Relationship between the degree of improvement in glucose metabolism and oxidative stress in type 2 diabetes patients

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Background and AIM

Previous clinical studies have reported an association between the activation of oxidative stress and daily glucose variability. Likewise, our group previously reported that oxidative stress was associated with both daily and day-to-day glucose variability. Before now, however, there have been no reports of a relationship between glucose variability and oxidative stress from an intervention study. In this study, we sought to evaluate whether glucose variability and markers of diabetic control help to improve oxidative stress in type 2 diabetes(T2DM).

Methods and Materials

The study subjects were 36 type 2 diabetes outpatients. The patients underwent 72 hours of continuous glucose monitoring (CGM) and the diacron-reactive oxygen metabolites (d-ROMs) test before and after a 6-month intervention period(Treatment target were defined FPG<130mg/dl, 2hrPG<180mg/dl, HbA1c<7%). The fasting plasma glucose (FPG), mean glucose level (MGL), mean amplitude of glycemic excursions (MAGE), mean of daily differences (MODD), and area under the postprandial plasma glucose curve (AUC_{PP}) were calculated from CGM data. Finally, the relationship between the glucose metabolism improvement and oxidative stress improvement in T2DM was evaluated.

Baseline clinical characteristics of subjects

Clinical characteristics	Means ± SD, n (%)	Clinical characteristics	Means ± SD, n (%)
Age (years)	61.6 ± 11.9	HbA1C (%)	8.4 ± 1.6
Sex (male)	28 (77.8)		
Body-mass index (kg/m²)	26.1 ± 4.7	MGL (mg/dl)	174.4 ± 40.2
Smoking (%)	6 (16.7)		
Duration of diabetes (years)	11.4 ± 8.5	MAGE (mg/dl)	116.0± 34.5
Hypertension	23 (63.9)		
Dyslipidemia	24 (66.7)	MODD(mg/dl)	28.6 ± 8.3
Blood pressure (mm Hg)			
Systolic	128.6 ± 18.1	FPG(mg/dl)	142.8 ± 24.0
Diastolic	73.0 ± 10.3		
Low-density lipoprotein cholesterol (mg /dl)	106.4 ± 29.3	AUC_{PP} (mg/dl/hr)	424.3± 279.5
High-density lipoprotein cholesterol (mg /dl)	48.6 ± 21.3		
Triglycerides (mg /dl)	148.7 ± 101.4	d-ROMs (U.CARR)	337.0 ± 58.0
estimated glomerular filtration rate (ml/min/1.73m²)	77.9 ± 24.7		

Diabetes Treatment

Diabetes treatment	Before intervention n (%)	After intervention n (%)
Diabetes therapy		
Diet alone	7(19.4)	0(0.0)
Metformin	9(25.0)	16(44.4)
Sulfonylurea	10(27.8)	3(8.3)
Glinide	3(8.3)	3(8.3)
α-glucosidase inhibitor	4(11.1)	6(16.7)
Thiazolidine	0(0)	3(8.3)
Dipeptidyl peptidase 4 inhibitor	16(44.4)	10(27.8)
Glucose-like peptide 1 receptor agonist	2(5.6)	16(44.4)
Insulin	9(25.0)	16(44.4)
Other treatments		
Lipid-lowering drugs(Statin)	11(30.6)	17(47.2)
Antihypertensive drugs(ARB)	12(33.3)	22(61.1)

Comparison of Glycemic Control and d-ROMs in the 1st and 2nd series

	1st series	2nd series	p
MGL(mg/dl)	174.4 ± 40.3	131.1 ± 24.5	<0.001
FPG(mg/dl)	142.8 ± 24.0	119.6 ± 30.5	<0.001
HbA1C (%)	8.4 ± 1.6	6.7 ± 0.9	<0.001
MAGE (mg/dl)	116.0 ± 34.5	88.8 ± 32.9	<0.001
MODD(mg/dl)	28.6 ± 8.3	26.0 ± 11.3	0.067
AUC_{PP} (mg/dl/hr)	424.3± 279.5	280.1 ± 248.9	0.025
d-ROMs (U.CARR)	337.0 ± 58.3	310.0 ± 57.5	0.030

Results

(Relationship of the change in the d-ROMs with the change in glucose metabolism variables non-glycemic clinical and laboratory variables)

	ΔFPG	ΔMGL	ΔHbA1c	ΔMAGE	ΔMODD	ΔAUC_{PP}	ΔHDL-C	ΔLDL-C	ΔTG
ΔMGL	0.642**								
ΔHbA1c	0.535**	0.693**							
ΔMAGE	0.258	0.542**	0.324						
ΔMODD	0.135	0.135	-0.010	0.515**					
ΔAUC_{PP}	0.351*	0.451*	0.304	0.671**	0.200				
ΔHDL-C	0.098	-0.225	0.099	0.056	0.039	-0.086			
ΔLDL-C	0.167	0.309	0.728**	0.166	-0.066	0.156	0.114		
ΔTG	0.268	0.269	0.206	-0.039	-0.038	-0.046	-0.188	-0.119	
ΔdROMs	0.574**	0.439**	0.403*	0.273	0.042	0.312	0.146	0.232	0.139

Results

(Independent effect of the change in markers of diabetic control on the change in the d-ROMs test results)

	Dependent variables: d-ROMs (U.CARR.)			
	β coefficient	t-value	P-value	Full-model R^2
			<0.001*	0.309
ΔMGL		0.651	0.520	
ΔHbA1c		0.802	0.428	
ΔFPG	0.574	4.083	<0.001*	

Conclusion

Improved glucose metabolism reduces oxidative stress in T2DM. Different from the cross-sectional study which is earlier data showing a strong correlation between glycemic variability and oxidative stress in T2DM, improved FPG, but not improved glucose variability or postprandial glucose, is strongly associated with oxidative stress reduction in T2DM.