To Find Out the Efficacy of Pancreatic Enzyme Supplement In Improving the Quality Of life in Patients with Chronic Pancreatitis

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ABSTRACT

BACKGROUND AND OBJECTIVE

Inflammatory pathology of pancreas resulting in irreversible tissue destruction and progressive conversion of pancreatic tissue to fibrous tissue is known as chronic pancreatitis. Management of chronic pancreatitis differs in different parts of our country and also differs between centers in same place. Pancreatic diseases have taken a great toll in our society in form of diabetes and pancreatitis. Chronic pancreatitis progressively, but definitely leads to malnutrition and diabetes. Prevalence in southern India is 114-200 cases per 1,00,000 populations.

Abdominal pain and malnutrition due to chronic pancreatitis goes in a vicious cycle and these patients become addicted to narcotic analgesic in addition to ethanol causing them to lose job, homes and families, spreading social insecurity

Pancreas secretes pancreatic juice rich in amylase, lipase and protease. When secretions in chronic pancreatitis fall below 10% of normal, then fat and protein digestion is impaired. After 10 years of chronic pancreatitis development of symptoms of PEI [pancreatic exocrine insufficiency] can be anticipated. Acinar cell loss of 90% leads to steatorrhea and diarrhea. Most of these patients with PEI and CP have abdominal pain and malnutrition.

Hence our humble effort is to study the efficacy of pancreatic enzyme supplements in improving the quality of life in these chronic pancreatitis patients in our part of the country.

METHODS

Chronic pancreatitis patients who come to Coimbatore Medical College hospital as out-patient and in-patient were enrolled in study after proper informed consent. Stool sample was collected for qualitative and quantitative stool fat globules test/analysis from patients who are CT and ultrasound proven cases of chronic pancreatitis. Those who have stool fat globule test positivity –fat globules of size larger than 50µ diameter, take average of size in 5 HPF-[X]. No. of fat globules in 5 HPF (high power field) take average of it –[Y]. The product of [X × Y] number-size product if > 500 is regarded as significant steatorrhea for any patient with fat globules in stool with 94% sensitivity and specificity. Fifty such patients with chronic pancreatitis and PEI are selected. Also they are having clinical steatorrhea and malnutrition. Malnutrition is regarded as loss of > 10% of body weight within last six months.

Study and control group are selected by randomization. Single blind prospective study is carried out for 35 weeks. Study group is given pancreatic enzyme supplement in adequate doses. Periodic follow up from baseline is done at 7, 14, 28 and 35 weeks. Body weight, BMI, nutritional laboratory parameters are measured. Hematological test for safety profile of enzymes are also done periodically. Stool fat globules also tested at 14 weeks to rule out failure of therapy. Quality of life is assessed using SF 36 health survey questionnaire at baseline and end of the study. Clinical symptom improvement is also assessed – pain, flatulence, stool characteristics

RESULT-

Enzyme supplementation in study group has shown a significant improvement in body weight and BMI (P value=0.01) , S. Albumin ( P value = 0.01), total protein (P value = 0.006) ,hemoglobin ( P value =0.01).when compared to controls. Quality of life is assessed using SF 36 health survey questionnaire at baseline and end of the study. Clinical symptom improvement is also assessed – pain, flatulence, stool characteristics

CONCLUSION

There was improvement in Quality of life in patient with PEI due to chronic pancreatitis to statistically
significant levels with pancreatic enzyme replacement therapy. Pancreatic enzyme supplements were satisfactory in terms of safety, tolerability and patient compliance.

KEY WORDS - Chronic Pancreatitis, Pancreatic exocrine insufficiency, Pancreatic enzyme replacement therapy, Pancreatic enzyme supplements, Quality of life.

1. INTRODUCTION

Chronic pancreatitis is a chronic inflammatory disease of pancreas where there is irreversible tissue destruction and progressive conversion of pancreatic tissue to fibrous tissue, eventually leading to malnutrition and diabetes. Less than five percent prevalence is demonstrable in autopsies. As per recent survey conducted in various countries in the Asia-pacific region, the prevalence of chronic pancreatitis in southern India is estimated to be 114-200 cases per 1,00,000 populations. In western population its 27.4 cases per 1,00,000 population is regarded as overall prevalence1.

Pain in chronic pancreatitis is what brings the patient to medical care. Pain is usually multifactorial - inflammation, duct obstruction, high pancreatic tissue pressure, neuropathy, fibrosis and other causes. Pain and malnutrition goes in a vicious cycle and they become addicted to narcotic analgesics causing social insecurity by losing job, homes and families2.

Fifteen to forty percentages of patients do not experience pain relief even after drainage procedures. Head of pancreas is considered ‘pacemaker’ of disease in chronic pancreatitis pain. So surgical excision is a debilitating procedure and requires high volume centres.

Pancreatic juice plays an important role in digestion. Secretion of pancreatic juice occurs more importantly during intestinal phase when chime enters the duodenum. Presence of fatty acids, amino-acids and HCl acid in duodenum is most potent stimulant, for exocrine pancreatic secretion. Pancreatic juice contains lipase, protease and amylase. Prevalence of pancreatic exocrine insufficiency in CP increases in proportion to disease duration3.

Pancreatic Enzyme supplement contain digestive enzymes to help digestion. They are available as over-the-counter products as nutritional supplements, also as prescriptive forms. Dosage is patient tailored.

Starting with smallest dose and should not exceed 2500 lipase units/kg of body weight per meal4. Enzyme replacement will lead to increased quality of life due to relief of steatorrhea and abdominal pain. Enzyme supplementation leads to weight gain, improvement in malnutrition and also complications like osteoporosis and micro-nutrient deficiency. Progression of disease can be delayed5.

With available facilities in our set up, our efforts to study patients with chronic pancreatitis (CP) non-invasively at variable points in time. Study shall allow us to find out the improvement in quality of life (QOL) in these CP patients in our part of the country by providing pancreatic enzyme Replacement therapy (PERT)

REVIEW OF LITERATURE

In chronic pancreatitis bizarrely distributed pathological changes are seen. Inflammation resets to nodular scarring and lobular fibrosis and healing by indurations. Thicker the sheets of fibrosis, the lesser the acinar cell mass occur and there is ductular dilatation. Ductular dilatation is accompanied by dysplasia and cuboidal cells predominate. Mononuclear infiltrates and patchy necrosis are not uncommon. In minor cases acini and islets are preserved but for cost of cystic changes. Severe cases fibrosis coalesce over broad areas and there is destruction of acinar architecture and loss of islet cells. Thickened vessels and neural trunk become prominent due to tissue loss. In small ductal dilatation sometimes small calculi can be found out. Here hypertrophied ductular epithelium found in minor ductules, together with peri lobular fibrosis.

