Exocrine Pancreatic Dysfunction in Diabetes: An Observational Study

Dear Editor,

Chronic pancreatitis is a condition characterized by irreversible destruction and fibrosis of the pancreatic parenchyma, leading to exocrine insufficiency and progressive endocrine failure leading to diabetes. Fibrocalculous Pancreatic Diabetes (FCPD) refers to the diabetes secondary to fibrocalculous pancreatitis.[1] Due to chronic exocrine insufficiency, there is diminished entry of nutrients due to malabsorption which can eventually lead to absent or blunted incretin response to meals and reduce postprandial insulin secretion.[2] However, the pancreatic enzyme replacement therapy (PERT) with mixed meals to evaluate changes in glycemic state have yielded variable results.[3]

The objective documentation of insufficiency of the exocrine pancreas is difficult and controversial. Examination of stool collected over 72 h following the intake of 100 g of oral fat daily is gold standard but the procedure is cumbersome, time-consuming, and may be unacceptable because of dyspepsia and worsening steatorrhea. Pancreatic elastase remains stable during intestinal transit[4] and can be measured in fecal elastase by an enzyme-linked immunosorbent assay (ELISA). The use of fecal elastase does not require cumbersome stool collection or a special high-fat diet, and it has a high negative predictive value and a high sensitivity in moderate to severe disease when formed stools are analyzed. Subjects with FEC <200 µg/g are considered to have pancreatic exocrine insufficiency (when FEC is <100 µg/g, insufficiency is considered severe). We undertook this study to see the prevalence and severity of exocrine insufficiency in subjects with fibrocalculous pancreatic diabetes (FCPD) and compared it with subjects of type 1 diabetes, type 2 diabetes and healthy control subjects using fecal elastase as a marker of pancreatic exocrine function.

In this observational study, 31 consecutive subjects with FCPD, 24 subjects with Type 1 diabetes, 24 patients with Type 2 diabetes and 23 healthy controls were included. Data on age, sex, symptoms of steatorrhea, duration of diabetes, and treatment details were recorded. FCPD was diagnosed by the criteria laid by Mohan *et al*.[5] Fasting blood glucose, HbA1c and fecal elastase were estimated in all. Fecal elastase was measured by the ELISA method. A fresh sample of stool was collected in a sterile container after proper labeling, immediately stored at 2 to 8°C, and tested within a week. Approximately 30 to 100 g of stool was thoroughly mixed with extraction buffer and vortexed, and then the homogeneous mixture was allowed to settle for 15 to 30 min. The supernatant was then collected and mixed with washing solution and tested. After the ELISA reaction was over, the reading was taken using a wavelength of 450 nm within 10 min of stopping the reaction. The reagent was manufactured by Merck Millipore USA. All statistical analysis was performed using the software IBM SPSS 21.0. Appropriate statistical tests like Chi-Square and Spearman Rho correlation were used.

The median (IQR) of fecal elastase in healthy control was 500 µg/g (373.45-500). In FCPD group all had severe exocrine insufficiency. The prevalence of pancreatic insufficiency in type 2 diabetes was 37.5% (severe deficiency in 25%) and in type 1 diabetes was 37.9% (severe deficiency in 16.7%). As compared to subjects with FCPD (with 100% deficiency), the FEC deficiency with significantly lower in type 2 (37.5%, $P < 0.001$) and type 1 diabetics (37.9%, $P < 0.001$). In FCPD group there was no significant correlation between fecal elastase with HbA1c, duration of diabetes. On the other hand, in subjects with type 2 diabetes fecal elastase was negatively correlated with duration of diabetes ($r = –0.582$, $P = 0.002$) and HbA1c ($r = –0.519$, $P = 0.009$).

The deficiency of fecal elastase in FCPD is not surprising. Exocrine insufficiency in FCPD is already manifest by the time the patients present with diabetes. The documentation of exocrine insufficiency may also indicate that PERT may have some therapeutic effect in better glycemic management of FCPD subjects. In subjects with T2DM, fecal elastase was negatively correlated with duration of the disease and HbA1c.[6] This is also in line of the hypothesis that suggests a significant endocrine-exocrine association of the pancreas in the pathogenesis of T2DM. Exocrine pancreatic deficiency is already documented in Type 1 DM.[7]

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Conflicts of interest

There are no conflicts of interest.

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