Clinical factors associated with daily and day-to-day glucose variability determined by continuous glucose monitoring and the glucagon stimulation test in type 2 diabetic patients

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Background and AIM

For glucose variability induces endothelial dysfunction through oxidative stress , the risk of developing diabetic complications is related to glucose variability. We reported that oxidative stress was associated with both daily and day-to-day glucose variability in cross-sectional study. There has been no report that investigate the relationship between clinical factors including glucagon stimulation test and simultaneously daily and day-to-day glucose variability in T2DM. We studied the clinical factors associated with daily and day-to-day of glucose variability as determined by continuous glucose monitoring (CGM) and the glucagon stimulation test.

Methods and Materials

We performed a cross-sectional analysis of type 2 diabetes (T2D; insulin-treated, n=80; not insulin-treated, n=115) patients who underwent over 72 h of continuous glucose monitoring between October 2013 and April 2017 at Showa University Hospital. Correlations of clinical factors with the mean amplitude of glycemic excursions (MAGE) and mean of daily differences (MODD) in CGM were analyzed by multiple regression.

Baseline clinical characteristics of subjects

Clinical characteristics	Insulin-treated T2DM (n=80)	T2DM without insulin therapy (n=115)
Age (years)	65.3 ± 11.7	62.7 ± 13.0
Sex (male:female)	50 : 30	79 : 47
Body-mass index (kg/m^2)	25.8 ± 4.4	25.9 ± 4.5
Duration of diabetes (years)	15.8 ± 10.7	11.1 ± 8.3
Blood pressure (mm Hg)		
Systolic	129.2 ± 18.3	126.5 ± 20.6
Diastolic	73.4 ± 12.8	74.1 ± 12.1
Low-density lipoprotein cholesterol (mg /dl)	95.1 ± 25.9	99.1 ± 37.0
High-density lipoprotein cholesterol (mg /dl)	49.4 ± 14.7	46.8 ± 16.0
Triglycerides (mg /dl)	129.4 ± 75.0	137.4 ± 75.3
estimated glomerular filtration rate (ml/min/1.73㎡)	73.3 ± 24.9	77.8 ± 21.1
Fasting Plasma Glucose state (mg/dl)	129.5 ± 35.5	138.0 ± 35.6
HbA1C (%)	7.5 ± 1.3	8.0 ± 1.5
Mean sensor Glucose (mg/dl)	148.4 ± 43.2	167.4 ± 43.1
MAGE (mg/dl)	110.8 ± 43.2	110.5 ± 38.3
MODD (mg/dl)	33.2 ± 17.4	27.0 ± 9.5
Fasting C-peptide(ng/ml)	1.6 ± 0.9	2.3 ± 1.0
ΔC-peptide(ng/ml)	1.5 ± 0.9	1.9 ± 1.5

Diabetes Treatment

Clinical characteristics	Insulin-treated T2DM (n=80)	T2DM without insulin therapy (n=115)
Diabetes therapy		
Diet alone	0 (0.0)	14 (12.2)
The number of Oral hypoglycemic agent	1.3 ± 1.1	1.8 ± 1.3
Metformin	27 (33.8)	28 (24.3)
Sulfonylurea	4 (5.0)	46 (40.0)
Glinide	3 (3.8)	38 (7.0)
α-glucosidase inhibitor	23 (28.7)	24 (20.9)
Thiazolidine	13 (16.3)	15 (13.0)
SGLT2 inhibitor	4 (5.0)	8 (7.0)
Dipeptidyl peptidase 4 inhibitor	32 (40.0)	55 (47.8)
Glucose-like peptide 1 receptor agonist	14 (7.5)	28 (24.3)
Insulin		
The number of insulin injection	2.8 ± 1.4	N/A
Insulim dose (U/kg)	0.3 ± 1.3	N/A
Statin therapy	46 (57.5)	65 (56.5)

Results

(Correlation between glycemic variability and clinical factors associated with glycemic variability.)

Clinical characteristics	Insulin-treated T2DM (n=80)		T2DM without insulin therapy (n=115)	
	MAGE	MODD	MAGE	MODD
Age (years)	0.335*	0.232*	0.202*	0.252**
Body-mass index (kg/m^2)	-0.021	-0.062	0.116	0.093
Duration of diabetes (years)	0.188	0.239*	0.157	0.204*
Blood pressure (mm Hg)				
Systolic	0.001	0.181	-0.039	0.089
Diastolic	-0.178	0.006	-0.027	0.072
Low-density lipoprotein cholesterol (mg /dl)	0.055	0.082	0.235*	0.130
High-density lipoprotein cholesterol (mg /dl)	0.156	0.217	0.068	-0.053
Triglycerides (mg /dl)	-0.141	-0.073	0.313**	0.112
estimated glomerular filtration rate (ml/min/1.73㎡)	0.015	-0.095	-0.035	0.072
Fasting Plasma Glucose state (mg/dl)	0.315**	0.395**	0.426**	0.289**
HbA1C (%)	0.532**	0.318**	0.610**	0.365**
Fasting C-peptide(ng/ml)	-0.116	-0.056	0.117	-0.001
ΔC-peptide(ng/ml)	0.432**	-0.308**	-0.032	-0.094

*P<0.05, **P<0.01

Values represent Spearman`s correlation coefficients

Results

(Multivariate analysis of clinical factors associated with glycemic variability.)

Clinical characteristics	Insulin-treated T2DM (n=80)		T2DM without insulin therapy (n=115)	
	MAGE	MODD	MAGE	MODD
Age (years)				0.308**
Blood pressure (mm Hg)				
Diastolic				0.308**
Fasting Plasma Glucose state (mg/dl)	0.339**	0.365**		
HbA1C (%)			0.474**	0.383**
ΔC-peptide(ng/ml)	-0.365**	-0.273**		
Use of Sulfonylurea	0.200*		0.266**	

*P<0.05, **P<0.01

Values represent unstandardized regression coefficient (b) estimated by stepwise multiple regression analysis.

Adjusted for age, duration of diabetes, body-mass index, Systolic blood pressure, Diastolic blood pressure High-density lipoprotein cholesterol, Low-density lipoprotein cholesterol, Triglycerides, estimated glomerular filtration rate, Fasting plasma glucose, HbA1c, Fasting c-peptide, Δ c-peptide insulin use, Sulfonylurea use, Dipeptidyl peptidase 4 inhibitor use, α-glucosidase inhibitor use, Glinide use, The number of insulin injection

Conclusion

Insulin secretion is related to glucose variability in insulin-treated T2D. Poor glycemic control greatly contributes to glucose variability in T2D. SU administration increases daily glucose variability in T2D with or without insulin therapy.