



The Emphasis on Remission of Type 2 Diabetes through Diet

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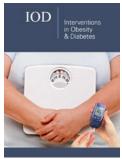
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Opinion

Five years ago, bringing type 2 diabetes into remission would not have been a serious treatment option. Looking at guidelines and evidence today makes clear that health professionals have accepted this possibility on many occasions and settings [1]. However, the question of which dietary steps make remission actually happen has not been answered to a final extent. Type 2 diabetes accounts for more than 90% of the of the ever growing number of patients with diabetes, and remission would not only mean improvement of the quality of life of patients, but could also reduce health care costs extensively. Type 2 diabetes is the end stage of a long lasting Insulin Resistance (IR). Already in the nineties of the last century Reaven and Hotamisigl and their research groups made clear that a diet rich in saturated fat and carbohydrates leads through a cascade of steps to weight accumulation in the abdomen, to visceral fat storage, inflammation of the fatty tissue and other organs, and finally, insulin resistance [2]. The first step in the process is the change of the microbiome caused by an unhealthy food pattern leading to the leaky gut, which enables Liposaccharides (LPS) to enter the system to set the stage for insulin resistance [3,4]. IR causes release of high insulin levels, not only after meals, but all day through many years [5], which is promoted by a lack of physical exercise, stress, sleep problems, low fiber diet, and genetic predisposition. Finally, the islets of Langerhans in the pancreas cannot keep up with the excessive continuous demand for insulin. Hence, type 2 diabetes is the result [6]. IR has also been linked to cardiovascular risk factors (age, blood pressure (SBP and DBP), Total Cholesterol (TC), Triglycerides (TG), HDL-C, LDL-C concentration), and cardiovascular disease [7]. During the chronic process of type 2 diabetes progression the islets of Langerhans deteriorate more. Up to six years after diagnosis reversion is possible [1]. The glucose levels at the time of diagnosis, which are used to determine who is fit for remission should not be the final cut off point, but rather a choice between: glucose levels related to carbohydrate intake; or fasting insulin; or C-peptide. Any of those will tell the HP more about the insulin production of the pancreas. Even glucose levels >10mmol/l. may seem a great risk, but they may reduce quickly on a remission scheme.

The simple physiological explanation of the emergence of type 2 diabetes, being insulin resistance, should lead to a clear path in the management of the disease, by taking away its cause, IR, and letting the body restore itself. This fact in itself has remained controversial in diabetes management, and is certainly not mentioned in most studies on T2DM management [1], or explained to patients, which is peculiar, because taking away the cause is the best way to treat a problem. But most scientific manuscripts regarding T2DM never even mention IR as the problem to tackle. Rather, one looks at the symptoms, hyperglycemia and high HbA1C; hypertension and dyslipidemia, and treats them. Because T2DM is in many cases diagnosed in late-stage comorbidities, such as high blood pressure and dyslipidemia, are already present and demand action as well. They are also caused by insulin resistance [7] but dealing with their symptoms may overshadow the main treatment. Medication to treat them often

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prevents substantial weight loss. Additionally, weight loss, which should be the main concern to resore insulin sensitivity, is regarded as one of the issues, instead of the main target. Weight loss is also something that is decided upon in close alliance with the patient: are they up to it? If not, a more modest approach is taken [1]. It is important to prioritize the main objectives in T2DM management. And they are: reduction of insulin resistance and weight loss. The two are closely connected. Insulin resistance being the cause of T2DM and the cause of overweight/obesity must be put into remission. Remission of T2DM is only possible when the abundant weight is lost. Therefore the approach should primarily focus on weight loss. Weight loss in patients with severe IR needs to address IR as the main physiological problem. This implies cutting down on carbohydrate intake, not as an option, but as a necessity. Low carbohydrate intake leads to low insulin levels, which will enable the body to start losing weight. Only low carbohydrate of less than 50 grams per day lead to lower HbA1C [8,9] and have more potency to improve the HbA1C than other diets, such as Mediterranean diet or low fat diet [9]. A point of notice is that HbA1C levels reveal the state of T2DM in a patient, whereas fasting glucose levels do not.

Obese patients often have changing and elevated fasting glucose levels, due to the insulin resistance. Weight loss is further promoted by low energy intake, as shown in the DIRECT study with 46% remission, with 85% of participants who lost >15kg achieving remission at 1 year [10]. The DIADEM study showed 61% remission after one year compared to controls [11]. These studies both offered their intervention groups diets of 800-850 calories per day, low energy, low carbohydrate and high protein through meal replacements. But it is the combination of low energy and low carbohydrate that makes the most impact. The Look Ahead study gave their participants 1200-1800 calories, leading to a remission of 11% of the study population [12], meaning that results were not even close to those of the DIRECT and DIADEM studies. Although the outcomes of DIRECT and DIADEM show how specific the treatment to put T2DM in remission must be: recent NMAs do not confirm the results [13]. This may be due to the fact that low carb diets included in NMAs and SRs show great variety in their carbohydrate content, and their outcomes. What to conclude from them is therefore biased. What does this tell us? First of all: weight loss is crucial. A weight loss of more than 10% will lead to remission. Secondly, the lower the carbohydrates, the better the remission, suggesting the pancreas is reset in this process. The DIRECT study showed that the pancreas morphology changed: it's volume increased and the borders were more smooth in those showing remission, suggesting a reversal of the organ. And, this is the good news: remission may result in restoration of the pancreas [14]. Finally, we need to acknowledge that treating T2DM consists of several stages [1]. The first stage being aimed at remission. Remission is only possible within the first six years after diagnosis, so we need to start with it right away [1]. A calorie restriction as well as a carbohydrate restriction is mandatory, preferably <50 grams carbohydrate per day and a calorie intake of <1000kcal.day. The protein intake may be as high as 1,2 grams/kilo body weight [15]. Weight loss should

be 10-15% of initial weight. This combination makes weight loss possible at a steady speed. That will keep the patient motivated. The second stage is aimed at weight maintenance, installing healthy habits such as exercise, mental coaching to overcome psychological barriers that keep the patient from improving himself. The third phase is the hardest: maintaining healthy habits and incorporating them in life, as well as relapse management. In this phase a variety of dietary patterns is recommended, e.g., the Mediterranean diet, or products that are part of that diet pattern, such as olive oil, pulses, seeds, high amounts of vegetables. This is a pattern that is beneficial for prevention of cardio vascular disease. In patients that have recovered from T2DM carbohydrate intake should never go back to the levels the patients used before, but must stay restricted to the point where weight and glucose/HbA1C levels stay stable.

Conclusion

Remission of T2DM is preferably started right after the diagnosis, but can be successful for up to six years. The success depends on the restoration of the insulin sensitivity obtained by 10-15% weight loss. Weight loss is best on a low carbohydrate (<50 grams/day), low energy (<1000kcal/day), 1-1,2 grams protein/day diet in the weight loss phase

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