Royal Surrey
NHS Foundation Trust

Diabetes and pancreatic cancer

Karen Mackie – Diabetes Specialist Dietitian RSCH

Bev Tuthill – Diabetes Specialist Nurse RSCH

We would like to thank Mary Phillips BSc (Hons) RD DipADP *Advanced Specialist Dietitian (Hepato-pancreatico-biliary surgery)*

WORLD CLASS CARE
FOR OUR COMMUNITY

Content

- Different types of diabetes (brief overview)
- Type 3c diabetes – causes, characteristics and diagnosis
- Relationship between diabetes and pancreatic cancer
- Therapeutic management of diabetes
- Nutritional management of diabetes
- The challenges and importance of glycaemic control
- Managing diabetes at the end of life

Different type of diabetes

- Type 1 diabetes – autoimmune (insulin deficiency)
- Type 2 diabetes – insulin resistance and insulin deficiency
- MODY - genetic
- Gestational diabetes…..

- Type 3C diabetes – concurrent deficiency in both pancreatic endocrine and exocrine function (insulin, glucagon and pancreatic enzyme deficiency)

Causes of Type 3C diabetes

- Pancreatic cancer
- Chronic pancreatitis
- Acute pancreatitis
- Cystic Fibrosis
- Pancreatic surgery
- Haemochromatosis, Fibrocalculous, Pancreatopathy, Pancreatic Agenesis

Suspecting Type 3C diabetes

- **Misdiagnosis is common:**

  2017 Nov;40(11):1486-1493. **Incidence, Demographics, and Clinical Characteristics of Diabetes of the Exocrine Pancreas (Type 3c): A Retrospective Cohort Study** Chris Woodmansey 1, Andrew P McGovern 1, Katherine A McCullough 1 2, Martin B Whyte 1 2, Neil M Munro 1, Ana C Correa 1, Piers A C Gatenby 1 3, Simon A Jones 1 4, Simon de Lusigna

  Of the 559 cases of Type 3C diabetes 87.8% were initially misdiagnosed as Type 2 diabetes

- **Red flags – sudden weight loss, rapid progression, no family history, back pain, sudden bowel changes, minimal osmotic symptoms**
- **HbA1c <6.5% does not rule out type 3c diabetes**
  - Glucose tolerance test if any concern
  - Be aware fasting glucose will be reduced due to low glucagon levels
- **CT scan – not the full picture**
- **All patients with chronic pancreatitis should be screened at least 6 monthly, even if asymptomatic. Pancreatic cancer patients should be screened more regularly**

Proposed diagnostic criteria for Type 3C

Major criteria

- Pancreatic exocrine insufficiency – faecal elastase
- Pathological pancreatic imaging
- Absence of Type 1/ autoimmune markers

Minor criteria

- Absent pancreatic polypetide secretion (PP)
- Impaired incretin secretion
- No excessive insulin resistance
- Impaired beta-cell function
- Low serum levels of lipid soluble vitamins (A, D, E &K)

Diagnosis and treatment of diabetes mellitus in chronic pancreatitis, Ewald N and Hardt P (2013) World Journal of Gastroenterology

Diagnosis of Type 3C diabetes

Pancreatology

Review

Pancreatology 2011;11:279–294
DOI: 10.1159/000329188

Pancreatogenic Diabetes: Special Considerations for Management

YunFeng Cui[a, b] Dana K. Andersen[a]

[a]Department of Surgery, Johns Hopkins Bayview Medical Center, Johns Hopkins University School of Medicine, Baltimore, Md., USA; [b]Department of Surgery, Tianjin Nankai Hospital, Nankai Clinical School of Medicine, Tianjin Medical University, Tianjin, China

Parameter	Type 1 IDDM juvenile onset	Type 2 NIDDM adult onset	Type 3c pancreatogenic postop. onset
Ketoacidosis	common	rare	rare
Hyperglycemia	severe	usually mild	mild
Hypoglycemia	common	rare	common
Peripheral insulin sensitivity	normal or increased	decreased	increased
Hepatic insulin sensitivity	normal	normal or decreased	decreased
Insulin levels	low	high	low
Glucagon levels	normal or high	normal or high	low
PP levels	normal or low (late)	high	low
GIP levels	normal or low	normal or high	low
GLP-1 levels	normal	normal or high	normal or high
Typical age of onset	childhood or adolescence	adulthood	any

IDDM = Insulin-dependent diabetes mellitus; NIDDM = non-insulin-dependent diabetes mellitus.
Modified from Slezak and Andersen [13], with permission.

