Nutritional assessment and treatment for patients diagnosed with pancreatic cancer.

Anna Burton
Specialist Pancreatic Dietitian

Patients and carers struggle with the lack of dietary information and support.
(Gooden and White, 2013)

Bozzetti and Group (2009) recommend early involvement of dietitians and nutritional assessment to guide management due to high nutritional risk in pancreatic cancer
Discussion topics

• Pancreatic anatomy and physiology
• Nutritional assessment
• Pancreatic enzyme replacement therapy (PERT)
• Secondary diabetes (type 3c)
• Psychological therapies
• NICE guidelines (2018)
• Case study and nutritional treatment
Histology and function

- **Endocrine** (Islets of Langerhans)
  - Alpha cells – glucagon
  - Beta cells - insulin
  - Delta Cells - Somatostatin

- **Exocrine** (Acinar cells and ducts)
  - Trypsinogen and chymotrypsinogen - protein
  - Lipase
  - Amylase carbohydrates
  - Bicarbonate alkaline ph 7-8

- **Controlled by**: gastrin, CCK, Secretin, incretins (Glucagon-like peptide-1 (GLP-1), Glucose dependent insulinotrophic polypeptide (GIP)
Pancreatic enzyme response to a meal

Lipase, amylase, trypsin and chymotrypsin

(Taken from Keller and Layer, 2005)
Lipase secretion rates

(Adapted from Keller and Layer 2005)

<table>
<thead>
<tr>
<th></th>
<th>Interdigestive</th>
<th>Maximal</th>
<th>2 hours postprandial</th>
</tr>
</thead>
<tbody>
<tr>
<td>U/min</td>
<td>1000</td>
<td>3000 – 6000</td>
<td>2000 – 4000</td>
</tr>
<tr>
<td>U/hour</td>
<td>60 000</td>
<td>180 000 – 360 000</td>
<td>120 000 – 240 000</td>
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</table>
Exocrine tumours – adenocarcinoma (95%)
65 - 75% in the head of the pancreas
Presenting symptoms affecting nutritional status

- Abdominal pain
- Jaundice
- Weight loss
- Poor appetite
- Nausea
- Vomiting – duodenal/gastric obstruction
- Indigestion
- Diarrhoea
- Steatorrhoea
- Constipation
- Taste changes
- Lethargy
- Feeling full
- Depression (33 – 70%) Torgerson and Wiebe 2013, Gooden et al 2016
- Physical activity
- Diabetes (Misdiagnosed/undiagnosed Ewald et al 2013)

1 Physical
2 Endocrine insufficiency
3 Exocrine insufficiency –
   Pancreatic enzyme insufficiency (PEI)
   Pancreatic head 60 -90%
   Pancreatic body/tail 30 -50%
   (Sikkens et al, 2014)

4 Metabolic
   Hyper metabolism and catabolism
   Complex metabolic disorder which is poorly understood and difficult to treat
   (Fearon, et al, 2011, 2013)

Cancer cachexia
Weight loss
Different to simple starvation

- Weight loss
  - 40% of patients at time of surgery have cancer cachexia (Bachmann, et al, 2008)
  - 40% overweight/obese patients have sarcopenic obesity (Tan et al, 2009)

  - **Weight loss is an independent predictor** for reduced response rates to chemo/radiotherapy (Bachmann, et al 2008, 2009)
  - Reduced post operative outcomes (Pausch, et al, 2012)
  - Reduced survival (Tan, et al, 2009)

Affects quality of life due to reduced functional status and body image
Less then 10% weight loss – responds to nutritional support
Symptoms of fat maldigestion and Steatorrhoea

- 90% reduction in function before evidence of maldigestion
- Lipids are the most sensitive to deactivation due to ph. 7-8 and proteases
- Digestion of carbohydrate and protein throughout the gut starting in the mouth
- Reduction in oral intake of fat to manage symptoms – check if patients have done this

Any combination of or all:
- Pale
- Floating
- Difficult to flush
- Greasy
- Sticky
- Large volume stool
- Diarrhoea/constipation
- Foul smelling
- Wind and bloating
- Pain
- Urgency
Pancreatic Enzyme Replacement Therapy (PERT)

- Source: Porcine (allergy, vegetarian/vegan and religious reasons)
- Capsule containing enteric coated granules (less than 2mm)
- Temperature and pH sensitive
- No clear maximum treatment guidelines
  - 400 000 units of lipase per day
  - 10 000 units per kg/day
  - 5000 – 4000 IU lipase per g fat
## PERT Preparations