Fibrosis generates from PSC activation. Pancreatic stellate cell (PSC) cytoplasmic processes engulf acinar cells normally. They are rich in lipid vacuoles and pliable. Once activated and loss of lipids and proliferation leads to perilobular fibrosis as they transform themselves to myofibroblasts. They respond to various growth factors but they importantly secrete collagen type I & II and fibronectin.

Definition

PEI is defined as maldigestion because of inadequate pancreatic enzyme activity. This can be due to
- insufficient enzyme production
- insufficient enzyme activation
- early enzyme degradation

Classification of PEI (PANCREATIC EXOCRINE INSUFFICIENCY)

1. Primary PEI:
Problems in the pancreas
- destruction
- innervation
Chronic pancreatitis, cystic fibrosis, post necrotizing acute pancreatitis status are some of the parenchymal diseases.
Deficiency of Parenchyma

- Obstruction (papillary tumor)
- Decreased endogenous stimulation (Celiac disease, Crohn's disease, DM)

Inactivation of enzymes

Zollinger Ellison syndrome due to duodenal hyperacidity, tetrahydrolipstatin.

2. Secondary PEI

Enzymes are released but do not work

- anatomical changes
- deregulated activation
- deregulated inactivation
- postcibal asynchronia

S/P Gastric surgery

- Gastric resections
- Short bowel syndrome
- Roux – en – y anastamosis

PEI associated with chronic pancreatitis

Alcohol consumption causes most cases of chronic pancreatitis - 60 - 70%. Cholelithiasis, Hereditary Pancreatitis, infantile malnutrition, cystic fibrosis and of anatomic variants like pancreas divisum, annular pancreas, papillary stenosis constitute 10% of cases. Rest 20% has idiopathic etiology.

Alcohol affects intracellular transport and Secretion of enzymes, so enzymes tend to co-localise and activation of lysosomes leads to auto digestion of cells. Cell destruction leads to a high protein and loss of acini leads to low bicarbonate secretion classical of chronic alcoholic pancreatitis. Together with reduced volume and increased concentration leads to precipitation of proteins in ducts. Naturally Calcium Carbonate precipitation is prevented by Lithostathine (Protein in Pancreatic Juice). Lithostathine is lacking in chronic pancreatitis. Small ductules are plugged with zymogen membrane associated protein GP2, which usually precipitates in chronic pancreatitis.

CHRONIC PANCREATITIS AND PEI

Pain is common symptom for which treatment is sought in chronic pancreatitis. It will cause decrease oral intake and will worsen the quality of life. 90% of acinar cell loss can lead to steatorrhea, diarrhea. Malnutrition can lead to anemia, osteopenia. Diabetes can develop in 40-80% of cases. Usually develops after PEI has developed.

Course of disease of chronic pancreatitis is that at least 12 months interval to detect complications.

CT of pancreas helps to diagnose chronic pancreatitis findings being

1. Dilated pancreatic duct (68%)
2. Parenchymal atrophy (54%)
3. Pancreatic calcifications (50%)

Others are focal pancreatic enlargement, peri pancreatic fluid collection, biliary duct dilatation and irregular pancreatic parenchyma contour.

Who will develop pancreatic exocrine in sufficiency?

In principle at diagnosis, more though after 10 years of disease, development of symptoms of PEI can be anticipated at time of diagnosis pancreatic function test should be employed. A typical symptom of advanced PEI is steatorrhea. Elevated blood amylase has become one of cornerstone in diagnosis of (acute) pancreatitis.

In a study, parameters such

- Pre-albumin
- Mg, Zn
- Vit 25-OH Cholecalciferol
- Retinal binding protein.

A decrease in these parameters in chronic pancreatitis can be taken as PEI. But pancreatic function tests are ultimate

- A non-invasive acceptable study is measurement of fecal elastase1 level

<table>
<thead>
<tr>
<th>Test</th>
<th>Normal</th>
<th>Mild to moderate PEI</th>
<th>Severe PEI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fecal elastase-1 test</td>
<td>&gt;200 mg/g</td>
<td>100-200 mg/g</td>
<td>&lt;100 mg/g</td>
</tr>
</tbody>
</table>

Fecal fat and weight estimation test(24 hr fecal fat test)

If stool fat exceeds 7g/day after a nutritional intake of 100 g of fat/day over 3 days suggests steatorrhea.

- Secretin test (SPT) is gold standard but it is rarely done and it is invasive test.
- C13 breath test (mixed triglyceride) is an alternative radiolabelled triglycerides given if digested and absorbed. It is detected in breath in percentages. 100%-Normal <90% -Severe.

It is not available widely in India.

- A practical test in India is qualitative and quantitative microscopic detection of fecal fat globules in fecal sample.

The No. of fat globules were estimated separately in the diameter ranges of <25 μm , 25 to 50 μm, and greater than 50μm.
Five high-power fields (HPF) are counted. The average number of globules [X] determined within each size-range from the 5 HPF, was multiplied by the midpoint size-range (i.e., 2.5, 8, 15.5, 30.5, and 60.5 μm) [Y] to get a statistically significant size-number product [XY]. It is calculated for all size ranges.

Average size of the fat droplets [Y] within each size range represents, the size range midpoint. In any fat globule size-range, it was found that--

Product [XY] of less than 200 rules out steatorrhea, product between 200-500 is indeterminate and have to go for further tests for steatorrhea.

**If more than 500 confirms steatorrhea**
with 94% sensitivity and specificity.  

So in India, even if these tests are not available, a patient with CP having malnutrition and clinical white/watery stools (steatorrhea) can be regarded as having PEI. And can be given enzyme supplement, nutrition improvement can be assessed. If malnutrition is corrected it shows it was due to PEI. PEI test are mainly in detecting steatorrhea, which is the leading symptom. This is because pancreas although secrete lipase, protease and amylase only lipase has no substitution from anywhere inside body. Amylase and protease are also present in salivary and intestinal secretions.

**Pancreatic Enzyme supplement**

Ideal pancreatic enzyme supplement should be mimicking pancreatic enzyme function in body.