WORLD CLASS CARE
FOR OUR COMMUNITY

Type 1 or 2 DM developing exocrine insufficiency	Pancreatic disease developing diabetes
Exocrine secretion reduced with insulin deficiency Increased risk pancreatic cancer	Resection / disease of the pancreas causes destruction of endocrine cells
May present with deteriorating nutritional status but often nutritionally well	Often concurrent malnutrition – dietary restrictions not appropriate
Change in bowel habit	Rapid deterioration onto insulin
Glycaemic control responds to enzymes	Requires careful monitoring
Normal nutritional status achieved with enzymes	Hyperglycaemia may worsen with increased enzymes (absorbing CHO)
RED FLAG - Exclude pancreatic cancer - Lifestyle advice if diagnosing chronic pancreatitis	**RED FLAG** – exclude disease recurrence in patients with pancreatic cancer or pancreatic cancer in those with chronic pancreatitis

With permission of Mary Phillips – HPB dietitian

Characteristics of Type 3C diabetes

- **Generalised pancreatic cell damage----**

- **B cell damage – insulin deficiency**
- **Alpha-cell damage – glucagon deficiency**
- **PEI – pancreatic enzyme insufficiency**

- ***Wang W, Guo Y, Liao Z, Zou DW, Jin ZD, Zou DJ, Jin G, Hu XG, Li ZS. Occurrence of and risk factors for diabetes mellitus in Chinese patients with chronic pancreatitis. Pancreas. 2011;40:206–212.***

Symptoms

- Stomach/back pain
- Weight loss
- Indigestion
- Loss of appetite
- Change of bowel habits
- Jaundice
- Recently diagnosed diabetes (especially if low weight, no family history…)
- Bloating, wind, burping, feeling full quickly
- Feeling or being sick
- Feeling exhausted

Relationship between diabetes and pancreatic cancer

- If you have pancreatic cancer there is a high risk of developing diabetes ie: poor glycaemic control
- If you have Type 1 or Type 2 diabetes there increased risk of developing pancreatic cancer – linked to pancreatic atrophy

Therapeutic management of diabetes

WORLD CLASS CARE
FOR OUR COMMUNITY

HanPanEU

United European Gastroenterol J. 2017 Mar; 5(2): 153–199. United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU) J Matthias Löhr,[1] Enrique Dominguez-Munoz,[2] Jonas Rosendahl,[3] Marc Besselink,[4] Julia Mayerle,[25] Markus M Lerch,[5] Stephan Haas,[1] Fatih Akisik,[6] Nikolaos Kartalis,[7] Julio Iglesias-Garcia,[2] Jutta Keller,[9] Marja Boermeester,[4] Jens Werner,[10] Jean-Marc Dumonceau,[11] Paul Fockens,[4,8] Asbjorn Drewes,[12] Gürlap Ceyhan,[13] Björn Lindkvist,[14] Joost Drenth,[15] Nils Ewald,[16] Philip Hardt,[16] Enrique de Madaria,[17] Heiko Witt,[18] Alexander Schneider,[19] Riccardo Manfredi,[20] Frøkjer J Brøndum,[21] Sasa Rudolf,[22] Thomas Bollen,[23] Marco Bruno,[24] and HaPanEU/UEG Working Group

HanPanEU - *Harmonizing diagnosis and treatment of chronic pancreatitis across Europe*

- In mild hyperglycaemia – metformin can be used if not contra-indicated (Grade 1B)
- In more severe cases – Insulin is the treatment of choice (Grade 1B)

- **Sulphonylureas** – risk increased and prolonged hypo, often contraindicated secondary to accompanying liver disease. Advised against ….

