Nutritional Problems (and Solutions)

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Overview

- Refeeding syndrome
- Pancreatic exocrine insufficiency
- Malignant bowel obstruction
- Nutrition impact symptoms
Refeeding syndrome
Refeeding syndrome

A CLINICAL STUDY OF MALNUTRITION IN JAPANESE PRISONERS OF WAR (A CLINICAL STUDY OF MALNUTRITION IN JAPANESE PRISONERS OF WAR*)

MAURICE A. SCHNITZER, M.D., F.A.C.P.; PAUL F. MATTMAN, M.D.; THEODORE I. BLISS, M.D., F.A.C.P.
Refeeding - Definition

- Abnormalities in electrolyte levels and fluid balance with resultant organ dysfunction that occurs in a malnourished individual on reintroduction of an energy substrate.

- Clinically we see
  - Significant reductions in serum phosphate; magnesium and potassium levels
  - Insulin resistance (high blood sugars)
  - Respiratory compromise; cardiac arrhythmia; oedema and multi-organ failure
  - Ultimately death
Hypokalaemia
Hypomagnesaemia
Hypophosphataemia
Thiamine deficiency
Salt and water retention - oedema

Starvation / Malnutrition
Glycogenolysis, gluconeogenesis and protein catabolism

Refeeding syndrome

Refeeding (switch to anabolism)
Fluid, salt, nutrients (CHO major energy source)

↑ Glucose uptake
↑ Utilization of thiamine
↑ Uptake of K⁺, Mg²⁺ & PO₄³⁻

↑ Protein and glycogen synthesis

Insulin secretion
Starvation: Pathophysiology

- Catabolism - use of stored body fat / protein for energy
- Basal Metabolic rate reduces by 20-25%
- Muscles and other tissues switch from ketone to free fatty acids as an energy substrate
- Blood levels of ketones increase
- Brain switches from glucose to ketones as energy source
- Reduced rate of gluconeogenesis in liver, thus preserving muscle stores
- Total body depletion in electrolytes but serum levels remain normal
  - Most electrolytes are stored in the cells (not in the blood)
  - Electrolytes are preserved by reduced renal excretion
  - Reduction in intracellular compartment size
Refeeding: Pathophysiology

- Increased insulin and reduced glucagon secretion
- Insulin stimulates production of glycogen, fat and protein
  - requires phosphate, magnesium and thiamine
- Insulin stimulates uptake of potassium, magnesium and phosphate into cells
- Water follows as an osmotic process

Consequences
- Low levels of serum phosphate, potassium, magnesium
- Fluid overload
Refeeding - risk factors

One or more of the following:
- BMI less than 16kg/m²
- Unintentional weight loss > 15% in the last 3-6 months
- Little or no nutritional intake for >10 days
- Low levels of potassium, phosphate or magnesium prior to feeding

Two or more of the following:
- BMI less than 18.5kg/m²
- Unintentional weight loss >10% within the last 3-6 months
- Little of no nutritional intake for >5 days
- History of alcohol abuse, use of drugs including insulin, chemotherapy, antacids or diuretics

NICE, 2012
Refeeding - management

- Referral to a trained HCP
- B vitamin supplementation
- Slow reintroduction of carbohydrates
- Daily blood tests (Phosphate / Magnesium / U&E’s)
- Blood glucose monitoring
- Daily weights
- Strict fluid balance charts
- Intravenous correction of electrolyte abnormalities
- ICU monitoring in those with severely deranged electrolytes

NICE, 2012
In summary

- Assess risk
- Refer to a dietitian
- Monitor refeeding bloods
- Prescribe thiamine 100mg or pabrinex for 10 days ONLY

- Serum electrolytes likely to be normal until patient refed
Pancreatic Exocrine Insufficiency (PEI)
PEI - definition

“...deficiency or absence of digestive enzymes leading to maldigestion of food and consequently malabsorption of nutrients” (Whitcomb et al, 2010)

“Exocrine pancreatic insufficiency results from a progressive loss of acinar pancreatic cells which leads to the secretion of an insufficient amount of digestive enzyme into the duodenum.” (Pezzilli et al, 2013)

Failure of the pancreas to secrete sufficient enzymes to achieve normal digestion

“...pancreas is unable to deliver sufficient amounts of digestive enzymes to the small intestine, leading to maldigestion” (Sikkens et al, 2012)
## Digestive enzymes

