PANCREAS, NUTRITION in Cystic Fibrosis, and Total Parenteral Nutrition

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Objectives

At the end of the session the participant will be able to:

- Describe the current diagnostic testing used in assessing pancreatitis

- Assess the importance of nutritional management of cystic fibrosis

- Explain some of the concepts behind total parenteral nutrition in the newborn
Case Study—Pancreatitis

- Clinical presentation
- Lab tests
- Amylase vs Lipase
- Genetic testing
CF-topics

- Pancreatic Sufficient vs Pancreatic Insufficient
- Nutritional monitoring in cystic fibrosis
Indications for TPN
The TPN prescription
Monitoring TPN
Mr. Spink, 51 y presented to ER with acute abdominal pain radiating to the back. He bends forward to relieve the pain.

Lab tests ordered
- Lipase 240 IU/L (<60 IU/L)
- P–Amylase 120 U/L (<100U/L)

Diagnosis – pancreatitis
Lipase vs Amylase

- More specific than amylase for acute pancreatitis

- Levels of lipase remain elevated in serum longer than amylase (8–14 vs 3–4 days)

- $T_{1/2}$ for lipase is 7–14h, $T_{1/2}$ for amylase ~2h
Lipase and Amylase

- Hydrolyses glycerol esters of long chain fatty acids.
- Catalyzes the hydrolytic degradation of complex carbohydrates by cleaving the 1,4 α–glucosidic bonds. P–amylase is typically in greater concentration in adults.
Some Risk factors for acute pancreatitis

- Chronic alcohol consumption
- Autoimmune disease (SLE)
- Gallstones
- Hypercalcemia, hyperparathyroidism
- Hypertriglycerideridemia (>1000mg/dL or 11.3mmol/L)
Other lab tests?

- ALT
- CRP
- Ca
- TG
- Creatinine
- Glucose
- WBC
Case

- Mr. Spink is a moderate drinker
- No other illnesses, and no respiratory conditions
- No family history of pancreatitis
Case

- This was Mr. Spink’s 4th episode in the last decade
- Further testing indicated a mutation in the serine protease inhibitor gene (SPINK 1)
- Note also CFTR mutations (mild phenotype) may be associated with CP
Case Study  (Cindy Fir)

- Birth history
  - 34 wk gestation
  - Normal pregnancy
  - Weight at birth = 3kg
  - Height = 50cm

- NBS result homozygous for δF508
- Sweat test ordered
  - Positive Result (110/120)
Question

- Should Cindy Fir be started on enzyme replacement therapy?
Of importance is correcting the maldigestion/malabsorption associated with pancreatic insufficiency
Clinical presentation–CF

- Acute or persistent respiratory symptoms
- Malabsorption /malnutrition (PI)
- Failure to thrive
- Combination of the above
- Newborns with meconium ileus
  - 80–90% newborns with M.I. have CF
- Infertility
In the US survival has increased from 25% in 1986 to > 36% in 2010

Reasons include

- Early diagnosis
- Management of the disease
  - Nutrition
  - Lung function
Survival

- Survival is related to % ideal body weight and lung function
- >85 % IBW better prognosis at 5y than those with <85% IBW.
- Survival also decreases with decreasing lung function
  - (Sharma et al. Thorax 2001)
Figure 3: Estimated probability of death within 5 years of patients with cystic fibrosis according to percentage predicted FEV₁ and percentage ideal weight.
Survival

- Normal ranges of
  - weight-for-age,
  - height-for-age, and
  - weight-for-height percentiles

  are associated with better pulmonary function percent predicted (FEV$_1$) and survival for adults and children

(J Am Diet Assoc, 2008)
Survival

- Increased survival led to recognition of
  - Osteoporosis/bone health
  - CF related diabetes
  - Liver disease

In older individuals
Includes

- Measurement of fat soluble vitamins
- OGGT
- Liver enzymes
Energy requirements

- 150–200% energy requirements of a healthy child
  - Increased work of breathing, and decreased appetite

- Markers of nutritional adequacy
  - Linear growth
  - Weight gain
Energy Requirements

- Macronutrients are also important for skeletal muscle mass and better exercise ability.

- Exercise important for better longevity.

  - (Lands, Paediatr Resp Rev 2007, 8, 305-12)
Supplementation of vitamins at doses beyond the DRI

Additional supplementation depending on lab findings (e.g. anemia)
CF care and the laboratory

- Also recommended
  - PFT
  - CBC
  - Fat soluble vitamins, A,D,E,K?
  - OGGTT
  - Liver enzymes
PS implies enough residual pancreatic function so that pancreatic replacement therapy is not required

PS patients have better nutritional status


PS patients may develop chronic pancreatitis as they get older
- PI is associated with Class I–III mutations (< 5% CFTR function).
- PI requires Pancreatic Enzyme Replacement Therapy

Some PI associated mutations
Assessing pancreatic function

- 3 day stool fat
- Fecal elastase
- ≈ 80% CF patients are PI
- Pancreatic replacement therapy
Fecal Fat

- 72h stool collection
- Adequate fat intake, (ideally this is documented).
- Methods
  - Van De Kamer et al. J. Biol. Chem. 1949, 177: 347
  - JeeJheeboy et al Clin Biochem 1970, 3:157 (this is often required when babies are supplemented with MCT)

- Normal
  - >95% of fat intake is absorbed
Fecal Elastase

- This test reduces the need for fecal fat determinations and is helpful in the newborn period.
- Spot test (<5g stool)
- Enzyme linked immunoassay
- Adult Values are applicable >2 weeks (term babies)
- PI cutoff
  - <100μg/g
Cindy Fir

- Is PI
- Started on PERT and vitamin supplementation
- At first visit after 3 months she is assessed for growth by the dietitian
- Some blood work is ordered
Blood work includes liposoluble vitamins.

