PANCREAS, NUTRITION in Cystic Fibrosis, and Total Parenteral Nutrition

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Inspiring Innovation and Discovery

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

TPN –topics

- Indications for TPN
- The TPN prescription
- Monitoring TPN

Case

- Mr. Spink , 51y presented to ER with acute abdominal pain radiating to the back.
- He bends forward to relieve the pain.

- Lab tests ordered
  - Lipase 240IU/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 pancreatits

- Chronic alcohol consumption
- Autoimmune disease (SLE)
- Gallstones
- Hypercalcemia, hyperparathyroidism
- Hypertriglyceridemia (>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?

CF

- 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

Survival rates

- 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)

Sharma et al
Thorax ,2001

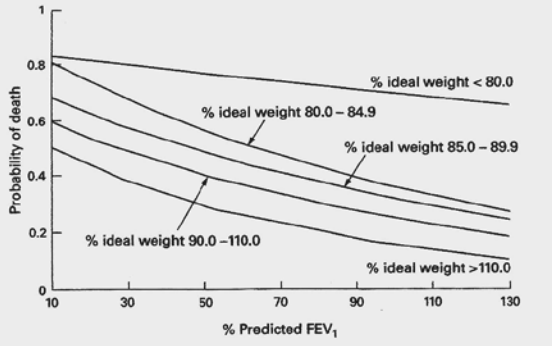

Figure 3 Estimated probability of death within 5 years of patients with cystic fibrosis according to percentage predicted FEV, and percentage ideal weight.

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

CF Care

includes

- Measurement of fat soluble vitamins
- OGTT
- 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?
- OGTT
- Liver enzymes

Cindy Fir– PI or PS?

- PS implies enough residual pancreatic function so that pancreatic replacement therapy is not required
- PS patients have better nutritional status
- Some PS associated mutations R117H, R347P, A455E ,R334W□□ G178R ,R352Q

- 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

- F508del , G542X, G551D, N1303K, W1282X R553X, R1162X, I507del, R560T, 1078delT

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

Cindy Fir

- 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)

Recommendations for vitamin D testing– CF foundation

- 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

Vitamin K

- 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

TPN

- 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.

Labs

Day	Na Mmol/L	Glucose Mmol/L/ mg/dL	TG Mmol/L/ mg/dL)	Creat µmol/L/ mg/dL	Tbil µmol/L / mg/dL	Dbil µmol/L / mg/dL	ALT U/L	GGT U/L	ALP U/L
3	134	5.5/99	0.52/46	62/0.7	64/3.7	5/ 0.3			
6	141	5.1/92	0.68/60	70/0.8	88/5.2	11/ 0.6			
18	135	3.4/61	1.70/ 150	57/0.65	46/2.7	27/ 1.6			
32	142	3.7/67	2.16/ 191	42/0.5	61/3.5	45/ 2.7			
53	137	3.7/67	1.13/ 100	35/0.4	213/ 12.5	149/ 8.7	34	69	478
58	135	4.7/85	1.24/ 110	27/0.3	275/ 16.0	207/ 12.0	52		957
65							61	152	

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

Hyperlipemia

- 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)

Self Assessment

- 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**
    or
  - **Fecal elastase**
  - CFTR mutation analysis
  - Pancreatic amylase

Self-Assessment

- Patients on long term TPN are at risk for
  - **Cholestasis**
  - Anemia
  - Sepsis