  In early type 3c diabetes mellitus, oral therapy with insulin segretagogue (sulfonylurea and glinides) may also be considered. World J Gastroenterol. 2013 Nov 14; 19(42): 7276–7281. Published online 2013 Nov 14. **Diagnosis and treatment of diabetes mellitus in chronic pancreatitis** Nils Ewald and Philip D Hardt

- **Glinides** – increased risk hypo but *shorter half-life* so can be considered at low doses before insulin start

WORLD CLASS CARE
FOR OUR COMMUNITY

- **Thiazolidines –** Advise against owing to side effects (bone fractures, fluid retention, congestive heart disease)
- **Alpha-glycosidase inhibitors –** advised against as can exacerbate exocrine insufficiency
- **Incretin-based therapies –** high frequency gastro side-effects and currently under review due to potential increased risk of pancreatitis.
- **Sodium glucose co-transporter-2 (SGLT-2) inhibitors –** potentially able to induce euglycaemic DKA in insulin-deficient patients (T1 and T3C DM) therefore advised against

Progression to insulin

2017 Nov;40(11):1486-1493. Incidence, Demographics, and Clinical Characteristics of Diabetes of the Exocrine Pancreas (Type 3c): A Retrospective Cohort Study
Chris Woodmansey 1, Andrew P McGovern 1, Katherine A McCullough 1 2, Martin B Whyte 1 2, Neil M Munro 1, Ana C Correa 1, Piers A C Gatenby 1 3, Simon A Jones 1 4, Simon de Lusigna

- **The following is the incidence of insulin usage within 5 years of diagnosis**
  - 4.1% in Type 2 diabetes
  - 20.9% after acute pancreatitis
  - 45.8% in those with chronic pancreatitis

Insulin regimens

Options:

- Basal bolus – more flexible, more precise, 4 or more injections a day
- Mixed insulin – only 2 injections a day, less change required, need to keep carbohydrate consistent
- Pumps – flexible, more precise, can fine-tune dosing, need to carbohydrate count, need to be confident with technology, no pen injections but set change every 3 days.

Which option is best?

Injection techniques

Seems simple but this can significantly impact management

WORLD CLASS CARE
FOR OUR COMMUNITY

Pancreatic Cancer UK

Supported by OncoSil MEDICAL VIATRIS

Break

Diabetes and pancreatic cancer

Thursday 10th February 2022, 09.00 – 11.00am, Zoom Webinar

#PCUKStudyDay

Nutritional management of diabetes in pancreatic cancer

- **Nutritional status and glycaemic control**
- **Focus of this session is on glycaemic control *BUT***
- **Part of the assessment involves the following:**
  - *If low weight or lost weight – oral nutrition support*
  - *Pancreatic Enzyme Insufficiency – need enzymes and annual micronutrient blood tests*
    - *Education on dosing and dietary relationship*
- **Carbohydrate awareness/counting**
  - Education on carbohydrates (individualised)

Carbohydrates

- **Awareness progressing to dose adjustment as competent to do so**
- **Stepwise process of education**

What are carbohydrates and how do they effect blood glucose

↓

Relationship between insulin and carbohydrate content

↓

Carbohydrate counting

↙ ↘

Set carbohydrates variable carbohydrates

WORLD CLASS CARE
FOR OUR COMMUNITY

Carbohydrate counting

- **Educate on the different tools available**
  - Carbs and Cals
  - Food labels
  - Weighing
  - Reference tables
  - Apps/internet

WORLD CLASS CARE
FOR OUR COMMUNITY

Dose adjustment

- **Routine diet with set carbohydrates – can be on mixed insulin or set rapid acting insulin doses**
- **Variability in diet – working towards dose adjustment**
  - Get them counting carbohydrates and reviewing patterns (understanding?)
  - Ratios eg: 1unit : 10g carbohydrates
  - ISF (Insulin sensitivity factor) eg: 1 unit to lower blood glucose by 2mmol/l
  - Target blood glucose: individually agreed
  - Snacks: Individual *remember they may require small and often secondary to poor appetite*

Other factors that effect blood glucose

- Activity
- Alcohol
- Stress
- Infection
- Pain
- Enzymes

WORLD CLASS CARE
FOR OUR COMMUNITY

Challenges and importance of glycaemic control

- **Acute: Significant day-to-day variability**
  - **Enzymes** *(have they taken the right amount of enzymes?)*
  - **Insulin management** *(are they appropriately managing their insulin doses?)*
  - **Understanding** *(Do they understand the relationship between carbohydrates and blood glucose/insulin? Can they manage intensive carbohydrate counting for dose adjustment?)*
  - **Lack of glucagon** *(overnight/hypo recovery/activity…)*
  - **Emotional health ---** *impacts management*
- **Chronic - complications if long-term raised levels**
  - Microvascular and macro-vascular
- **End of life**

WORLD CLASS CARE
FOR OUR COMMUNITY

Are they taking their enzymes correctly

- Bowels – colour, Bristol stool charts, floating, frequency
- Weight stability – nutritional assessment and blood glucose assessment
- Micronutrient screen

- Be aware that blood glucose is likely to rise once enzymes taken appropriately

Insulin management

- **May need to review the insulin regimen and injection technique**
- **Are they**
  - Taking the basal insulin routinely and at the same times
  - Are they bolusing before meals
- **Is the basal insulin covering the full 24 hours?**
- **Are they adjusting based on their carbohydrates?**

Understanding

- Do they understand the relationship between blood glucose, insulin and carbohydrates?
- Do they understand how the different insulins act?
- It is a complex system so need to base on the individual's understanding
- Would a mixed insulin be simpler and safer?