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Product name</th>
<th>Lipase /U</th>
<th>Enteric coated</th>
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<tbody>
<tr>
<td>Abbott (Mylan)</td>
<td>Creon 10 000</td>
<td>10 000</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Creon 25 000</td>
<td>25 000</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Creon 40 000</td>
<td>5000/g</td>
<td>gastro resistant granules</td>
</tr>
<tr>
<td></td>
<td>Creon micro</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Merck</td>
<td>Nutrizym 22</td>
<td>22 000</td>
<td>Yes - minitablets</td>
</tr>
<tr>
<td>Janssen - Cilag</td>
<td>Pancrease HL</td>
<td>25 000</td>
<td>Yes - minitablets</td>
</tr>
<tr>
<td>Essential</td>
<td>Pancrex granules</td>
<td>5000 /g</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Pancrex V capsules</td>
<td>8000</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Pancrex V 125 capsules</td>
<td>2950</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Pancrex V Forte tablets</td>
<td>5600</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Pancrex V Powder</td>
<td>25 000/g</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Pancrex V tablet</td>
<td>1900</td>
<td>Yes</td>
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Right time, right place....... Right ph.

- **Goal**........ enough active enzymes in the duodenum with food
- 44 000 - 75 000 with a meal and 22 000-50 000 with a snack/nutritious fluids/supplements
- Adjust to fat content of meal/snack
- Take at the start of eating, during and at the end of a meal (Dominguez-Munoz, 2013)
- Small amount of cold liquid
- Take capsules whole (do not sprinkle on food, crush or chew)
- If need to open – mix microspheres with acid fruit puree or yogurt
- Omit enzyme with small portions of fat free foods/liquids
- Varies from patient to patient:
  - Functional pancreatic tissue
  - Differing amounts of fat in the diet
  - Anatomical
- **Side effects** – Flatulence, abdominal bloating, nausea, mouth ulcers, anal irritation
- Constipation ?due to improved digestion.
- Fibrosing colonopathy (50 000 U lipase/kg/body weight)
Improving nutritional status

- Manage symptoms (liaise with GP/hospital)
- Pancreatic enzyme replacement therapy (PERT) understanding, compliance, dose adjustments, timings
- Diagnose and treat endocrine insufficiency - nutritional messages for secondary diabetes
- Provide nutritional support
  - Exercise – lean body mass (Fearon, 2014)
  - Psychological support
Unresolved symptoms

- Check compliance and understanding
- “sounds like a lot”
- ? Is dose sufficient (increase)
- Add PPI (lipase active ph 5.5)
- Antidiarrheal agent

- Consider other causes:
  
  Small bowel Bacterial Overgrowth (SBBO)
  Bile salt malabsorption
  Coeliac disease (Bustillo, et al. 2009)

- Type 2 diabetes and obesity risk factor for pancreatic cancer.
- Diabetes develops up to 24 - 36 months prior to diagnosis of pancreatic cancer ?tumour affecting insulin resistance?
- Limited research in the UK

- Various terms used within the literature: pancreatogenic, secondary, pancreatic cancer diabetes mellitus (PC-DM), Type 3c, Type3cDM

- Since 2008 Type 3c has increasingly been used in the literature

- Prevalence ????? 5 – 10% of all diabetics

- 50% of type 3c misclassified in specialist centres (Ewald, 2013)

- Lack of resources and understanding –
  - under and misdiagnosis
  - Inappropriate health messages and nutritional advice

- ? Newly diagnosed diabetic with weight loss – screen for pancreatic cancer
Classification


3c Diseases of the exocrine pancreas

- Fibrocalculous pancreatopathy
- Pancreatitis
- Trauma/pancreatectomy
- Neoplasia
- Cystic fibrosis
- Haemochromatosis
- Other
Incidence of diabetes vs. methods used to diagnose hyperglycaemia in pancreatic cancer patients

<table>
<thead>
<tr>
<th>% diagnosed as diabetic</th>
<th>Patient history or medical records</th>
<th>Fasting blood glucose</th>
<th>HbA1c</th>
<th>OGTT 75g</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12 – 29%</td>
<td>47%</td>
<td>41.7%</td>
<td>77% (diabetic and glucose intolerance)</td>
</tr>
</tbody>
</table>
Pathophysiology