1. Its activity for all three composants (fat, protein, carbohydrate) should be similar to pancreatic enzyme function.

2. Gastric acid should not hamper efficiency of the supplement.

3. It should be comfortable to the patient.

A Dutch Alexander Fles in 1859 grounded “veal pancreas” in a mortar, freshly prepared for a patient and given as a “sandwich” (between wafers). So it was a raw material and difficult for the patients. Later on, pancreatic enzyme powder was refined but it was instable in acid milieu. Later on tablet form came but, if there was a delayed pyloric passage it becomes unstable in acid medium.

So tablets were coated with films and made acid resistant. But large particles mixed insufficiently with food and delayed passage through pylorus and it was ineffective. So micro tablets were produced particles of size 2mm but still it had inadequate pyloric passage. And released enzymes became inactive. Micro spheres were pancreatic enzyme preparations which are acid resistant and pyloric passage easy and equal mixture with chymus. Released enzymes were active.

When secretions in chronic pancreatitis falls below 10% of normal then fat and protein digestion is impaired, so we have to supplement amylase, lipase and proteases that is pancreatic enzyme supplements.

Two major preparations in used are  
1. Pancreatin
2. Pancrelipase

Alcohol derived extracts of hog pancreas with limited amount of lipase and proteolytic enzymes are pancreatin. Pancrelipase is an enriched preparation. On a per weight basis pancrelipase has a dozen times lipolytic activity and four times proteolytic activity when compared to pancreatin. So pancrelipase is widely used.

As stated above pancrelipase is available worldwide as enteric coated and non-enteric coated preparations. Non enteric coated preparations (viokase tablets or powder) should be given along with proton pump inhibitors or H2 antagonists for acid suppression.

Acid suppression therapy was not required if enteric coated formulations was used, in 2006, FDA announced that pancreatin is a prescription medicine not a dietary supplement. All products must undergo re-approval process. No simplified approval of “OTC” (over the counter) at present. Three formulations are approved for use (Creon, Pancreaze and Zenpep) all being enteric coated.

Dosing of pancrelipase should be patient tailored according to age and weight of patient, extend of pancreatic insufficiency and dietary fat consumption. Enzyme activity indicated in international units or USP units One IU is equal to two/three USP units. Initiating dose is usually 20,000 to 30,000 IU (90,000 USP) of lipase activity in the prandial and post prandial period.

This dose is considered adequate to treat steatorrhea and bring it to clinically insignificant level. Poor mixing of granules with food and slow dissolution and release of enzyme are cause of ineffectiveness of enteric-coated formulations. Response can be improved by Gradually hiking dose, changing to a different formulation Suppression of gastric acid, ryles tube patients microspheres can be mixed with enteral feeds and given, Pancreatic enzyme are well tolerated. Oropharyngeal mucositis can be avoided by swallowing the capsules rather than chewing. Diarrhea and abdominal pain can occur due to excessive dosing. Hyperuricosuria and kidney stones may occur due to high purine content of pancreas extracts. Colonic strictures were only reported in cystic fibrosis. Who received high dose...
and had high lipase activity. High dose formulations were banned.

Pre requisites for PERT:
Pancreatic enzyme replacement therapy (PERT) has certain prerequisites
1. Diagnosis is established by fecal elastase1 test in borderline cases. Evident steatorrhea in a chronic pancreatitis patient only do tests for fecal fat globules, if present suggests chronic pancreatitis with PEI. Also ultra sound and CT evidence of chronic pancreatitis with some malnutrition or under nutrition clinically can be taken as PEI.

PANCREATIC ENZYME REPLACEMENT THERAPY – PERT

What is sufficient dose?
Dose depends on the severity of disease, and symptoms of the patients. Initial dose is 20,000 to 30,000 IU of lipase. This is considered adequate to treat steatorrhea and bring it to clinically insignificant levels. Our aim is to treat not only symptoms but also malnutrition in such cases it may be necessary to use slightly higher dose and the patient should be improving such cases 30,000 IU lipase as starting dose is recommended. In case of insufficient effect pancreatic dose should be doubled or tripled provided no side effects are there. Pancreatin granulates and / or gastric acid blockade (PPI) can also be helpful to increase the effectiveness.

How to evaluate success of PERT
Success or Compliance can be monitored by variety of options.Clinical improvement of the patient, decrease in pain and improvement of gastrointestinal symptoms are sufficient criteria to evaluate success. There is a remarkable reduction in stool frequency. Formed stool consistency is regained.

➢ Flatulence will decrease remarkably.
➢ BMI Increase
➢ Fecal elastase test percentage is reduced or becomes negative.
➢ Fecal fat excretion is quantified after a standardised meal (24hr fecal fat).
➢ Disappearance of fat globules
➢ 13C MCT breath test-Radiolabelled Carbon-13 is given in medium chain triglycerides and its digestion leads to detection of C13 in CO2 after metabolism.
➢ It can be quantitatively measured. In non-responders we can use CFA, 13C Breath Test.

MATERIALS AND METHODOLOGY

STUDY DESIGN

➢ It is a prospective study design. The research population is all patients with chronic pancreatitis and PEI attending General Surgery Department as in-patient and out- patient in Coimbatore Medical College Hospital
➢ Randomised ,single blind study and study was conducted in best manners and was approved by independent Ethics Committee of CMCH
➢ Sample size: 50 patients
➢ Duration of study is 12 months ( september 2013 – september 2014)

PRIMARY OBJECTIVE :

1) To assess the efficacy of pancreatic enzyme supplements in improving quality of life in patients of chronic pancreatitis with PEI

SECONDARY OBJECTIVE:

2) to find out the safety & tolerability of pancreatic enzyme supplements in chronic pancreatitis with PEI, also patient compliance

STUDY DESIGN FORMATION

To analyze patients attending CMCH out-patient department and those who get admitted due to acute exacerbations of chronic pancreatitis
Group 1: chronic pancreatitis patients >18yrs age
Group 2: control group consisting of age & sex matched chronic pancreatitis patients

MATERIALS:

➢ Study data collection formats
➢ SF-36 questionare in local language.
➢ Paper
➢ Pencil
➢ Pancreatin tablets
➢ Weighing machine
➢ Inch tape

PERSONNEL:

➢ Surgeons of CMCH General surgery department
➢ Nursing staff
➢ Laboratory personnel
➢ Radiologist

INCLUSION CRITERIA:

➢ All patients diagnosed of chronic pancreatitis and pancreatic exocrine insufficiency
➢ Not on PERT preparations for 3 months

EXCLUSION CRITERIA:

➢ In all groups individuals suffering from known systemic diseases such as gout ,renal diseases ,cardiovascular diseases ,liver
disorders, thyroid and lipid metabolism disorders, malabsorption syndromes.

