Supporting patients to achieve remission of Type 2 diabetes

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Introduction

Type 2 diabetes (T2D) currently affects 7% of the total population in the UK, and someone new is diagnosed every 2 minutes (Whicher et al. 2020). The prevalence has doubled in the past 20 years with 4.7 million people affected and this is expected to rise to 5.5 million by 2030 (Diabetes UK 2019). The economic burden of diabetes is high, and accounts for 10% of the NHS expenditure (Hex et al. 2012). Roughly 18% of hospital beds are filled with patients with diabetes (NHS Digital 2020). The long-term complications of T2D are well documented, including retinopathy, neuropathy and nephropathy (Fowler 2008). Diabetes also causes macrovascular complications and is thought to be responsible for 530 myocardial infarctions each week in the UK, in addition people with T2D have double the risk of experiencing a cerebrovascular accident (NHS Digital. 2016).

Being overweight or obese increases a person's risk of developing T2D by 80-85% (Ng et al. 2014) and worryingly 63% of adults in England are overweight or obese (NHS Digital 5/05/2020). It has been estimated that over a third of the UK population has pre-diabetes, this is a state when blood sugars are higher than normal but below the threshold for a diagnosis of diabetes (Mainous et al. 2014) Nationally there is a drive to prevent T2D and the Healthier You: NHS Diabetes Prevention Program (DPP) has been running since 2016 and it is hoped that after the 5 year program, 18000 cases of diabetes may have been prevented (NHS England. 2016)

Until recently a diagnosis of T2D was thought to be irreversible and progressive (UK prospective, 1995). Several recent studies (Counterpoint, Counterbalance and the Diabetes Remission Clinical Trial (DiRECT)) have shown that in people who have had diabetes for less than 10 years there is potential for remission of the condition if significant weight loss (more than 10% of their original body weight) is achieved (Lean et al.; Lim et al. 2011; Steven et al. 2016)

How has remission been achieved?

Our understanding regarding the onset of T2D has progressed. The Beta cells which are found in the pancreas are responsible for the production of insulin, which is essential for the maintenance of glycaemic levels. Previously it was thought that Beta cell death or dysfunction led to the onset of diabetes but evidence to support the twin cycle hypothesis has improved our understanding of the condition (Taylor 2008). Historically studies have shown that Bariatric surgery could be effective in the treatment of T2D in obese patients, reversing the metabolic abnormalities of the condition in a number of weeks (Gumbs et al. 2005). Although the full mechanisms of how the weight loss affected the beta cell function was not understood. The twin cycle hypothesis suggests that long term surpluses of calories lead to an accumulation of liver fat with a subsequent overflow into the pancreas, ultimately these repeated cycles between the liver and pancreas result in an inhibition of insulin secretion after meals with a resultant hyperglycemia (Taylor 2013). The calorie deficient experienced post bariatric surgery was replicated in the Counterpoint study, where participants were given a very low-calorie diet for 8 weeks (Lim et al. 2011). Interestingly this study confirmed that people were able to tolerate a low calorie liquid diet for a short

period of time (Steven et al. 2016). Over this period, the mean weight loss was 15kg, similar to weight loss achieved over the same period post gastric bypass. The participants levels of liver fat dropped dramatically and their insulin sensitivity improved, these finding provided evidence to support the twin cycle hypothesis (Taylor 2013). Adding to this, we now also know that Beta cells can de-differentiate after excess fat exposure, resulting in an inability to secret insulin (Cinti et al. 2016), once normal levels are achieved there is potential for Beta cell recovery.

Not all people with T2D are obese but T2D is characterized by an accumulation of fat in the liver and pancreas. Everyone has their own threshold (personal fat threshold), and this explains why some people with a healthy Body Mass Index develop diabetes. This accumulation of fat results in insulin resistance and positively this can resolve once the fat levels normalize (Taylor and Holman 2015).

Research into diabetes remission

Following the initial Counterpoint study (Lim et al. 2011) where the potential for the remission of diabetes was shown using a very low energy diet to support weight loss, public interest was sparked. Motivated individuals who had heard about the research sought information from the researchers and a website containing information of how to achieve remission of diabetes was made available (Steven et al. 2013). A group of determined individuals (n=77) followed this advice, half using liquid meal replacements and half restricted their calorie intake. Overall, in this non research environment the participants lost more than 10% of their weight and 61% reported remission of their diabetes (Steven et al.

2013). This study showed that remission of diabetes should be a goal in the management of T2D. Importantly these successes were seen in very motivated individuals and therefore more research was necessary.

