CRITICAL CARE

LETTER

Choosing the correct metrics for glucose control

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See related research by Kaukonen et al., http://ccforum.com/content/17/5/R215

In an attempt to determine whether strict glucose control (SGC) [1] was adopted in ICUs in Australia and New Zealand (ANZ) before or after the publication of NICE-SUGAR (Normoglycemia in Intensive Care Evaluation and Surviving Using Glucose Algorithm Regulation) [2], Kaukonen and colleagues examined the 'mean of the highest and lowest blood glucose level in the first 24 hours after ICU admission' (Glu_1) [3]. Assuming that a median Glu_1 of less than 6.44 mmol/L is an indicator of adoption of SGC, they conclude that SGC was not adopted before NICE-SUGAR and that this trial led to an even looser glucose control in their continent.

As the Glu_1 is calculated from blood glucose values in the first 24 hours, this metric by definition will not reflect what happens beyond the first day of ICU admission. Second, ICU algorithms for glucose control will never affect the first blood glucose level, which usually is the highest value in the first ICU day. We calculated median Glu_1 before and after successful implementation of a SGC algorithm in a large cohort in The Netherlands [4]. Whereas important metrics of glucose control changed, median Glu_1 did not (Table 1). Notably, we found a much higher median Glu_1 compared with that of Kaukonen and colleagues.

Numerous metrics are suggested as quality indicators of glucose control [5]. Most metrics differ in their definitions and many are not precise, prohibiting their applicability and hence reproducibility and comparability of research results. Median Glu_1 is not a good indicator of SGC, because of the aforementioned points, and will consequently differ among research cohorts.

Authors' reply

Kirsi-Maija Kaukonen, Michael Bailey, David, Pilcher, Neil Orford, Rinaldo Bellomo and the Australian & New Zealand Intensive Care Society (ANZICS) Centre for Outcomes & Resource Evaluation (CORE)

In our study of glycemic control in ANZ, we used Glu_1 values (mean of the lowest and highest glucose values of the first 24 hours in ICU) to determine glucose control during ICU stay [3]. van Hooijdonk and colleagues argue that Glu_1 is not sufficiently representative of glucose control over the whole ICU stay. However, previously, Glu_1 was specifically assessed for its potential use as a surrogate glucose control marker throughout the ICU stay in ANZ. To establish such a link, we studied more than 8,000 critically ill patients and 197,227 blood glucose measurements [6]. The difference between Glu_1 and the mean of all glucose measurements in ICU was 0.17 mmol/L. Accordingly, we consider Glu_1 to be a robust and validated surrogate of glucose control throughout the ICU stay in ANZ.

We agree that the first glucose value is usually high and is not affected by interventions. However, the lowest glucose within 24 hours will be measured after reaching normoglycemia (9.8 to 14.3 hours in the van Hooijdonk data) and, therefore, is affected by interventions. Accordingly, Glu_1 values are also affected. Glu_1 did not decrease in the van Hooijdonk data, even though the mean glucose level did. As we do not have access to their data, we cannot make any assumptions about why this happened. In contrast, Egi and colleagues [6] showed differences between Glu_1 and mean glucose of 0.26, 0.13, 0.12, and 0.37 mmol/L in the four different ANZ ICUs. Thus, we consider that our assumptions are sufficiently robust and our conclusions likely correct.

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Table 1 Metrics of glucose control before and after implementation of strict glucose control [4]

	1 year before implementation	2 years after implementation	*P* value
	n = 1,321	n = 2,175	
Glu_1 in mmol/L, median [IQR]	7.7 [6.6-9.3]	7.7 [6.5-9.3]	0.96
Mean blood glucose level in mmol/L per patient of all measured blood glucose levels during ICU admission, median [IQR]	7.1 [6.4-8.1]	6.5 [5.9-7.7]	<0.001
Time in hours to reach normoglycemia, median [IQR]	14.3 [7.3-26.7]	9.8 [5.2-16.7]	<0.001
Patients who reached normoglycemia, number (percentage)	1,044 (79)	1,818 (84)	<0.001

Glu_1, mean of the highest and lowest blood glucose level in the first 24 hours after ICU admission; IQR, interquartile range.

Abbreviations
ANZ: Australia and New Zealand; Glu_1: Mean of the highest and lowest blood glucose level in the first 24 hours after ICU admission; NICE-SUGAR: Normoglycemia in Intensive Care Evaluation and Surviving Using Glucose Algorithm Regulation; SGC: Strict glucose control.

Competing interests
RTMvH did consulting work for Medtronic Inc. (Minneapolis, MN, USA) and GlySure Ltd (Abingdon, UK) and received research support from Medtronic Inc. and OptiScan Biomedical (Hayward, CA, USA). PES declares that he has no disclosures to report. MJS received consultant fees from Medtronic Inc., GlySure Ltd, Edwards Life Sciences (Irvine, CA, USA), and Roche Diagnostics (Basel, Switzerland) and financial support from Medtronic Inc. and OptiScan Biomedical; all fees and financial support were paid to the institution.

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