Glucagon insufficiency

- Slower to recover from hypoglycaemia
- Activity needs to be more carefully managed

Emotional health

- **Consider picture up to their diagnosis**
  - Feeling awful for some time
  - Managing with news of diagnosis
  - Undergone surgery
  - Managing with treatment regimen
- **Consider personal circumstances and support**

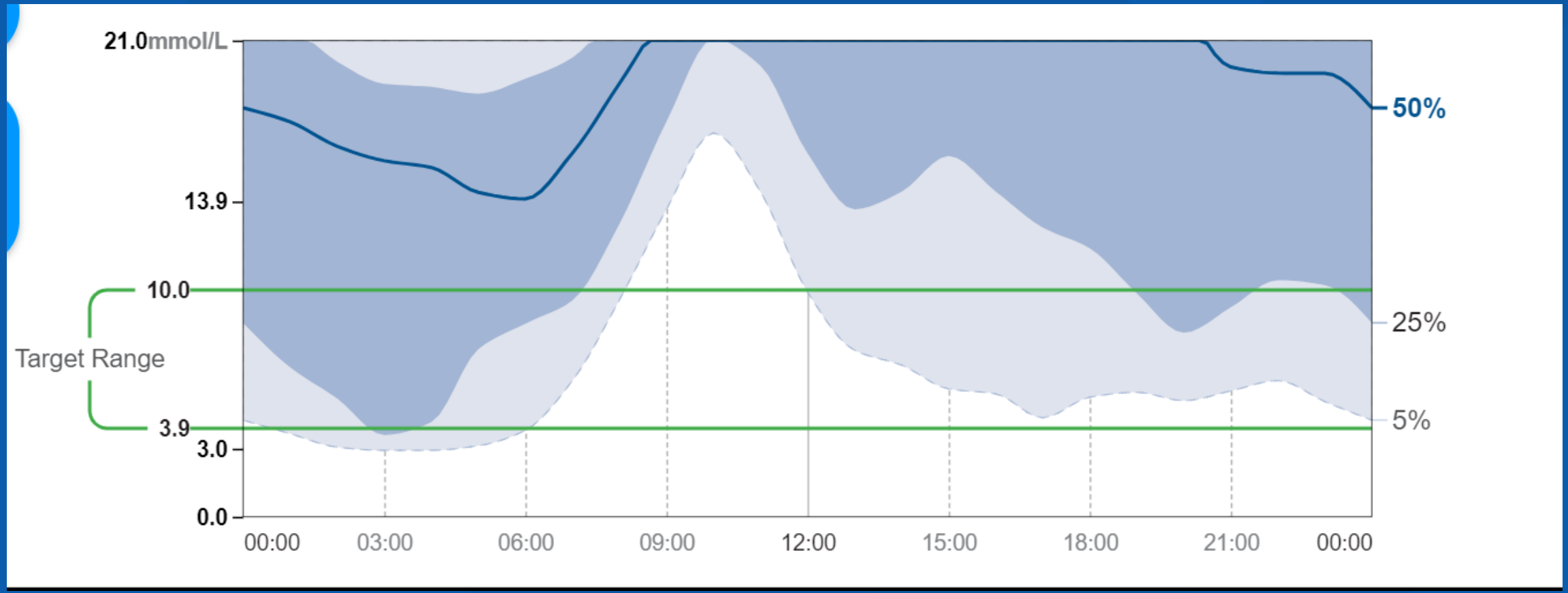
End of life

- Management aims change
- Aim: Minimise symptomatic glycaemic variation, but the focus moves away from tight targets to reduce chronic complications
- Blood glucose testing will need to continue but less rigid targets
- More flexibility with diet – appetite likely impacted so small and often and as tolerated.

