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ARE FIBROCALCULOUS PANCREATIC DIABETICS MORE INSULIN-SENSITIVE THAN INSULIN DEPENDENT DIABETICS ?

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Fibro-calculous-Pancreatic-Diabetes (FCPD) subjects are known to be 'ketosis-resistant', despite severe hyperglycemia which requires large doses of insulin for its control. This contrasts with 'ketosis-prone' behaviour of classic IDDM patients. Ketosis Resistance in FCPD has been explained on the of basis various hypotheses, including preservation of /3-cell function,[1] simultaneous a-cell destruction, decreased availability of substrate for ketogenesis due to decreased adipose tissue 'volume', hepatic carnitine deficiency in patients with malnutrition, etc. We studied j3-cell function and intermediates of fat metabolism, in fasting state and after oral glucose, in FCPD and matched IDDM subjects to highlight the differences between the two groups.

Material and Methods

17 patients with FCPD and 14 patients with IDDM were included in the study. FCPD was diagnosed in a subject with characteristic clinical presentation and demonstration of pancreatic calculi on plain x-ray abdomen. IDDM was diagnosed in young diabetic subjects ketonuric at initial presentation and who tended to become ketotic after short-term insulin withdrawal. The clinical and biochemical profile of the subjects is presented in Table 1.

All subjects underwent a standard OGTT as recommended by WHO (1980).[2] Blood samples (—12, —2,60 and 120 mins.) were obtained through an indwelling cannula in the antecubital vein. All samples were analysed for glucose (GOD-POD method), C-peptide (Novo kit M1221), free fatty acids, glycerol and 3-HB (Enzymatic methods-Alberti & Williamson 1972).[8]

Results

As seen from Table 1, clinical and biochemical characteristics were comparable in the two groups. Their plasma glucose showed comparable rise during

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Table 1

Comparision of patients with FCPD and IDDM

	FCPD (n: 17)	IDDM (n: 14)
Age (yrs.)	21 (12-45)	24 (8-35)
BMI (kg/m^2)	14.9(11.2-24)	16.2 (13.2-20.6)
F-Glu-cose (mg%)	206 (82-657)	297(113-499)
HbAiC (mol/1 Fru.)	99 (40-232)	122 (64-155)
Duration (mths.)	4 (1-72)	1 (1-38)
TG (mmol/1)	1.1 (0.6-9.4)	0.9 (0.5-4.5)
Cholesterol (mmol/1)	3.3 (1.8-4.7)	3.3 (1.8-5.0)

Median (Range)

OGTT (Table 2). Both groups had detectable fasting C-peptide levels, which showed small but significant rise following oral glucose (Table 2). Fasting and post-glucose C-peptide levels were comparable in the two groups. Fasting levels of NEFA, glycerol & 3-HB were all higher in IDDM subjects compared to FCPDs. After glucose load, concentration of the metabolites fell and the fall was numerically higher in IDDM (Table 3). This was because the fall was proportional to the fasting levels. Calculated as percentage of fasting levels the fall was similar in two groups.

Discussion

Ketosis resistance observed in FCPD subjects has been explained in various ways. Mohan et al found that fasting and stimulated C-peptide levels were significantly higher in FCPD subjects as compared to IDDM patients.[1]

Samal et al found that the total fasting C-peptide immunoreactivity was near normal in FCPD, but the 'reserve' was lower than controls, though higher than that of IDDM.[4] These findings imply that the jS-cell function is better preserved in FCPD as compared to IDDM, explaining thereby the ketosis resistance. It is also conceivable that there is a concomitant «-cell destruction in FCPD, leading to deficiency of glucagon-the major ketogenic hormone.

In our study, fasting levels of metabolites (products of lipolysis and ketogenesis) were significantly higher in IDDM than in FCPD. This difference persisted following glucose, the fall in the levels being parallel in two groups.

Table 2

Glucose and C-peptide response during OGTT in FCPD and IDDM patients

	FCPD (n=17)	IDDM (n-14)	FCPD v IDDM
Glucose mg/dl			
Fasting	268 ±43	285±30	—
60 min	392±40	450±37	—
120 min	403 ±37	465±34	—
C-peptide nmols/1			
Fasting	0.08±0.02	0.11 ±0.02	n.s.
60 min	0.15±0.06	0.17±0.04*	n.s.
120 min	0.20±0.100***	0.19±0.05*	n.s.

Fasting Vs 60 and 120 mins.: *p<0, .05 ***p<0.001.
mean±S.E.M.

Table 3

Metabolite response during OGTT in FCPD and IDDM patients

	FCPD (n=17)	IDDM (n=14)	FCPD Vs IDDM
NEFA mmols/l			
Fasting	0.75±0.17	1.03±0.19	n.s.
60 min	0.71±0.20*	0.75±0.14	n.s.
120 min	0.69±0.22	0.90±0.17	n.s.
Glycerol mmols/l			
Fasting	0.09 ±0.02	0.23 ±0.04	0.001
60 min	0.09 + 0.01	0.15±0.03**	n.s.
120 min	0.07 ±0.01	0.12±0.02**	0.00
3-HB mmols/l			
Fasting	0.08 + 0.03**	0.18 + 0.08	n.s.
60 min	0.05 ±0.02*	0.16±0.08	0.04
120 min	0.04 + 0.02*	0.12 ±0.04*	n.s.

Fasting Vs. 60 and 120 mins.: *p<0.05 **p<0.0
mean±S.E.M.

Thus, higher levels of metabolites in IDDM suggests better insulin action, either quantitative or qualitative, in FCPD as compared to IDDM. Since insulin and C-peptide levels, both fasting and post-glucose, were similar in the two groups, it appears that insulin sensitivity and hence insulin action is better in FCPD than in IDDM. However, the glucose response during OGTT was comparable in the two groups, This suggests that better insulin sensitivity in FCPD is differential probably only with respect to antilipolytic action of insulin.

Thus, this study implies that FCPD subjects are insulin-sensitive, which could contribute to their ketosis resistance. This is in contrast with the common belief that these subjects are 'insulin-resistant'.

However, we feel that larger doses of insulin required for control of diabetes in subjects with FCPD could be related to other causes of insulin resistance, e.g. binding with insulin antibodies. Further studies are needed to clarify this.

References

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