- Patients below 18 years
- Patients undergoing surgical procedure for chronic pancreatitis
- Patients on medications affecting uric acid & lipid levels but medications affecting duodenal, gastric pH, gastric emptying, bile secretion were permissible at stable doses.

**METHOD**

- Patient admitting with acute exacerbation of chronic pancreatitis and chronic pancreatitis patients attending OP department with c/o abdominal pain, previous history of acute pancreatitis will be examined & detailed clinical history will be taken for all the patients. Thorough physical examination will be done for all patients.

- Stool sample was collected for qualitative and quantitative stool fat globules test/analysis from patients who are CT and ultrasound proven cases of chronic pancreatitis. Those who have stool fat globule test positivity –fat globules of size larger than 50µ diameter, take average of size in 5 HPF-[X]. No. of fat globules in 5 HPF (high power field) take average of it – [Y]. The product of [ X × Y ] number-size product if > 500 is regarded as significant steatorrhea for any patient with fat globules in stool with 94% sensitivity and specificity.

- Fifty such patients with chronic pancreatitis and PEI are selected. Also they are having clinical steatorrhea and malnutrition. Malnutrition is regarded as loss of > 10% of body weight within last six months.

- Those patients with diabetic features are described as confounding factor and shall be eliminated by proper matching.

- Randomization will be done using table of random numbers

- Informed consent will be taken

- Detailed personal history-smoking, tobacco chewing, gutka & alcoholism will be taken. Abstinence from ethanol and tobacco is followed strictly.

- Each patient will be followed up for 35 weeks; study group will be given pancreatic enzyme capsules 2 per large meal, thus 3 times a day. Medication will be provided in packets when they come for study visit.

- Pancreatic enzyme supplements (pancreatin) are alcohol derived extract of hog pancreas with relatively low concentrations of lipase and proteolytic enzyme. Pancrelipase is enriched preparation 12 times the lipolytic and 4 times proteolytic activity of pancreatin. Pancrelipase are rapidly inactivated by gastric acid so they are enteric coated. Enzymatic activity listed in international unit or USP units. Therapy is initialized at doses that provide 60,000 – 90,000USP units (20-30,000 IU) of lipase activity sufficient to reduce steatorrhea to clinically insignificant levels. Pancreatic enzyme supplements are well tolerated. The capsules should be swallowed not chewed as may cause Oropharyngeal mucositis. Excessive dose may cause diarrhea and abdominal pain and may increase incidence of gout.

- Body weight, BMI to be measured at screening, baseline, 7wks, 14wk, 28 wks and end of study 35 wk.

- Nutritional laboratory parameters-total cholesterol, TG, HDL, LDL, Total protein, serum Albumin, sampled at baseline,14wk and 35 wk

- Stool fat globules will be seen at baseline and 14wk(to rule out failure of therapy) and 35wk.Subjects provides information on number of stools per day, their consistency(hard/formed, normal/soft/watery) flatulence(none/mild/moderate/severe) abdominal pain (none /mild/ moderate/ severe)

- Quality of life was assessed using the SF36 HEALTH SURVEY questionnaire at baseline and at end of study

- Safety evaluation for recorded adverse effects of drug were assessed,vital signs (at all point of time),physical examination(all time points)lab safety tests (baseline , 7 wks,14wks and 35wks)include haematological analyses(Hb, PCV,RBC count,WBC count and platelets)biochemical analyses (fasting glucose, creatinine urea ,total bilirubin ,SGOT,SGPT,ALP,URIC ACID)

- In addition to standard treatment regimen administered in our institution for patients of chronic pancreatitis the study group (cases) is additionally receive oral supplementation of pancreatic enzymes;

- Standard of care in our institution includes- analgesics like paracetamol, tramadol, tricyclic antidepressants, Multivitamine tablets, Proton pump inhibitors, ranitidine

- Efficacy of our treatment was assessed using improvement in clinical symptoms and proportion of patients having stool fat globules negative at end of study, and improvement in BMI is taken as face value, Improvement in albumin and cholesterol values and clinical global impression of
disease compared to start of study will be evaluated.

DEFINITION OF VARIABLES

✓ Age is a continuous variable
✓ Sex is considered nominal discrete variable
✓ Body mass index is a continuous variable.

RESULTS

DATA COLLECTION

- The data we have are not the data we want
- The data we want are not the data we need
- The data we need are not available

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The study comprised of 50 patients who were studied prospectively for a period of 12 months and observations were as follows, one patient withdrew consent and another patient lost to follow up.

DESCRIPTIVE STATISTICS

AGE DISTRIBUTION

Study patient’s age ranged from 19 yrs to 60yrs and most of them fall in age range of 41 – 50 Yrs of age.

Table 7: Age Distribution

<table>
<thead>
<tr>
<th>AGE RANGE</th>
<th>NO. OF PERSONS</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-20 YEARS</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>21-30 YEARS</td>
<td>6</td>
<td>12%</td>
</tr>
<tr>
<td>31-40 YEARS</td>
<td>16</td>
<td>32%</td>
</tr>
<tr>
<td>41-50 YEARS</td>
<td>20</td>
<td>40%</td>
</tr>
<tr>
<td>51-60 YEARS</td>
<td>6</td>
<td>12%</td>
</tr>
</tbody>
</table>

Graph 1 : Age Distribution

Table 8: Statistics of Age

<table>
<thead>
<tr>
<th>AGE</th>
<th>MEAN</th>
<th>STANDARD DEVIATION</th>
<th>NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>CASES</td>
<td>40.52</td>
<td>10.01</td>
<td>25</td>
</tr>
<tr>
<td>CONTROLS</td>
<td>41.16</td>
<td>9.31</td>
<td>25</td>
</tr>
<tr>
<td>TOTAL</td>
<td>40.84</td>
<td>9.67</td>
<td>50</td>
</tr>
</tbody>
</table>

Least common age group is less than 20yrs 4%
Percentage of patients fall in 31-40 yrs 32%
Percentage of patients falls in 21-30 and 51-60yrs 12%
Median age = 42. Max age = 60

SEX DISTRIBUTION

Out of 50 patients six females and rest 44 were male patients. Male to female ratio being — 7.3 : 1

Graph 2: Sex Distribution

PRESENTING SYMPTOM

Patients mostly presents with an abdominal pain, they may be admitted with an acute exacerbation of chronic pancreatitis or it can be abdominal pain due to maldigestion. Site and further distinction are not made in the study.