Case study 1

- 52 year old lady
- Significant weight loss, pancreatic insufficiency, bouts of acute pancreatitis followed by diagnosis of chronic pancreatitis with calcification on head of pancreas. During this time her HBA1c was elevated at 118mmol/mol and managed with Lantus and Metformin. Poor blood glucose testing (2-3 times a week)
- Later in the year she had a total pancreatectomy
- Commenced on basal bolus regimen
- Ongoing pain so was on Oromorph for a few months
- Regular carer for grandchildren. Often quite anxious.
- Ongoing difficulty optimising glycaemic control
- Saw dietitian - discussed carbohydrates, enzymes reviewed. Diet variable and limited understanding in relation to carbohydrates and insulin

Libre graphs



WORLD CLASS CARE
FOR OUR COMMUNITY

Which management changes would you consider?

A. Consider an insulin pump
B. Continue on the basal bolus regimen with further education
C. Switch to mixed insulin

Case study 2

- 45 year old man
- Necrotising pancreatitis with repeat admissions secondary to pancreatitis
- On basal bolus regimen and enzyme replacement
- Ongoing difficulty with extreme fluctuations (black out with head injury while hypo) but HBA1c in range – commenced on flash glucose monitoring
- Started Humulin I but moved to Degludec
- Referred dietitian late 2019 for carbohydrate education
- Progressed to insulin pump early 2020 resulting in much less variability
- in his levels

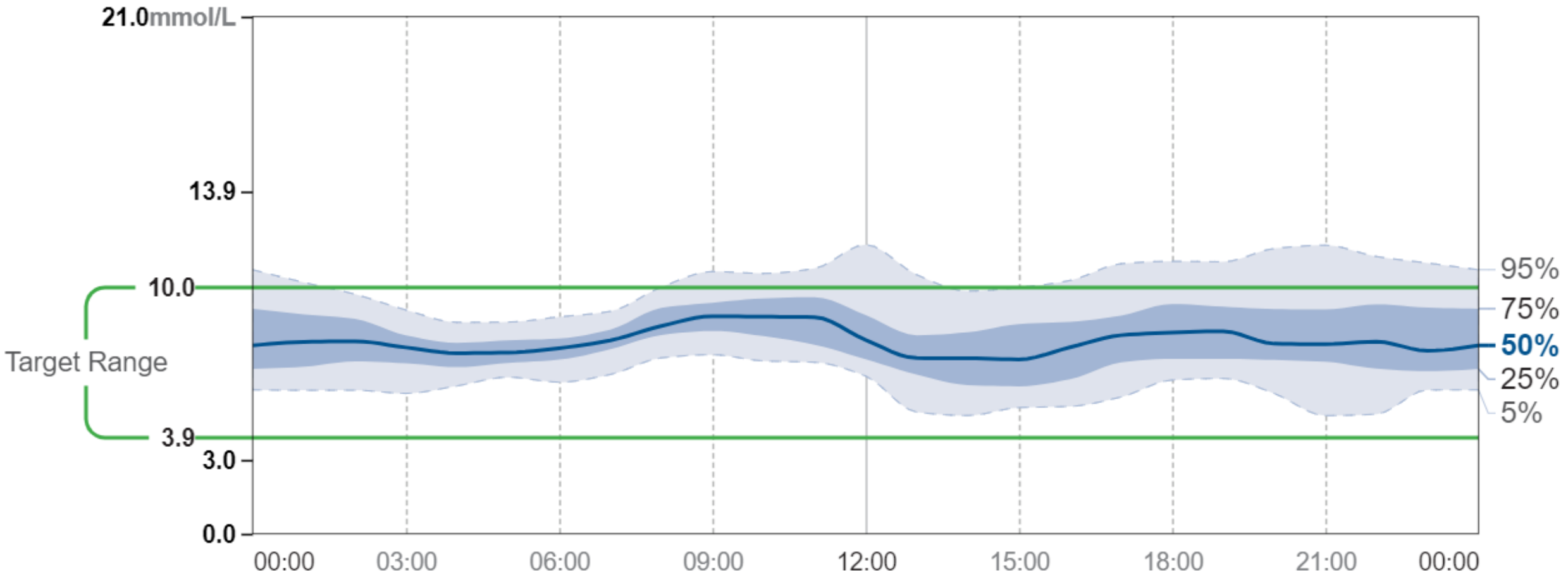
Would looping improve his management?

