Glycemic variability in patients with idiopathic chronic pancreatitis: association with pancreatic exocrine insufficiency and GLP-1

N. Tandon MD, Ph.D¹, Pramod Garg MD. DM², M.Kalaivani M.Sc, Ph.D³ Neelam Pandey MD,DM¹
Departments of ¹Endocrinology, ²Gastroenterology, and ³Biostatistics
All India Institute of Medical Sciences, New Delhi, India

Background

- Exocrine insufficiency causes malabsorption which, through several mechanisms including interference with GLP-1 secretion, may contribute to glycemic variability (GV).

Objective

- To estimate GV using continuous glucose monitoring system (CGMS) and post prandial GLP-1 responses in patients with idiopathic chronic pancreatitis (CP) with exocrine insufficiency.

Method

- Inclusion: Idiopathic CP patients
- Exclusion: Patients with pancreatitis due to alcoholism, gall stones, dyslipidemia ; any past history of GI surgery or altered gastric emptying or any other form of diabetes.
- 21 insulin treated idiopathic CP patients were hospitalised and put on a standard diet and CGMS was installed for 3 days.
- Exocrine function assessed by fecal elastase and 24 hour fecal fat estimation. Gastric emptying was estimated by 99mTc sulphur colloid scintigraphy.
- On the third day, a mixed meal test was conducted on all 21 patients and 10 healthy controls.
- Baseline and post-meal blood samples of GLP-1 (Total), Glucagon and C-peptide at 0, 30 and 60 minutes were collected and analyzed.
- Glycemic variables - SD, mean amplitude of glycemic excursions (MAGE), Lability Index (LI), J-Index, Low Blood Glucose Index (LBGI), continuous overlapping net glycemic action (CONGA), mean of daily differences (MODD), were calculated using “Medtronic CareLink iPro Software.

Results

- Out of 21, in 1 patient CGMS data was unrecorded and in 4 patients fecal fat estimation could not be done .

Results

- Patients were further categorized as those with (PEI) and without (PES) pancreatic exocrine insufficiency, based on fecal fat excretion(> or < 7gm/day) and their GV and post- prandial hormonal responses were compared.

Clinical Parameters	CP+DM+PEI (n=10)	CP+DM+PES (n=6)	p value
Age (yrs)	32.7±7.7	33.7±10.1	0.832
Sex (Male : Female)	8:2	4:2	1.000
BMI (Kg/m ²)	20.5±3.4	22.9±3.8	0.157
Duration of DM (yrs)	3 (0.5-21)	2.8 (0.5-8)	0.492
Fecal Elastase (ug/g)	20 (5-73)	41 (29-132)	0.056
HbA1c (%)	9.6±2.6	9.0 ± 0.8	0.618

CGMS Parameters	CP+DM+ PEI(n=10)	CP+DM+ PES(n=6)	p value
No. of excursions in 48 hours	6 (4-13)	5 (4-7)	0.147
High excursions in 48 hours	5 (3-7)	4 (2-5)	0.181
Low excursion in 48 hours	1 (0-6)	1 (0-2)	0.635
(%)Time spent in hyperglycemia (>3.8 mmol/l)	47 (19-81)	66 (7-83)	0.635
(%)Time spent in euglycemia (3.8-7.6 mmol/l)	44 (19-81)	33.5 (17-90)	0.792
(%)Time spent in hypoglycemia (<3.8mmol/l)	6.5 (0-25)	2 (0-13)	0.562

GV Parameters	CP+DM + PEI (n=10)	CP+DM + PES (n=6)	p value
Mean glucose (mmol/l)	9.0 ± 1.8	10.4 ± 2.5	0.205
SD (mmol/l)	3.3 ± 1.6	3.5 ± 1.2	0.768
MAGE (mmol/l)	5.7 (2.2-10)	5.9(2.8-10)	0.792
CONGA (mmol/l)	8.0 ± 1.8	9.5 ± 2.5	0.196
MODD (mmol/l)	3.6 (1- 8.2)	3.8(2.4-6.6)	0.689
Lability Index	5.2 (0.9-17)	4.6(1.5-6.5)	0.635
LBGI	2.6 (0-10.1)	2.0(0.9-3.3)	0.713

Results

- We saw preserved post-prandial GLP-1 response and glucagon response in patients with CP with coexistent DM with or without exocrine insufficiency

Discussion

- There was no statistically significant difference in CGMS data of PEI and PES groups. There was a trend towards more glycemic excursions and increased time spent in hypoglycemia in the PEI group, possibly as a result of unpredictability of meal absorption and inconsistent gut response to food products with variable fat content.
- Preserved post prandial GLP-1 response was observed in both exocrine sufficient and deficient groups, probably consequent to the stimulation of L cells by undigested food reaching the distal gut in CP patients.
- Similar observations were reported by Knop et al (2007) in a small study on eight CP patients.

Conclusions

- Our data suggest that exocrine insufficiency might modestly influence glycemic variability in patients with idiopathic CP with DM.
- Exocrine insufficiency does not influence circulating GLP-1 (Total) level and post prandial hormone responses in these patients