [0.0–933], and 622 [103–1037] kcal/day, respectively. Median per-patient results: BG: 5.8 [5.3–6.4], 6.4 [5.9–6.9], and 8.3 [7.6–8.8] mmol/L; Insulin Rate: 3.0 [2.0–3.0], 1.5 [0.8–2.0], and 0.5 [0.0–1.0] U/hr; and carbohydrate administration: 384 [207–498], 104 [0–829], and 207 [0–726] kcal/day. Overall, SPRINT gave ~2x more insulin with a 3-4x narrower, but non-zero, range of carbohydrate input to achieve tighter TGC with less hypoglycemia (2% SPRINT vs 7.7% and 2.9% for Glucontrol-A,B). SPRINT had less BG<3.0 mmol/L and less hyperglycemia (BG>8.0 mmol/L).

Conclusions: Protocols that dose insulin “blind” to carbohydrate administration suffer greater glycemic variability, even if cohort-wide glycemic targets are met. TGC protocols must be explicitly designed to account for carbohydrate administration to minimise BG variability and thus mortality outcomes across cohorts and/or centres.

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