Stool consistency-complain of watery stools

Flatulence

Abdominal pain is there for 100 % of all patients, but only 24 patients had severe pain at start of study. Patients with stool frequency more than 5 times a day are 20 in number. Watery stools occurred in 31 patients. Flatulence was problematic for 40 patients. Deranged blood sugar was found in 4 patients and diabetes being considered as confounding factor all was eliminated by matching, so anapcreatic diabetes will not be discussed in results of this analysis as a symptom of chronic pancreatitis. Diabetes is only 8% in our study.

Table 9: Symptoms of Cases

<table>
<thead>
<tr>
<th>SYMPTOMS</th>
<th>At baseline</th>
<th>At 35 wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain(severe)</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Abdominal pain(moderate)</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Stool consistency (Watery)</td>
<td>15</td>
<td>72%</td>
</tr>
<tr>
<td>Stool frequency (&gt;5/day)</td>
<td>13</td>
<td>76%</td>
</tr>
<tr>
<td>Flatulence</td>
<td>Moderate = 19</td>
<td>Moderate = 76%</td>
</tr>
<tr>
<td>Mild = 4</td>
<td>Mild = 16%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mild = 17</td>
</tr>
</tbody>
</table>
At start of study:

**GRAPH 3: SYMPTOMS AT BASELINE**

- Abdominal pain
- Stool frequency
- Stool consistency
- Flatulence

At end of 35 completed weeks we notice the following abdominal pain severity has come down to less than 5. Watery stools are also not bothersome. Flatulence has also decreased considerably.

**GRAPH 4: SYMPTOMS AT 35 WKS**

**GRAPH 5: ABDOMINAL PAIN AT BASELINE**

After giving pancreatic enzyme supplements the pain has come down and patients had improved quality of life.

**GRAPH 6: ABDOMINAL PAIN AT 35 WKS**

**GRAPH 7: FLATULENCE AT BASELINE**

**GRAPH 8: FLATULENCE AT 35 WKS**

After giving pancreatic enzyme supplements flatulence has come down to minimal for most patients.

**GRAPH 9: STOOL FAT GLOBULES**
Stool fat globules were tested for all patients, was found 100% positive for all patients with clinically evident Steatorrhea. Patients in whom enzyme preparations were used showed disappearance of fat globules in 50% by 2 weeks of study. Controls continue to have fat globules positivity. Stool fat globule positivity is taken as significant only when stool sample showed fat globules of size larger than 50µ (X) and their number in 5 high power field average is taken (Y). They are multiplied \[X \times Y\] and product is more than 500 is considered Positive.

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>No. of patients</th>
<th>percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>44</td>
<td>88%</td>
</tr>
<tr>
<td>idiopathic</td>
<td>4</td>
<td>8%</td>
</tr>
<tr>
<td>tropical</td>
<td>2</td>
<td>4%</td>
</tr>
</tbody>
</table>

Most common etiology found out in study was Ethanol abuse. Some young patients 20 and 19 years of age had tropical pancreatitis. Some middle aged female patients had no reason found out, so idiopathic.

Graph 13 – Etiology of chronic pancreatitis

Graph 14 : Complication of Chronic pancreatitis

Stool frequency has decreased from 5 times per day to less than 2 times per day. By giving pancreatic enzyme supplements. Initially 20 people had frequency more than 5/day but toward end of 35 wks it decreased to 6 patients.

TABLE 10: RISK FACTORS OF CHRONIC PANCREATITIS
TABLE 11: ASSOCIATED COMPLICATIONS OF CHRONIC PANCREATITIS

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>No. of patients</th>
<th>percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudocyst</td>
<td>7</td>
<td>14%</td>
</tr>
<tr>
<td>Pancreatic fistula</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pancreatic head mass</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pancreatic ascites</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Portal/splenic vein thrombosis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Acute Attack on chronic pancreatitis</td>
<td>2</td>
<td>4%</td>
</tr>
</tbody>
</table>

Common complication encountered is pseudocyst of pancreas; most of the Patients were 2.6cm size. Site was body and head of pancreas. So conservative management was suggested. A 20 yr lady with chronic pancreatitis had pseudocyst of 4cm size so surgery was planned if it increases in size to more than 6cm and after improving general condition of patient. Acute exacerbations of chronic pancreatitis was there for 2 patients in course of study and one of them withdrew consent and other patient lost follow up. Alcohol abuse is considered as reason for acute exacerbation.

INFERENTIAL STATISTICS

I. WEIGHT

Table 12: Analysis of weight for control

<table>
<thead>
<tr>
<th>parameters</th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)-baseline</td>
<td>53.02</td>
<td>2.46</td>
<td>25</td>
</tr>
<tr>
<td>Weight (kg)-35wks</td>
<td>53.21</td>
<td>2.79</td>
<td>24</td>
</tr>
</tbody>
</table>

Weight measurements were made in baseline, 7,14,28,35 weeks and results obtained shows that cases has significant improvement in weight over 35 weeks as compared to controls, p value being 0.01.

Table 13: Analysis of weight for case

<table>
<thead>
<tr>
<th>parameters</th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)-baseline</td>
<td>51.39</td>
<td>4.48</td>
<td>25</td>
</tr>
<tr>
<td>Weight (kg)-35wks</td>
<td>54.14</td>
<td>2.34</td>
<td>24</td>
</tr>
</tbody>
</table>

Weight improvement for cases was achieved by careful dietary advice and giving pancreatic enzyme supplements and avoiding alcohol. Fat restriction was not advised and was encouraged to take normal fat diet and small frequent meals.

GRAPH 15: WEIGHT ASSESSMENT

BMI

Similar results for Body Mass Index of patient was expected as increase in weight. BMI is calculated by weight divided by height squared in meters. Normal range of BMI is 18.5 to 24.99. If below 18.5 it is regarded as underweight and more than 30 is regarded as obesity. Most of our patients were in range of underweight to normality.

Table 14: Analysis of BMI for controls

<table>
<thead>
<tr>
<th>parameters</th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI(kg/m2)-baseline</td>
<td>20.31</td>
<td>.87</td>
<td>25</td>
</tr>
<tr>
<td>BMI(kg/m2)-35wks</td>
<td>20.40</td>
<td>.97</td>
<td>24</td>
</tr>
</tbody>
</table>

5 of controls had reduction in body weight and BMI, indicating the chances of malnutrition due to chronic pancreatitis. Multi-vitamins were given including fat-soluble vitamins vit A,D,K,E. Vitamin A is anti-infective and it plays an important role in maintaining integrity of epithelial and glandular linings of intestine and elsewhere.

