Remission in Type 1 Diabetes - What's New?

Chwalba Artur and Ewa Otto-Buczkowska
Medical Specialist Centre in Gliwice, Jasnorzowska 26/21, 44-100 Gliwice, Poland

Corresponding author: Ewa Otto-Buczkowska, Medical Specialist Centre in Gliwice, Jasnorzowska 26/21, 44-100 Gliwice, Poland, Tel: +48 502 094 599; E-mail: em.buczkowski@pro.onet.pl

Rec Date: Dec 3, 2014; Acc Date: Dec 12, 2014; Pub Date: Dec 14, 2014

Copyright: © 2015 Artur C, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Type 1 diabetes is an autoimmune disease, in which there is a destruction of pancreatic islet β cells. In the natural course of the disease we deal with a gradual progress during the few years of reduction of cell mass. The symptoms of diabetes appear when the mass of insulin-secreting β cells will be reduced by about 80-90%. In this state, the amount of insulin is insufficient to ensure normoglycemia. Many patients shortly after diagnosis of diabetes type 1 and initiation of insulin therapy come to partial cell β renewal and consequently to reduce the need for exogenous insulin. This phenomenon is called the remission of the disease. The period is also called honeymoon. The glucose concentration decreases so the insulin dose should be also reduced, however complete cessation of insulin is not recommended. Accuracy to determine and compare the prevalence of type 1 diabetes remission is difficult because of ambiguous criteria for its diagnosis: most remission criteria take into account the following parameters: glycated hemoglobin (HbA1c), daily need for exogenous insulin, and the concentration C-peptide in the blood. In all definitions of remission, although different criteria are used, residual insulin secretion is underlined, as well as demonstrated measurement of C-peptide and low demand on exogenous insulin.

Keywords: Type 1 diabetes; Clinical remission; Insulin secretion; Insulin therapy; C-Peptide level

Abbreviations:

IDDM: Insulin-dependent Diabetes Mellitus; DM: Diabetes Mellitus; T1D: Type 1 Diabetes; A1C: Glycosylated Hemoglobin; DKA: Diabetic Ketoacidosis

Introduction

Type 1 diabetes is an autoimmune disease, in which there is destruction of pancreatic islet β cells. In the natural course of the disease we deal with a gradual progress during the few years of reduction in cell β mass. The symptoms of diabetes appear when the mass of insulin-secreting β cells will be reduced by about 80-90%. In this state, the amount of insulin is insufficient to ensure normoglycemia. Many patients shortly after diagnosis of diabetes type 1 and initiation of insulin therapy come to partial cell renewal β and consequently to reduce the need for exogenous insulin. This phenomenon is called the remission of the disease. The remission period often follows the clinical onset of insulin-dependent (type 1) diabetes, and is characterized by residual β cell function, reduced insulin requirements, and good metabolic control. Studies on the occurrence of remission in diabetes have a long history. In 1946, Glassberg presented a description of diabetes remission [1]. In subsequent years there have been many reports on the occurrence and behavior of remission in juvenile diabetes mellitus and of insulin secretion during this period [2-7]. This assessment of insulin secretion also allowed for the exclusion of patients with diabetes mellitus with other type than juvenile diabetes. The first description of juvenile diabetes patients remission in Polish literature was presented in 1971 [8]. Many studies have shown that early diagnosis and rigorous intensive insulin therapy as well as very careful metabolic disease control from the time of diagnosis determine beginning and duration of remission. These studies have a long history [9-12].

Factors Promoting T1D Remission

A number of factors promote to the occurrence of remission. Böber et al. conducted a retrospective study performed on patients diagnosed with IDDM [13]. In conclusion, history of infection prior to presentation and DKA at diagnosis was associated with young age and were the most important factors negatively influencing the remission rate in newly diagnosed IDDM patients. Knip et al. demonstrated that the boys had a remission more often and of longer duration than the girls. The children with remission had lower blood glucose, milder hyperketonemia and ketonuria, higher pH and PCO2 at onset than those without remission [14]. Swedish multicenter study showed remissions in 43% of the patients with a median duration of 8 months (range 1-73) [15]. In islet antibody-positive diabetes, normal body weight was the strongest factor for entering remission, whilst a low number of islet antibodies were of importance for the remission duration. Yetter et al. in the present study have used the HbA1c concentration at the time of diagnosis as an indicator of the duration of the remission phase in 23 juvenile diabetic children [16]. The results suggest that the initial HbA1c concentration may serve as a useful indicator to predict the duration of the remission phase in juvenile-onset diabetic patients. Researches conducted in recent years indicate that the low prevalence of remission is observed in the youngest children, aged<5 year and in adolescents aged>12 year [17]. It is possible that the low frequency of honeymoon phase in young children reflect more aggressive β-cell destruction in young children. In adolescents insulin resistance contributes to less likelihood of having partial remission. Other authors have similar observations [18]. They asserted that young age and severe disease in initial period are associated with decreased residual beta-cells function what is reflected by a lower incidence of partial remission. Many authors indicates β cell
demonstrated a correlation between lower C-peptide levels and Tregs administration with the potential to prolong remission in Type 1 Diabetes. This suggests that the use of immunosuppressive drugs may not be necessary in all cases to achieve and maintain remission. 

It is important to note that the duration of remission can be extended with the use of immune modulators, such as anti-CD3 monoclonal antibodies, which can improve insulin secretion and reduce the frequency of clinical remission. Efforts are also being made to use other medications, such as alefacept protein complex of molecules CD58/LFA-3 and human IgG, to help in the prevention of autoimmune processes in newly diagnosed Type 1 Diabetes patients. The infusion of autologous Tregs prolongs remission in recently diagnosed Type 1 Diabetes, and the use of sitagliptin in Type 1 Diabetes patients could help to decrease daily requirements of insulin by delaying β-cell loss and improving endogenous insulin production. It is also important to consider the use of insulin sensitizers, such as metformin, which can help to improve insulin sensitivity and reduce the risk of developing Type 2 Diabetes.

The final results of clinical studies are still awaited, and further research is needed to understand the mechanisms leading to the occurrence of partial remission and how they can be exploited to improve outcomes for patients with Type 1 Diabetes.