<table>
<thead>
<tr>
<th>Site</th>
<th>Carbohydrate</th>
<th>Fat</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saliva</td>
<td>Amylase</td>
<td>Salivary lipase</td>
<td></td>
</tr>
<tr>
<td>Gastric Secretion</td>
<td>Gastric Amylase</td>
<td>Gastric Lipase</td>
<td>Pepsin; Rennin; Gelatinase;</td>
</tr>
<tr>
<td>Pancreatic Secretion</td>
<td>Amylase</td>
<td>Lipase; Steapsin</td>
<td>Trypsin; Chymotrypsin; Carboxypeptidase; Elastase</td>
</tr>
<tr>
<td>Jejunal / Ileal Secretion</td>
<td>Sucrase; Maltase; Isomaltase; Lactase</td>
<td>Intestinal Lipase</td>
<td>Brush Border Peptidases</td>
</tr>
</tbody>
</table>
PEI - clinical symptoms

Steatorrhoea
- Loose watery yellow/orange stool
- Floats / difficult to flush away
- Oily / visible food particles

LIMITATIONS
- Low fat diet
- Constipating drugs
- Late symptom
PEI - clinical symptoms

- Large volume stool
- Undigested food in the stool
- Post-prandial abdominal pain
- Nausea / colicky abdominal pain
- Gastro-oesophageal reflux symptoms
- Bloating / flatulence
- **Weight loss despite good oral intake**
- Vitamin deficiencies (especially A,D,E,K)
- *Hypoglycaemia in patients with diabetes*
  

- Borborygmy (gurgling)
- Belching (if constipated)
PEI - management

- No 2 patients are the same

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<thead>
<tr>
<th></th>
<th>Mean Intra-digestive</th>
<th>Post Prandial Peak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipase</td>
<td>up to 1000u/min</td>
<td>3000 - 6000u/min</td>
</tr>
<tr>
<td>Amylase</td>
<td>50 - 250u/min</td>
<td>500 - 1000u/min</td>
</tr>
<tr>
<td>Proteases (Trypsin)</td>
<td>50 - 100u/min</td>
<td>200 - 1000u/min</td>
</tr>
</tbody>
</table>

- Enzymes release continues for approximately 2 – 3 hours post prandially (360,000 - 720,000u) (Keller & Layer, 2005)
PEI practicalities

Timing
- Mix with food
- Allow for slow meals / multiple courses

Storage
- <25°C

Dose
- Minimum starting dose
  - 50,000u with meals
  - 25,000u with snacks
- Increase until symptoms are under control
- Snacks vs. meals
Enzymes should be:
- Taken with all food, snacks and nutritional supplements
- Swallowed with a cold drink
- Spread out through out the meal
- Taken with milky drinks

Enzymes should not be
- Sprinkled on food
- Chewed
What if they don’t work?

- Adequate dose?
- Adequate timing?
- Correct storage?
- PPI?
- Correct preparation?
- Co-morbidity?
Differential diagnosis: BAM

- Bile acid malabsorption

- Gallbladder resection (Ruis-Campos et al, 2019)
- Bile salts may bind to mal-digested protein, carbohydrates and fibre
- Reduced pH in proximal small bowel may cause precipitation of bile salts
- High bile acid losses seen in children with CF (Weber et al, 1976)
Differential diagnosis: SIBO

- Small intestinal bacterial overgrowth

- Documented in 36% of patients with CP; 26% in those who had not had surgery (Capurso et al, 2016)

- May precipitate bile acid malabsorption

- Pezzilli (2009) proposed PERT may normalise small bowel luminal conditions thereby avoiding bacterial overgrowth

- Pancreatic resection increased incidence of bacterial overgrowth over chronic pancreatitis alone (Bordin et al, 2013)
Differential diagnosis: Other

- Octreotide? Opiates? Chemotherapy? Radiotherapy?
- Delayed gastric emptying
- Other GI pathology
  - Intestinal inflammation (Pezilli et al, 2007)
  - Lactase deficiency
  - Coeliac disease (Leeds et al, 2007)
- Functional disorders
In summary

- Ask detailed questions about bowels and symptoms
- Adjust doses
- Explain to increase compliance

- Faecal elastase
  - <250ug/g = PEI
Malignant bowel obstruction (MBO)
MBO: background

- Bowel obstruction is common
  - 10-28% bowel (Antony et al, 2007)
  - 20-50% ovarian (Tuca et al, 2019)
  - Appendicular and pseudomyxoma peritonei
  - HPB (pancreas, gallbladder)
  - OG
  - Primary peritoneal malignancy
  - Peritoneal mesothelioma
  - Metastatic melanoma
  - Lobular breast cancer
Nutritional management: TPN

- Prognosis > 2 months (Arends et al, 2017)

- Cochrane review 2018
  - Survival and QoL
  - No RCTs
  - 13 observational studies (n=721)
  - All on PN
  - 3 measured QoL
  - Survival 3-1278 days
  - More research needed
MBO: dietary management