A. Yes
B. No

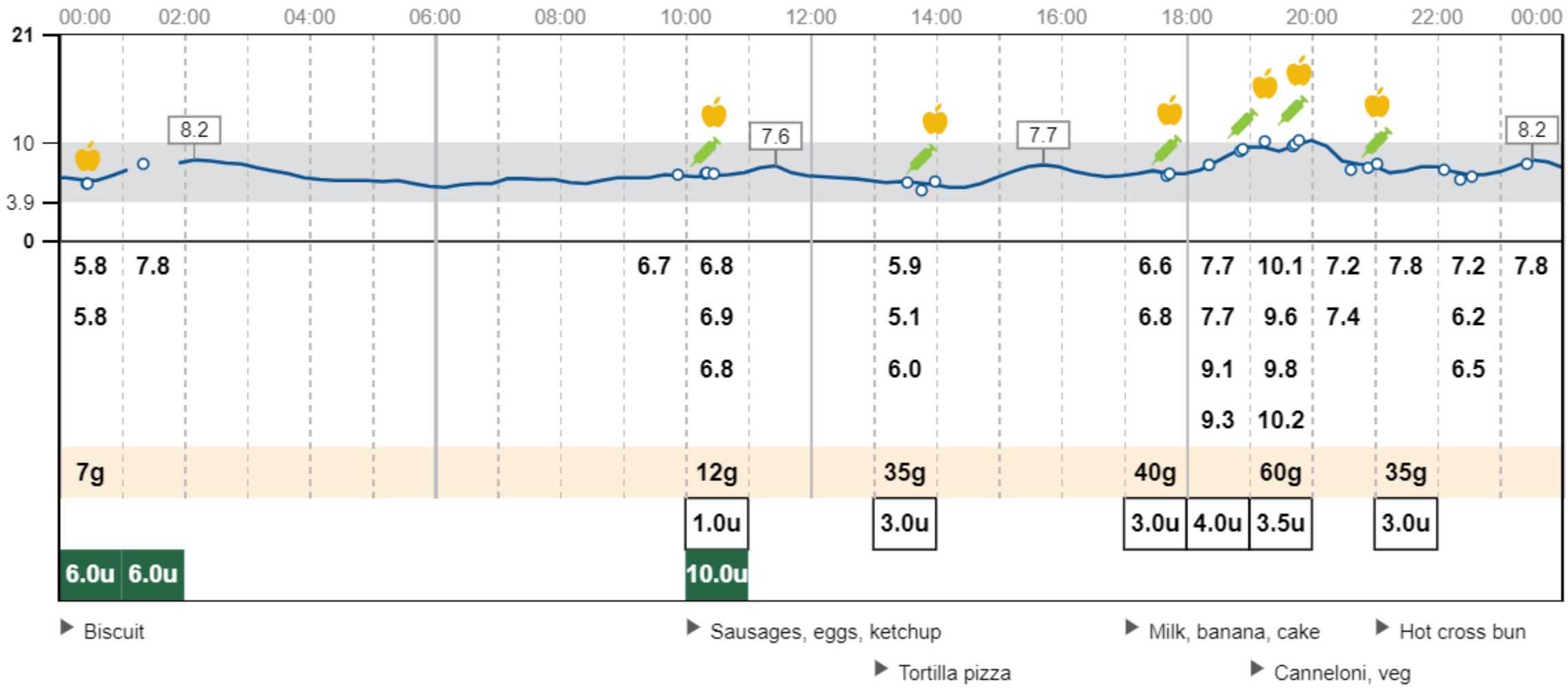
WORLD CLASS CARE
FOR OUR COMMUNITY

Case study 3

- Severe acute necrotising pancreatitis with 6 month hospital admission
- Pancreatic exocrine insufficiency – on Creon
- Type 3c diabetes – insulin requiring on basal bolus
- Naso-jejunal feeding – secondary to delayed gastric emptying and progressed onto normal diet
- Referred to dietitians for carbohydrate advice post-discharge
- Likely PTSD



WORLD CLASS CARE
FOR OUR COMMUNITY



WORLD CLASS CARE
FOR OUR COMMUNITY

Would you advise to continue with basal bolus or switch to insulin pump therapy?

A. Continue with basal bolus
B. Switch to insulin pump therapy

WORLD CLASS CARE
FOR OUR COMMUNITY

Many thanks for listening
Any questions?

WORLD CLASS CARE
FOR OUR COMMUNITY