- **Absence of islets** – total pancreatectomy
  - (absolute deficiency of insulin, glucagon and pancreatic polypeptide)
- **Partial absence of functional islets** – chronic
  - pancreatitis, partial pancreatectomy, severe acute
  - pancreatitis
- **Paraneoplastic** – pancreatic ductal adenocarcinoma

Potential mechanisms of hyperglycaemia

- Insulin deficiency
- Immunopathogenesis
  - Hepatic insulin resistance caused by reduction in pancreatic polypeptide
  - Peripheral insulin resistance
  - Reduced incretin effect due to malabsorption of carbohydrate

- **Treatment and medication choice?**
- **Effect of diabetes on overall outcome and survival in pancreatic cancer?**
- **Need for evidence based guidelines on diagnosis and treatment?**
Case study – 68 year old female

• 2 week cancer wait referral

• Pancreatic head mass – suspected adenocarcinoma pancreas

• Referred to dietitian whilst attending MDT pancreatic clinic

• Struggling with poor appetite, lethargy, weight loss (8kg over previous 8 weeks), steatorrhoea, taste changes, jaundiced, polyuria and thirst

• Weight 57kg  Height 1.68m  BMI 20kg/m2
• Previous weight 65kg (12% weight loss over 2 months)

• Random blood glucose 28mmol/l

• Inoperable

• Referred to oncology for assessment for chemotherapy
Nutritional requirements
Out with the old in with the new!

**Henry (2005)**
- $10.2 \times 57 + 572 = 1153$
- 10% SF
- 1.25 PAL

- **Kcal** 1585
- Protein 0.2g/kg hyper metabolic
- **71g day**

- Previous BMI 23kg/m2
- Repletion

**PENG (2018)**
- Pancreatic cancer 24kcal /kg REE
- Range 22 – 27kcal/kg
- PAL 1.25

- **Kcal** - 1567 – 1923
- Protein 1g/kg if possible up to 1.5g/kg
- **57g – 85g**
Causes of weight loss

1. Hyperglycaemia - Newly diagnosed diabetic – type 3c/secondary
2. Maldigestion due to blocked pancreatic and biliary duct
3. Reduced oral intake due to GI symptoms, taste changes, lethargy
4. Tumour mediated hyper metabolism and cachexia

Treatment

Management of diabetes
Diabetic medication – gliclazide 40mg bd started by oncologist (4pm Friday)

Management of maldigestion
Commenced Pancreatic Enzyme Replacement 75 000 with meals and 50 000 with snacks

Nutritional support
Dietary advice – nutritional support – little and often, avoid simple sugars, High protein/high kcal, oral nutritional supplements
Nutritional management:

- Offer enteric-coated pancreatin for people with unresectable pancreatic cancer

- Consider enteric coated pancreatin before and after pancreatic cancer resection

- Do not use fish oils as a nutritional intervention to manage weight loss in people with unresectable pancreatic cancer

- For people who have had a pancreatoduodenectomy and who have a functioning gut, offer early enteral nutrition (including oral and tube feeding) rather than parenteral nutrition
Mental Health and CBT

Thoughts → Emotions → Cognitive Behavioral Therapy → Physical Sensation → Behaviors
Case study

- 72 year old male
- Diagnosed adenocarcinoma pancreatic head
- Surgical management with curative intent
  - (Pylorus Preserving Pancreaticoduodenectomy PPPD)
- Post operative day 5 – 12 Gastric outlet obstruction
- Post operative day 12 – 22 struggling with severe loss of appetite
- NG fed from day 7 – 22
Cognitive Behavioural Therapy

- Explored and managed physical symptoms
- Socratic questioning and guided discovery
- Thoughts and recognition of thinking
- Own experiences and experiences of others

Sister in law – previous colonic surgery and BO

- Avoid reassurance and advice giving
References

• Ewald et al (2013). Diabetes mellitus secondary to pancreatic diseases (Type 3c) are we neglecting an important disease. Eur J Intern Med. Online.
• Gooden and White (2013) Pancreatic cancer and supportive care – pancreatic exocrine insufficiency impacts on QOL. Support Care Cancer 21 1835-1841
• Hardt et al (2008) Is pancreatic diabetes (type 3c diabetes) under diagnosed and misdiagnosed? Diabetes Care (31) 2 5165-5169
• NICE guidelines(2018) Pancreatic Cancer in adults: diagnosis and management (NG85)