GRAPH 16: BMI ASSESSMENT
Table 15: ANALYSIS OF BMI FOR CASES

<table>
<thead>
<tr>
<th>ANALYSIS FOR CASE</th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)-baseline</td>
<td>19.46</td>
<td>1.53</td>
<td>25</td>
</tr>
<tr>
<td>BMI (kg/m²)-35wks</td>
<td>20.53</td>
<td>.72</td>
<td>24</td>
</tr>
</tbody>
</table>

Body mass index is shown to have significant improvement in this study as expected and p value for cases found to be less than 0.005 which shows improvement in outcome due to intervention.

II. CHOLESTEROL

Table 16: Analysis of cholesterol for controls

<table>
<thead>
<tr>
<th>ANALYSIS FOR CONTROL</th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (mg/dl)-baseline</td>
<td>158.72</td>
<td>8.40</td>
<td>25</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)-35wks</td>
<td>162.50</td>
<td>17.00</td>
<td>24</td>
</tr>
</tbody>
</table>

Graph 17: Cholesterol values in cases and controls

Cholelithiasis is associated with hyperlipidemia and lithogenic bile. Bile acid-cholesterol mismatch is associated with supersaturation of bile and nucleation of cholesterol crystals and microstone formation. Pancreatic stones on contrary does not rely on cholesterol nidus. Instead has protein nidus around which calcium deposition occurs. In this study no significant difference in cholesterol levels was observed after giving pancreatic enzyme supplements ,cases and controls was having similar cholesterol levels and p-value was more than 0.05. Although Cholelithiasis is main cause of acute pancreatitis, its role in chronic pancreatitis is debatable. Alcoholism is the major cause in chronic pancreatitis. Only backpressure of main pancreatic duct blockage by a tumor or inflammatory mass causes chronic pancreatitis, bile stone blockade of similar nature usually presents with obstructive jaundice and is tackled before going in to a chronic problem. Repeated acute pancreatitis may lead to stricture or chronic inflammation of intra-pancreatic portion of CBD and in turn lead to chronic pancreatitis.

TABLE 17: Analysis of cholesterol for cases

<table>
<thead>
<tr>
<th>ANALYSIS FOR CASE</th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (mg/dl)-baseline</td>
<td>159.20</td>
<td>16.05</td>
<td>25</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)-35wks</td>
<td>162.83</td>
<td>7.92</td>
<td>24</td>
</tr>
</tbody>
</table>

III. TRIGLYCERIDE, LDL, HDL

As seen above total cholesterol was not affected by the study meanwhile some of the components of cholesterol like triglyceride and HDL showed a significant improvement in both controls and cases. Whereas LDL showed an improvement only in cases and controls didn’t had much increase. This may be due to the long study period of the population and different life styles and dietary habits. This is evidenced by fact that at 14 weeks mean values were similar to baseline value. So a definite conclusion could not be made although some parameters show an improvement. Further study for a longer period is advisable in that regard.

Graph 18: Triglyceride, LDL, HDL

Table 18: Analysis of Triglyceride for controls

<table>
<thead>
<tr>
<th>ANALYSIS FOR CONTROL</th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglyceride (mg/dl)-baseline</td>
<td>128.20</td>
<td>10.09</td>
<td>25</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)-35wks</td>
<td>130.79</td>
<td>10.58</td>
<td>24</td>
</tr>
</tbody>
</table>
Table 19: Analysis of Triglyceride for cases

<table>
<thead>
<tr>
<th>ANALYSIS FOR CASE</th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglyceride(mg/dl)-baseline</td>
<td>127.40</td>
<td>6.63</td>
<td>25</td>
</tr>
<tr>
<td>Triglyceride(mg/dl)-35wks</td>
<td>142.92</td>
<td>6.90</td>
<td>24</td>
</tr>
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</table>

TABLE 20: Analysis of HDL for controls

<table>
<thead>
<tr>
<th>2. ANALYSIS FOR CONTROL</th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL(mg/dl)-baseline</td>
<td>40.80</td>
<td>4.25</td>
<td>25</td>
</tr>
<tr>
<td>HDL(mg/dl)-35wks</td>
<td>44.58</td>
<td>6.06</td>
<td>24</td>
</tr>
</tbody>
</table>

Cessation of smoking improves the ‘good cholesterol’ HDL in previously known heavy and light smokers. This may be the reason for improvement in HDL in controls.

TABLE 21: Analysis of HDL for cases

<table>
<thead>
<tr>
<th>ANALYSIS FOR CASE</th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL(mg/dl)-baseline</td>
<td>40.60</td>
<td>4.41</td>
<td>25</td>
</tr>
<tr>
<td>HDL(mg/dl)-35wks</td>
<td>46.46</td>
<td>4.03</td>
<td>24</td>
</tr>
</tbody>
</table>

TABLE 22: Analysis of LDL for controls

<table>
<thead>
<tr>
<th>3. ANALYSIS FOR CONTROL</th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL(mg/dl)-baseline</td>
<td>54.60</td>
<td>4.77</td>
<td>25</td>
</tr>
<tr>
<td>LDL(mg/dl)-35wks</td>
<td>53.75</td>
<td>4.48</td>
<td>24</td>
</tr>
</tbody>
</table>

TABLE 23: Analysis of LDL for Cases

<table>
<thead>
<tr>
<th>ANALYSIS FOR CASE</th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL(mg/dl)-baseline</td>
<td>53.60</td>
<td>4.21</td>
<td>25</td>
</tr>
<tr>
<td>LDL(mg/dl)-35wks</td>
<td>58.75</td>
<td>4.48</td>
<td>24</td>
</tr>
</tbody>
</table>

IV. SERUM ALBUMIN, HEMOGLOBIN

Table 24: Analysis of S. Albumin for controls

<table>
<thead>
<tr>
<th>4. ANALYSIS FOR CONTROL</th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Albumin(mg/dl)-baseline</td>
<td>3.70</td>
<td>.25</td>
<td>25</td>
</tr>
<tr>
<td>Serum Albumin(mg/dl)-35wks</td>
<td>3.83</td>
<td>.49</td>
<td>24</td>
</tr>
</tbody>
</table>

Albumin comprises 60% of total protein in human plasma. It is produced by liver and carries out variety of function. Albumin and protein is the laboratory Nutritional parameters. In this study there was a significant improvement in serum Albumin of cases p-value being 0.01.