DiRECT (Diabetes Remission Clinical Trial) was a randomized control trial established in primary care to evaluate the effectiveness of a low-calorie diet with structured follow-up when compared with the conventional treatment of best practice management for T2D (Lean et al. 2018). Participants were selected who had had diabetes for less than 6years. The intervention included;

- Complete withdrawal of all antidiabetic and antihypertensive drugs
- Total Diet replacement (825-852kcal/day) for 3-5 months
- Stepped food introduction (2 – 8 weeks)
- Structured support for long term weight loss

Almost a third of people invited to participate in the trial agreed to partake and over the study the average weight loss was 10kg in the invention group compared with 1kg in the control group, with 46% (68/149) achieving remission at 12 months (Lean et al. 2018). After 24 months a third (53/149) of participants in the intervention group remained in remission (Lean et al. 2019). This study confirmed that B cell function was normalised in those who maintained their weight loss. The researchers of the DiRECT study wanted to further examine the impact of remission on the pancreas. People with T2D have a pancreas that is smaller and irregularly shaped when compared to people without the condition (Macauley et al. 2015). A subset of people from the DiRECT trial were compared against people without the condition. At baseline the pancreases in people with T2D were significantly

smaller and had irregular borders. Two years after the study the pancreases of the same participants who had progressed to remission had normalized (Al-Mrabeh et al. 2020).

Confirmation of Remission

The joint Association of British Clinical Diabetologists (ABCD) and the Primary Care Diabetes Society (PCDS) released a position statement clarifying the criteria to be met for diabetes remission to be confirmed (Nagi D 2019),

- Weight loss
- Fasting plasma glucose <7mmol/L or HbA1c <48 mmol/mol (WHO diagnostic thresholds) for two tests at least 6 months apart.
- Complete cessation of all glucose lowering medications prior to the attainment of the above parameters.

The ABCD and PCDS also highlight the importance of the use of uniform vocabulary to encourage consistent coding and language which will support regular follow-up and data collection and suggest that the term “diabetes in remission” should be adopted (Nagi D 2019). The latest research suggests that for those who have achieved remission the B cell function appears to remain stable if the weight loss is sustained. If the individual returns to their previous weight it is very likely that their diabetes will return (Taylor and Barnes 2019). Therefore, all those who achieve remission must continue to have their risk factors monitored and be supported to avoid any long-term weight gain (Nagi D 2019).

Can we predict who progress to “diabetes in remission”?

The DiRECT study showed that weight loss was the best predictor of remission, with 79% of participants who had achieved a weight loss of 10-15kg still in remission at 2 years (Thom et al. 2021). Following weight loss, the next best predictor was number of prescribed diabetes medication, with those on fewer diabetes medications more likely to progress to remission. People who suffered with anxiety or depression were less likely to achieve remission. Interestingly, baseline BMI, fasting insulin and duration of diabetes (all participants had diabetes < 6years) did not affect prediction of remission (Thom et al. 2021).

Which Diet is best to promote remission?

While it is clear that weight loss is the best predictor of remission (Thom et al. 2021). There has been a degree of uncertainty about the most effective weight reduction plans to promote diabetes remission. A recent systematic review (Churuangsuk et al. 2022) has examined the published data of weight reduction plans for diabetes remission. Seven studies were deemed high-quality and had 12-month data. It appeared that the highest remission rates were found in studies that included total diet replacement diets, with a 54% remission rate at 12months. In total diet replacement diets (TDR) normal food is replaced entirely are nutritionally complete shakes and/or soups, providing less than 900 calories per day. Interestingly, the very low carbohydrate ketogenic diet achieved a 20% remission rate, while the Mediterranean diet a 15% remission rate and a diet program that included some meal replacements 11% remission rate (Churuangsuk et al. 2022). The safely and effectiveness of a TDR diet was assessed in obese patients in the DROPLET (Doctor Referral of Overweight People to Low Energy total diet replacement Treatment) trial (Astbury et al, 2018). This trial assessed the merit of implementing a TDR diet with weekly support against a usual care diet program with reduce calorie intake. The results showed that the TDR diet

was successful in achieving a significant amount of weight loss in a reduced time and was tolerated well by many people (Astbury et al. 2018). Whilst these patients were not specifically noted to have diabetes, this study does support the effectiveness of the use of TDR diet in a primary care setting.