Why are these important?
Vitamin A

- Night vision
- Antioxidant

- Most common measure is Serum level
- Transport: RBP/prealbumin
Vitamin E

- Transport with lipids
- Cell integrity
- Neurological function
- Antioxidant
- Levels low at birth therefore early supplementation recommended
Vitamin E

- Assess serum levels

- Age specific Reference interval –
  - serum level or
  - serum /lipid (cholesterol)
All individuals with CF maintain a serum 25-hydroxyvitamin D goal of at least 30 ng/ml (75 nmol/liter)

Assess for adherence when the serum level of 25-hydroxyvitamin D level <30 ng/ml (75 nmol/liter).

Measurement of serum 1,25(OH)2D should not be used to assess vitamin D status

Routine measurement of PTH, osteocalcin, alkaline phosphatase, or other indirect markers to assess vitamin D status is not necessary
Supplementation is also recommended (Ares et al, JCEM 2005) but the optimal amounts not known

- Transport with lipids
- Too much may exacerbate vitamin K absorption

PT is still used routinely used for assessing K status but it is not sensitive
- Serum Vitamin K only assesses recent intake
- Other markers?
Parenteral Nutrition
Case Study

- **Cindy Fir**
  - Born with Meconium Ileus.
  - 3 days after birth she underwent intestinal surgery and a portion of her intestine was removed.
Indications for TPN

include

> Low birth weight patients

> High risk patients e.g. Short gut
Parenteral Nutrition

- Provision of macronutrients by IV route
- Complete nutrient intake by IV = TPN
- Sometimes as adjunct to enteral intake—this is important to prevent intestinal atrophy.
Metabolic Complications of TPN

- Disturbed calcium homeostasis
- Hyperglycemia, hypoglycemia
- Electrolyte balance
- Trace element and fat soluble vitamin deficiencies
- Fe deficiency
- Essential Fatty Acid deficiency
- TPN cholestasis
- Hyperlipemia
Cindy Fir was started on trophic feeds on day 3 of life but this was discontinued due to bowel distention. The following are some of her biochemistry labs.
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<th>Day</th>
<th>Na Mmol/L</th>
<th>Glucose Mmol/L/mg/dL</th>
<th>TG Mmol/L/mg/dL</th>
<th>Creat μmol/L/mg/dL</th>
<th>Tbil μmol/L/mg/dL</th>
<th>Dbil μmol/L/mg/dL</th>
<th>ALT U/L</th>
<th>GGT U/L</th>
<th>ALP U/L</th>
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<tbody>
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<td>3</td>
<td>134</td>
<td>5.5/99</td>
<td>0.52/46</td>
<td>62/0.7</td>
<td>64/3.7</td>
<td>5/0.3</td>
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<td>141</td>
<td>5.1/92</td>
<td>0.68/60</td>
<td>70/0.8</td>
<td>88/5.2</td>
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<td>18</td>
<td>135</td>
<td>3.4/61</td>
<td>1.70/150</td>
<td>57/0.65</td>
<td>46/2.7</td>
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<td>142</td>
<td>3.7/67</td>
<td>2.16/191</td>
<td>42/0.5</td>
<td>61/3.5</td>
<td>45/2.7</td>
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<td>1.13/100</td>
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<td>1.24/110</td>
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</table>
Trace elements

- Cu 8.8 (56) μmol/L (μg/dL)
- Mn 36.4 (0.2) nmol/L (μg/dL)
- Se 0.58(4.6) μmol/L (μg/dL)
- Zn 8.2 ((56) μmol/L (μg/dL)

(Discuss the Blood volume required for these lab tests and the implications).
TPN cholestasis

- Usually reversible if TPN is stopped
- Limit Cu and Mn to avoid toxicity
- Implement preventive measures
Hyperlipidemia

- Small for Gestational Age babies
- Sepsis
- Any patient receiving lipids

- Keep TG levels at <2.5mmol/L (224mg/dL)
Calcium homeostasis

- Assess serum Ca or ionized Ca status.

- Ca depletion
  - Limited solubility in TPN solutions
  - Urine Ca/Cr =0 signifies a problem

- Hypercalciuria or nephrocalcinosis
  - Urine Ca/Cr >1.0 – investigate
    - (Discuss random urine measurements)
In patients with CF, Vitamin D sufficiency is assessed by levels of

- Vitamin D
- 1,25dihydroxyvitamin D
- 25 hydroxyvitamin D
- PTH
- ALP
Self Assessment

- In CF, Pancreatic insufficiency is assessed with:
  - Fecal fat excretion
  - Fecal elastase
  - CFTR mutation analysis
  - Pancreatic amylase
Patients on long term TPN are at risk for

- Cholestasis
- Anemia
- Sepsis