Graph 19: Serum Albumin in Controls

Albumin for controls

35 weeks
14 weeks baseline
3.4 3.6 3.8

Graph 20: Serum Albumin in Cases

Albumin for cases

35 weeks
14 weeks baseline
0 5
Table 28: Analysis of Hemoglobin for controls

<table>
<thead>
<tr>
<th>5. ANALYSIS FOR CONTROL</th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin(g/dl)-baseline</td>
<td>9.46</td>
<td>.41</td>
<td>25</td>
</tr>
<tr>
<td>Hemoglobin(g/dl)-35wks</td>
<td>9.54</td>
<td>.45</td>
<td>24</td>
</tr>
</tbody>
</table>

Table 29: Analysis of hemoglobin for controls

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S.D</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin(g/dl)-baseline</td>
<td>9.40</td>
<td>.53</td>
<td>25</td>
</tr>
<tr>
<td>Hemoglobin(g/dl)-35wks</td>
<td>9.96</td>
<td>.23</td>
<td>24</td>
</tr>
</tbody>
</table>

There is significant improvement in haemoglobin concentration which is also regarded as a laboratory nutritional parameters, cases had significant p-value 0.01. as compared to controls.

CLINICAL SYMPTOMS
The clinical symptoms are subjective still most treasured is the patients words. I have done utmost sincerity in recording the symptoms and SF-36 questionnaire (Short form (36) health survey questionnaire) and counter checking with my colleagues for avoiding observer bias.

GRAPH 22: HEMOGLOBIN OF CASES AND CONTROL

There is significant improvement in haemoglobin concentration which is also regarded as a laboratory nutritional parameters, cases had significant p-value 0.01. as compared to controls.

GRAPH 23: CLINICAL SYMPTOMS FULL ANALYSIS

2. FLATULENCE

Flatulence is a distressing symptom moderate flatulence which is present more than half of day and interfere with day to day activity has come down in cases by giving pancreatic enzyme supplements over a period of 35 weeks in patients who didn’t receive enzymes it has remained same.

ABDOMINAL PAIN

Severe abdominal pain is which interfere with daily activities and confine patient to bed, in cases such severe abdominal pain has decreased to zero percent where as in controls severe and moderate abdominal pain has remained the same.
Quality of life (QOL) is assessed using SF-36 health survey questionnaire. The scores are calculated based on the RAND recommendation for scoring SF -36 health survey. Our patients were asked questionnaire in local language Tamil, accordingly scores were calculated ,out of 36 question—General health and emotional well being has 5 components each Pain and social functioning has 2 each Role limitation due to physical health and energy has 4 each Role limitation due to emotional problems has 3 each Physical functioning has 10 items.

Graph 24 : QOL

**QUALITY OF LIFE**

<table>
<thead>
<tr>
<th>Role-emotional</th>
<th>35 weeks</th>
<th>baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>38</td>
<td>45</td>
<td>62</td>
</tr>
<tr>
<td>47</td>
<td>62</td>
<td>76</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physical functioning</th>
<th>35 weeks</th>
<th>baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>58</td>
<td>72</td>
</tr>
<tr>
<td>55</td>
<td>62</td>
<td>78</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Social functioning</th>
<th>35 weeks</th>
<th>baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>38</td>
<td>58</td>
<td>75</td>
</tr>
</tbody>
</table>

**SF-36 SCORE**

**DISCUSSION**

Study of 50 patients with pancreatic exocrine insufficiency over a period of 35 weeks is a cumbersome exercise. In this single – blind study cases were given pancreatic enzyme supplement in adequate doses and were followed up meticulously.

Average age of our study of class is 40.84 which is fifth decade which was consistent with previous studies by Witt et al. Levy et al had conclusion of median age as 51 years and sex ratio of 5.07. Our study shows 6 females out of 50 patients with chronic pancreatitis. The discrepancy may be due to small sample size of 50 patients in contrast to Dr Levy and et al who studied on 1748 patients [10,11].

In this study most common etiology of chronic pancreatitis was found to be ethanol abuse-88%. Eight percent cases were idiopathic and 4% was tropical pancreatitis. It is in consistency with Levy et al study in 2006 suggesting 84% ethanol abuse and 9% idiopathic etiology [11].

Diagnostic help was by ultrasound, contrast enhanced CT and by testing fecal fat globules and clinical examination of stools. These were highly accurate in determining the study population. This was in consistency with studies of throat V et al and Levy et al. They used CT and ultrasound criteria for diagnosis and throat V et al used difficult methods of 24 hour fecal fat estimation for diagnosis and Lüth S et al used costly fecal elastase test for diagnosis. So our study was conducted in a cost effective best possible manner. Fecal fat globules microscopically more than 50 µ diameter and its number in 5 HPF, The multiplying average number[X] × average size [y]for all study population was more than 500 signifying steatorrhea. Later on it was found that steatorrhea disappeared in cases who received enzyme supplements and remained positive for controls. Kenneth D et al in his study observed similar findings of stool fat globules [12,13].

Chronic pancreatitis present with abdominal pain, malabsorption, decreasing weight and development of diabetes. In this study Abdominal pain, malabsorption and its symptoms of stool frequency, consistency, and flatulence were evaluated over a long period of 35 weeks and we found consistent improvement in these symptoms in cases receiving enzyme supplements. Throat V et al in their study was also able to came with similar findings. Peter A et al in study of chronic pancreatitis observed that in chronic pancreatitis 80% patients had abdominal pain at any point of time. Abdominal pain of type A will be frequently occurring short duration (less 10 days) followed by pain free interval. Type B Abdominal pain is experienced as months of intermittent interval of severe pain. Also there may be pain and discomfort of malnutrition and flatulence. In our study all patients had abdominal pain and 56% of patients had severe pain and is comparable to above studies. Diabetes was found in 8% in our study and it being an independent reason for pancreatic exocrine insufficiency was regarded as confounding factor and eliminated by proper matching. Mathew et al observed that prevalence of diabetes increases with disease duration. At onset of symptoms it ranges from 0 to 22% and reaches overall prevalence of 47% - 52% over 20 year period. So our observation tally with above studies [12].