Other type of interventions have also shown success. A population-based cohort study assessed the 5-year outcomes for patients newly diagnosed with T2D between the ages of 40- 69years. Patient in the intervention group received more support to achieve behaviour change but were not specifically encouraged to follow a TDR diet. Diabetes remission was achieved in 30% of the participants in the intervention group after 5 years (Dambha-Miller et al. 2020). This study showed that weight loss (>10%) soon after diagnosis was positive in achieving remission and could be achieved without severe calorie restriction. In this study for each kilogram of weight lost there was an associated 7% higher chance of remission (Dambha-Miller et al. 2020). All participant in this study had a duration of diabetes less than 2 years. Another recent service evaluation from a UK general practice which advised and supported patients (existing T2D's, newly diagnosed and those with pre-diabetes) to follow a low carbohydrate diet (50-130g/day) showed very positive long-term results, with significant improvement in weight, HbA1c and cardiovascular risk factors (Urwin et al, 2020). In patients with prediabetes, 93% returned to a non-diabetic threshold, while for those with T2D 46% were considered to have achieved remission of diabetes after the 23months. While this was not a randomized controlled trial it does show the positive impact motivated health care professionals can have within a community clinical setting and the effectiveness of promoting a low carbohydrate diet (Urwin et al, 2020).

There is recognition that no one intervention or diet will suit all, and there is acceptance that it is possible to achieve remission using a variety of dietary interventions (Taylor et al. 2021). The evidence does suggest that it is essentially about amount of weight lost (ideally more than 10%) and if this weight loss can be maintained

The role of the nurse in supporting patients to achieve remission

The evidence shows that the remission of diabetes should be a primary goal in the management of T2D (Steven et al. 2013). Nurses can play an important role in providing people with the information about the amount of weight loss required to achieve remission and can help motivate individuals to make a change (Steven et al. 2013). For some individuals any weight loss can be very challenging but promoting weight loss is essential, as even a 5% weight loss has been shown to have significant improvements on HbA1c, cholesterol, blood pressure and insulin sensitivity (Ryan and Yockey 2017).

Patient often approach nurses and other health care professionals for advice on what changes they should make to their diet. Recently there has been much debate about low carbohydrate diets versus low fat diets versus various intermittent fasts. The Diabetes UK 2018 guidelines (Dyson et al. 2018) were developed following a review of the many varied dietary approaches. The Diabetes UK nutrition guidelines recommend that overweight and obese newly diagnosed people with T2D should aim for 15kg weight loss and that this should be achieved through an individualized approach (Dyson et al. 2018). These guidelines have moved away from a “one-size fit all’ approach and recognize that a person-centered approach would be more beneficial, taking into account the person’s lifestyle, their cultural influences and incorporating joint decision making. The guidelines show that no single

approach is significantly superior but suggests that people with T2D should aim for a weight loss of 5% where appropriate. The guidelines support an approach which aims to reduce energy consumption and total and saturated fat intake, while increasing both fiber and physical activity. In addition, red and processed meat along with refined carbohydrates are discouraged. Nurses and all health care professionals are encouraged to provide a personalized approach to each patient, considering their lifestyle and culture (Dyson et al. 2018).

Primary care nurse are playing an important role in supporting the new NHS England low-calorie diet programme (NHS Soup and Shake programme) which has been launched in a number of areas across the country (NHS England). People who are eligible will be offered total Diet replacement products of 900 calories per day for up to 12 weeks. Individuals will be supported either on a one-to-one basis, in groups or even virtually (app/ online). The early pilot data has been very encouraging with the average weight loss after 3 month of 13.4kg (Diabetes UK 2022). Participants within this programme need to have a BMI > 27kg/m^2 but further research as part of the ReTUNE study is also been done to investigate the impact of weight loss in individuals with lower BMI and it seems the early results from this are also very encouraging (UK 2022)

Achieving significant weight loss will have many health benefits but it is imperative that this weight loss be maintained and that lifestyle changes be sustained and supported with regular physical activity (Wing and Phelan 2005). Were possible nurses should try and engage with their patients and make use of all opportunities with each patient to provide information and to promote change (Health Education England 2022). Through repeated

encouragement and support, nurses can help patients to modify their behaviour and improve their lifestyles. Weight regain is most common soon after the initial weight loss, and patients on the DiRECT study who gained 2-4kg were offered a "rescue plan" of either partial or total meal replacement to help them to reduce their weight again (Lean et al. 2019). This highlights the long-term commitment from both the patient and the nurse to sustain the lifestyle change and resultant weight loss.

Conclusion

It is possible to achieve diabetes remission, especially in those newly diagnosed with the condition, or who have had the condition for less than 10 years. This has very significant implications especially considering the possible complications that individuals with T2D often develop. Nurses have pivotal roles in ensuring their patients are aware of the latest research and then in supporting them in achieving weight loss to improve their health outcomes. This support needs to be sustained as patients who regain weight may develop diabetes again.

Conflict of interest

None declared

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