PANCREATIC ENZYMES: WHEN? WHY? WHAT DOSE?

Dr.Yogesh Waikar

Email: pedgihep@yahoo.com

Cell no: 8806319666

PANCREATIC ENZYMES: WHEN?

Because of the invasive nature, direct pancreatic function test is reserved for research purposes and in clinical practice, non-invasive testing is preferred. Discussion on various direct pancreatic function tests is outside the spectrum of this article which deals with options available and options that can be used in the current scenario at commercial level and are beneficial to patients suffering from pancreatic exocrine insufficiency.

Many non-invasive pancreatic function tests are available, but the perfect test does not exist. The test which has high sensitivity and good specificity to detect early pancreatic insufficiency is not available.

Qualitative measurement of a single stool specimen is useless because fat content varies with the dietary fat intake. Quantitative measurement of stool fat is cumbersome and only possible in few institutes. The 13C-MTG breathtesthasasensitivityof89%andspecificity of81% but again is available only in institutes with research settings.

Indications of Pancreatic enzyme replacement therapy are as follows:

1. Clinical: chronic pancreatitis evident with complications.

2. Endoscopy: EUS suggestive Chronic pancreatitis criteria > 3 criteria, parenchymal or ductal changes

3. E-PFT: Conwell and colleagues have replaced fluoroscopic placement of an oro-duodenal tube in an un-sedated patient with collection of duodenal fluid for bicarbonate determination by endoscopic collection while the patient is sedated, a technique that has been termed an endoscopic pancreatic function test (ePFT).2 Accuracy of the endoscopic pancreatic function test for the diagnosis of chronic pancreatitis needs to be compared properly with the gold-standardsecretin–pancreozymintest

4.S-MRCP: magnetic resonance pancreatography after intravenous secretin infusion (s-MRP) allows for a quantitative measurement of pancreatic secretion volume with a major advantage of of providing information about both ductal changes and function.3Further studies are needed.

5. Biochemical test: study, serum magnesium level of lower than 2.05 mg/dl has been shown to predict Pancretic enzyme insufficiency with a sensitivity of 88% and receiver operating characteristic area under the curve of 81%4

6. Stool: elastase 1: FE-1 reaches normal levels by day 3 in term newborns and by 2 weeks in infants born before 28 weeks of gestation. 5A faecal elastase concentration higher than 200 Ug /GM is considered as normal. Concentrations lower than 50 ug/g, are related to exocrine pancreatic insufficiency. Although faecal elastase quantification is not sensitive enough to detect patients with mild chronic pancreatitis ,its sensitivity in cases of moderate-to-severe disease is very high, close to100% Pancreatic elastase is highly stable along the GI transit and the faecal concentration of this enzyme significantly correlates with the amount of enzyme secreted by the exocrine pancreas. Methodology used to estimate the stool elastase 1 is human based hence porcine pancreatic enzyme supplement doesn't affect its value. Hence no need to stop PET before the test.6

The fecal chymotrypsintest is a less reliable test to evaluate EPI. But may be used to evaluate treatment efficacy and compliance.7 The chymotrypsin activity is measured from spot stool samples with a cut of value of <3 U/g Chymotrypsin can be variably affected during intestinal transport and may be diluted in the presence of concomitant diarrhoea. The test has a sensitivity ranging from 50% to 80% for advanced EPI but only 50% for mild to moderate EPI. Another disadvantage of this test is that patients have to stop PERT two days prior to the stool collection8

7. Trial: Empirical clinical response to PERT is also one of the ways to understand and detect chronic pancreatic insufficiency.

PANCREATIC ENZYMES: WhY?9.10

Clinically evident EPI with steatorrhoea occurs only when 90% of the pancreatic function is lost. Advanced maldigestion secondary to CP is associated with deficiencies of fat-soluble vitamins (vitamins A,D,E,andK),magnesium,calcium,zinc, and folicacid. Early detection and effective treatment of EPI is important to prevent morbidity and mortality.

Every patient with EPI and maldigestion, independent of the degree of steatorrhoea and presence or absence of associated symptoms, should receive PERT. The main focus in the management o f EPI is to prevent weightloss,EPIrelatedsymptoms,vitamindeficiencies, and to improve the nutritional status.

The most important clinical parameter to monitor treatment efficacy is body weight.