- Challenging
- No guidelines or consensus
- No previous studies or published evidence
Peritoneal metastases
Crohn’s disease stricture
Crohn’s: dietary management

- Guidelines: low fibre diet (Lee et al, 2014)
- 12 weeks enteral liquid diet:
  - Active remission in 81.4% (Hu et al, 2014)
Mrs H
50 yrs
Book binder
Married, no children
2009
- Diagnosed ovarian cancer
- Ileostomy

2010
- Chemo
- Surgery
- Chemo

2011
- Reversal of ileostomy

2012
- Disease recurrence
- Chemo
October 2014

- 4 hospital admissions with MBO
- Started elemental and liquid diet
- 114 days at home (Taxol, Caelyx)

Feb 2015

- PD (Cisplatin)
- Liquid diet and elemental ongoing

April 2015

- HPN, venting gastrostomy
- 5 admissions
- 296 days at home

April 2016

- RIP: 550 days since starting Elemental
Mrs B
79 yrs
2005 diagnosed ovarian cancer
Married, 3 dogs
Jan - Mar 2016: 4 hospital admissions with malignant bowel obstruction

21st March 2016
- Fit for surgery
- Stoma formation
- Chemotherapy

Feb - Dec 2017

Liquid diet and Elemental (3 months)
EDMONd
A feasibility study of Elemental Diet as an alternative to parenteral nutrition for patients with inoperable malignant bowel obstruction

RECRUITING
Royal Surrey County Hospital NHS Foundation Trust
Sussex Cancer Centre, Brighton
Velindre Cancer Centre, Cardiff
North Tees and Hartlepool NHS Foundation Trust
EDMONd - study objectives

▶ **Primary Aim**
▶ To provide ‘proof of concept’ of ED as an acceptable/useful feeding option for patients with inoperable malignant bowel obstruction

▶ **Secondary Aims**
▶ To provide evidence that ED:
  ▶ Is tolerated
  ▶ Has positive impact on quality of life
  ▶ Can meet some of the patient’s nutritional requirements
EDMONd - intervention

- Intervention
  - E028 introduced on consent during admission
  - Follow up for 2 weeks by telephone
  - Data collection:
    - Diet diaries: taste preferences, amount of E028
    - MSAS scores for vomiting and pain
    - QoL questionnaires
Mrs R

63 yrs

2013
Diagnosed ovarian cancer

Married
2013
Ovarian cancer → surgery → chemo

Aug 2015
Bowel obstruction → Admission: TPN → chemo → D/C on oral diet

Liquid diet
Nutrition & Dietetics Department

Low fibre diet
Nutrition & Dietetics Department

Soft Diet
Nutrition & Dietetics Department
Sept 2015 Admission: obstruction PD: Chemo stopped D/C with NGT CPCT: 9/52 prognosis

Champagne every Saturday with family x 9
RSCH 4 stage bowel obstruction diet

<table>
<thead>
<tr>
<th>Stage</th>
<th>Dietary advice</th>
</tr>
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<tbody>
<tr>
<td>Stage 1</td>
<td>Clear fluids only (including Elemental diet)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>ALL thin liquids</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Smooth or puréed foods only. Low fibre</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Soft sloppy foods. Low fibre</td>
</tr>
</tbody>
</table>
Jan 2016:
- replacement of NGT
- Bowels open
- tolerating supplements / liquid diet

April - Sept 2016, Aug 17 - Feb 18
- 6 cycles weekly Taxol x 2

- Maintained intake and weight with Bowel obstruction diet - Stage 1-4
BOUNCED: Managing oral diet following a diagnosis of sub-acute bowel obstruction: study exploring the efficacy of a 4 stage Bowel ObstrUctioN CancEr Diet
In summary

- One size does not fit all
- Symptom led
- Slow reintroduction
- Clear fluids with relapse
- More research and guidelines required
Nutrition Impact
Symptoms
We recommend .... the treatment of symptoms and derangements impairing food intake (nutrition impact symptoms) ...
3. **Symptoms:** I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply)

- [ ] no problems eating (0)
- [ ] no appetite, just did not feel like eating (3)
- [ ] nausea (1)
- [ ] constipation (1)
- [ ] mouth sores (2)
- [ ] things taste funny or have no taste (1)
- [ ] problems swallowing (2)
- [ ] pain; where? (3) ________________
- [ ] other (1)** ________________

**Examples: depression, money, or dental problems**  

*Box 3*
In Summary

- Ask questions
- Medications for symptoms
- Beware of under-reporting....
QUESTIONS?