Assessment of Glycemic Variability in Continuous Subcutaneous Insulin Infusion Therapy in Type 1 Diabetes Related to Anthropometry and Complication Status

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Introduction

We present an observational study assessing the relationship between glycemic variability (GV) and anthropometry (age, sex, body mass index [BMI]), microvascular complication status, and duration of diabetes in type 1 diabetes mellitus (T1DM) subjects treated with continuous subcutaneous insulin infusion (CSII) or multiple dose injection (MDI) therapy. Intraday GV was measured by standard deviation of glucose, mean amplitude of glycemic excursion (MAGE), *M* value, and *J* index, and interday variability was measured by the mean of daily differences (MODD).

Thirty-five subjects (19 on MDI and 16 on CSII therapy) were recruited, and the treatment groups were not significantly different. Glucose was monitored for a 48 h period for each subject using a Medtronic Gold continuous glucose monitoring system.

Overall glycemia, as measured by mean blood glucose (MBG) and hemoglobin A1c (HbA1c), was significantly lower (1.6 mmol/liter and 0.9%, respectively) in the CSII group than the MDI group (**Table 1**). Statistically significantly greater GV was found in the MDI group than in the CSII group (**Table 1**). This finding of lower GV in subjects with T1DM on CSII therapy is significant, as few studies have investigated this previously.[1] No significant difference in MBG and the degree of GV was found between males and females on both MDI and CSII therapy.

A statistically significant positive correlation was found between MAGE and HbA1c in all subjects, *M* value and HbA1c in all subjects, MAGE and HbA1c in the MDI group, and *M* value and HbA1c in the MDI group. This finding implies that HbA1c can be used to an extent to predict GV, especially in subjects treated with MDI.

A statistically significant positive correlation was found between MAGE and age in all subjects and *M* value and age in all subjects. No significant correlation was found between MAGE or *M* value and BMI or duration of diabetes.

A statistically significantly negative correlation was found between MAGE and estimated glomerular filtration rate (eGFR) in all subjects, the *M* value and eGFR in all subjects, and the *M* value and eGFR in the MDI group. The *M*

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Abbreviations: (BMI) body mass index, (CSII) continuous subcutaneous insulin infusion, (eGFR) estimated glomerular filtration rate, (GV) glycemic variability, (HbA1c) hemoglobin A1c, (MAGE) mean amplitude of glycemic excursion, (MBG) mean blood glucose, (MDI) multiple dose injection, (MODD) mean of daily differences, (T1DM) type 1 diabetes mellitus

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Table 1.
Results Comparing Glycemia and Glycemic Variability between Subjects on Multiple Dose Injection and Those on Continuous Subcutaneous Insulin Infusion

	MDI mean (standard deviation) $n = 19$	CSII mean (standard deviation) $n = 16$	p value
MBG	10.0 (2.00)	8.4 (1.5)	0.012[a]
HbA1c	8.7 (1.4)	7.8 (0.9)	0.027[a]
Standard deviation	3.8 (1.3)	2.8 (0.7)	0.008[a]
MAGE	7.5 (2.7)	5.0 (1.6)	0.003[a]
M value	14.0 (15.1)	4.8 (7.3)	0.031[a]
J index	64.9 (28.2)	44.2 (14.0)	0.013[a]
MODD	2.4 (3.1)	0.09 (1.9)	0.018[a]

[a] Indicates statistical significance at $p < 0.05$

value was found to be statistically significantly positively correlated with urine microalbumin:creatinine ratio in all subjects. No other significant correlations were found. These correlations may indicate that a higher degree of GV may be associated with, or contribute to, compromised renal function. This supports the hypothesis that GV may play a role in the development of microvascular complications in diabetes.[2,3] However, this is potentially confounded by the correlation of GV with HbA1c, itself an independent predictor of microvascular complications. No relationship between retinopathy stage and MAGE was found.

Further investigation is required in order to determine the clinical relevance of the difference in GV between the different treatment groups. Increased GV is associated with the overproduction of reactive oxygen species and may play a role in glucose-mediated endothelial damage and the development of vascular complications.[3] The findings from this study of an association between markers of nephropathy and GV may support the hypothesis of the involvement of GV in the development of microvascular complications in diabetes.

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References:

1. Bruttomesso D, Crazzolara D, Maran A, Costa S, Dal Pos M, Girelli A, Lepore G, Aragona M, Lori E, Valentini U, Del Prato S, Tiengo A, Buhr A, Trevisan R, Baritussio A. In type 1 diabetic patients with good glycaemic control, blood glucose variability is lower during continuous subcutaneous insulin infusion than during multiple daily injections with insulin glargine. Diabet Med. 2008;25(3):326–32.
2. Monnier L, Mas E, Ginet C, Michel F, Villon L, Cristol JP, Colette C. Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. JAMA. 2006;295(14):1681–7.
3. Brownlee M. Biochemistry and molecular cell biology of diabetic complications. Nature. 2001;414(6865):813–20.