Common complication encountered during period of study was pseudo cyst development in 14% of patients and acute episode of pancreatitis in 4% which required admission most common complication of chronic pancreatitis is 20 – 38% prevalence of pseudocyst [14]. Kim Ko, Kim TN in a study observed 14% of pseudo cyst in acute pancreatitis and 40% in chronic pancreatitis. This slight dissimilarity may be due to shorter duration of study and lesser study population. Kim Ko, Kim TN analyzed retrospectively 350 patients with pseudocyst. Peter A et al identified incidence of acute attacks of pancreatitis in chronic pancreatitis patients to be 6.4% which is in agreement with our study of 4% of acute episode.

Malnutrition is important concern in our study. Chronic pancreatitis and alcohol abuse may lead to malnutrition by way of lack of pancreatic lipase leading to steatorrhea. Chronic pain leads to low income, lack of purchasing power. Siddharath et al from AIMS, New Delhi found out that 50% of patients with chronic pancreatitis suffer from
malnutrition. Patients in study were considered malnourished if BMI was less then 18.5 or they lost 10% of their body weight in previous 6 months. In our study most patients 80% had history of weight loss more than 10% after starting symptoms of pancreatitis. Also 32% had BMI less than 19.5 mean BMI is 19.46 for cases. It is in agreement with above study. Pancreatic enzyme supplements improved body weight and BMI in chronic pancreatitis patients in our study. Similar observation was also found out by Throat V et al.12

In our Study there is overall decrease in stool frequency and stool consistency improved to formed stools. That is there was improvement in steatorrhrea. These same observations were found by Throat et al. There was marked improvement in flatulence, gas and loose stools in our study Whitcomb et al also found statistically significant well being in flatulence and stool consistency on giving pancreatic enzyme supplements.14

Absent lipase leads to altered lipid metabolism and malnutrition. Deficiencies occur in vitamin A,E and K and produce increased clotting time and neurological problems. Devi Mukkai Krishnamurthy et al identified elevated serum HDL but no difference in other lipoproteins (LDL, Triglycerides). He found it to be cardio protective effect. In our study total cholesterol had no significant change by use of enzyme supplements. But HDL has improvement in giving enzymes in cases as supported by above study.15

HDL also improved in controls in our study probably as a result of cessation of smoking and alcohol LDL was increased in cases in our study also triglycerides was increased significantly in cases and controls. These effects in controls can also be due to 35 week study, 14 week mean values of lipoproteins were similar to baseline value. So a authoritative conclusion cannot be made from our study regarding lipoproteins except for HDL and further follow up for a longer period is advisable.

Knop et al opined that there is enhanced post – prandial incretin response due to larger availability of nutrients as a result of enzyme supplements. Incretin is insulinotropic and causes anabolic effect, improvement of malnutrition and increase laboratory parameters of albumin, pre – albumin and protein increase in albumin and protein was also observed by Throat et al. Our study also confirms above studies by recording a significant increase in albumin and protein in case receiving enzyme supplements.12,15

With improvement in malnutrition and clinical symptoms there was an overall impact in life of patients receiving enzyme supplements as evidenced by improving clinical global impression of disease. Quality of life was assessed using SF – 36 questionnaire and was found to have excellent improvement when compared to controls not receiving enzyme supplements. similar findings were supported by Throat et al. There was improvement in mental health and social functioning also. Abstinence from alcohol and smoking has also contributed a lot.12

No adverse effects were found for pancreatic enzyme supplements during the study period. It was safe and tolerable. Patient compliance was satisfactory. Throat et al study had similar findings

Study was conducted single blind that was a limitation here. Data were analyzed SPSS 17 version software and using paired sample ‘t’ test.

Ensuring Patient Compliance with drug and winning patient rapport is utmost important in the study. Any treatment failure during the process was found and rectified.

There is no conflict of interest to disclose.

Further researches regarding this topic are to

1. Rectify challenges in effective therapy
   • Lipases presently available are porcine lipases, so we can have researches to produce recombinant human lipases.
   • Colipases are present in natural pancreatic Juice and assist in digestion.
   • Coupling of Colipases can increase efficacy of lipases.
   • Hyper acidity hinders treatment. Pancreatic Juice naturally has bicarbonate. Supplementing bicarbonates and its effects on treatment needs further study.
• Development of micro organisms and fruits by genetic engineering, we can be able to provide eco-friendly lipases without relying on capsules.

• Better delivery systems than microspheres like lipid droplets have to be devised.

• Rectify challenges in identifying treatment failures.

• We should be able to have test to identify early treatment failures in PEI.

• Diagnosis of PEI should also be cheap and patient friendly (Instead of collecting 24 hr stool sample).

CONCLUSION
• Chronic Pancreatitis is a disease of men mostly Male Female ratio being 7.3:1 it is most commonly found in the fifth decade age group of 41- 50 years.

• Ethanol consumption is most common cause (>80%).Idiopathic chronic pancreatitis occurs in 8% of Cases

• Computerized tomography, ultrasound helpful in diagnosis of chronic pancreatitis.

• Most common Complication seen in our study in chronic pancreatitis is pseudocyst 14%. Acute episodes of pancreatitis occurred in 4%.

• Pancreatic exocrine insufficiency is associated with chronic pancreatitis. It is diagnosed clinically by steatorrhea. Laboratory tests include 24 hour fecal fat estimation, fecal elastase rest, qualitative or quantitative fecal fat globules tested. We used fecal fat globule testing in our study, which was positive in all patients (100%).All cases that were given enzymes it became negative. chronic pancreatitis with pancreatic exocrine insufficiency present with abdominal pain malnutrition, watery, bulky, foul smelling stools (steatorrhea), Gas, Flatulence. Most common Symptom is Abdominal Pain, Severe Abdominal Pain being 56% and flatulence next common-52%.

• Pancreatic enzyme supplements improve symptoms of chronic pancreatitis with PEI. Decrease severity and duration of abdominal Pain. It improves stool consistency, decreases stool frequency. It decrease flatulence and gas formation.

• Enzyme supplements improve body weight, BMI and increase nutritional laboratory parameters like serum albumin, Protein, and hemoglobin (P Value less than 0.01) when compared to controls.

• Regarding lipid profile, enzyme supplements improves HDL value but regarding other lipoproteins no definite conclusion can be made.

• Quality of life shows significant improvement in patients given enzyme supplements by providing pain free period, emotional well being and increased weight gain. It has also shown better social functioning and energy.

Satisfactory safety, tolerability and compliance of patients to pancreatic enzyme replacement therapy was noted.

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Whitcomb D C et al. Pancrelipase delayed release capsules for exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatic surgery; doubleblind RCT. Am J Gastroenterology 2010;105