PANCREATIC ENZYMES: WHAT DOSE?11,15

Dose of pancreatic enzymes contains 1,000 to 2,500 U lipase/kg/meal. Adequacy of treatment is typically determined on clinical grounds.
Infants may require higher doses 2000-4000 lipase unit/120 ml
4year dose requirement may reduce to 400 to 500 lipase unit /kg/meal

For infants the capsule may be opened and spread over acidic food like rice or cereal.

For adolescence patients each meal may require 10,000 to 20, 000 lipase unit and up to 10, 000 lipase unit for each snack. Maximum dose suggested is 10,000 lp / kg/ day.Adult dose: 25,000 to 75,000 lipase unit / meal.

Comparative analysis of various enzyme preparations available in market has shown that enzyme contents were comparable, but the percentage of lipase activity after dissolution varied12

Half of the dose should be given 20 min prior to meal and remaining half in halfway of meal for appropriate delivery of enzymes.
Dietary counseling is also important. Patient or parent adjusted PERT dose is useful in most of the circumstances.

Most common cause of Treatment failure is under dosing. Max dose tested in adults/ cystic fibrosis children being 10,000 lipase unit / kg/ day. If the treatment response remains unsatisfactory, inhibition of gastric secretion can be attempted by administration of a proton pump inhibitor. If the patient still not responds, other diseases such as coeliac disease and bacterial overgrowth, which may also cause maldigestion and steatorrhoea, should be reconsidered.13,14

A last resort may be the restriction of fat. This should be imposed under supervision of a dietician.

SIDEEFFECTS:

Transient nausea, bloating, diarrhoea and hypersensitivity. Fibrosing colonopathy after using very high doses of the enteric-coated micro- minisphere preparations. 15

Refrences:

1. Chong AK, Hawes RH, Hoffman BJ, et al. Diagnostic performance of EUS for chronic pancreatitis: a comparison with histopathology. Gastrointest Endosc 2007;65:808-14
2. Conwell DL, Zuccaro G Jr, Vargo JJ, et al. An endoscopic pancreatic function test with synthetic porcine secretin for the evaluation of chronic abdominal pain and suspected chronic pancreatitis. Gastrointest Endosc 2003;57:37-40.
3. CsakóL.Diagnosisofearly-stagechronicpancreatitisbysecretin-enhancedmagneticresonancecholangiopancreatog-raphy.JGastroenterol2007;42(Suppl.17):113–7.
4. Lindkvist B, Dominguez-Munoz E, Luaces-Regueira M, Castiñeiras-Alvariño M, Nieto-Garcia L, Iglesias-Garcia J. Serum nutritional markers for prediction of pancreatic exocrine insufficiency in chronic pancreatitis. Pancreatology 2012;12:305–10

5. Kori M, Maayan-Metzger A, Shamir R, et al. Faecal elastase 1 levels in premature and full term infants. Arch Dis Child Fetal Neonatal Ed 2003;88:F106–8.
6. J.E. DomínguezMuñoz/BestPractice&ResearchClinicalGastroenterology24(2010)233–241)
7. LayerP,KellerJ,LankischPG.Pancreaticenzymereplacementtherapy.CurrGastroenterolRep 2001Apr;3(2):101e8
8. Lieb2ndJG,DraganovPV.Pancreaticfunctiontesting:heretostayforthe21stcentury.WorldJGastroenterol2008May 28;14(20):3149e58
9. BrunoMJ ,HaverkortEB, TijssenGP, etal. Placebo controlled trial of enteric coated pancreatin microsphere treatment in patients with unresectable cancer of the pancreatic headregion.Gut1998Jan;42(1):92e6.
10. MundlosS,KuhneltP,AdlerG.Monitoringenzymereplacementtreatmentinexocrinepancreaticinsufficiency usingthe cholesteryloctanoatebreathtest.Gut1990Nov;31(11):1324e8
11. Walker t/b of ped gastro.
12. CaseCL,HennigesF,BarkinJS.Enzymecontentandacidstabilityofenteric-coatedpancreaticenzymeproductsinvitro. Pancreas2005Mar;30(2):180e3.
13. RamoOJ,PuolakkainenPA,SeppalaK,etal.Self-administrationofenzymesubstitutioninthetreatmentofexocrine pancreaticinsufficiency.ScandJGastroenterol1989Aug;24(6):688e92.
14. DelchierJC,VidonN,SaintMarcGirardinMF,etal.Fateoforallyingestedenzymesinpancreatic insufficiency:comparison of two pancreatic enzyme preparations. Aliment Pharmacol Ther1991Aug;5(4):365e78
15. Best Practice&ResearchClinicalGastroenterology24(2010)337e347