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REVIEW ARTICLE

Type 1 diabetes: prevention and screening in focus

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Summary

It has been reported that the prevalence of type 1 diabetes (T1D) is increasing worldwide. Moreover, patients with T1D have a significant reduction in life expectancy, compared to their nondiabetic peers. In that context, prevention of T1D is a burning issue, having in mind multiple unsuccessful attempts in the past 50 years. However, recently there has been a turning point in this investigational area when it was shown that it is possible to delay T1D with immunotherapy in people with a high risk for T1D, in stage 2 of prediabetes. Teplizumab, a humanized IgG1 kappa CD3-directed monoclonal antibody modifies disease progression from stage 2 to overt T1D by preserving β-cell function. In future, T1D prevention studies should include combining immunomodulatory methods through the depletion of diabetogenic cells, strengthening regulatory cells, and islet regeneration, with a focus on the time of the onset of therapy and the duration of treatment. Primary prevention studies should start earlier, and secondary prevention studies should include more people at risk, which implies screening for T1D in the general population. People with immune markers of risk for T1D can now live without diabetes or with low metabolic risk for many years, which will allow for a reduction in acute and chronic complications of T1D and potentially a final cure. This review presents data from the newest primary, secondary, and tertiary prevention of T1D, as well as novelties in diagnostics, predominantly screening, and therapy of T1D.

Key words: type 1 diabetes, prevention, screening, therapy

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INTRODUCTION

The prevalence of type 1 diabetes (T1D) is increasing worldwide, and in the Europe and Central Asia region, it will increase by as much as 49% in the next 20 years. At the same time, the analysis of the prevalence by age category indicates that T1D is no longer a disease related exclusively to the pediatric age. In that context, data published in the latest International Diabetes Federation (IDF) atlas show that more than half of the people with newly diagnosed T1D in 2022 are over 20 years of age (1, 2). On the other hand, in patients who developed T1D before the age of 10, a significant reduction in life expectancy has been recently reported, up to 18 years compared to their nondiabetic peers. Moreover, reduced life expectancy up to 10 years, was registered in patients who developed T1D after 26 years of age (3). It is suggested that significant advancements in automated insulin delivery, along with the development of innovative software solutions for diabetes management and continuous glucose monitoring devices, will form the cornerstone of efforts to prevent and treat T1 D. Additionally, the integration of novel therapeutic approaches for immunomodulation and the preservation of β cells are expected to complement these technological advancements, further enhancing the efficacy of preventive and therapeutic strategies against T1D (4,5,6,7).

PATHOGENESIS OF T1D: BACKGROUND FOR PREVENTION STRATEGIES

It is a well-known fact that T1D is an autoimmune disease, a consequence of selective destruction of pancreatic β cells that secrete insulin (8). Previously, it was shown that diabetogenic, autodestructive T cells were not eliminated in the thymus due to negative selection, so they migrated into the circulation (9). Most likely, the initial meeting between the autoantigen and the autoreactive diabetogenic T cell, in genetically susceptible individuals, takes place in the pancreatic lymph node, from where, after differentiation and proliferation, the diabetogenic T cells migrate to the pancreatic islet and renew the encounters with autoantigens presented by antigen-presenting cells. They secreted numerous cytokines and chemokines that further attract macrophages, B, and other T cells, and destroy β cell mass. The destruction of the β cell mass is not linear, but rather a wavy line, with periods of relapse and remission (8). The immunological parameters of the intensity of immune response might be associated with residual β cell function as well as predictors of the clinical course of T1D (10,11, 12).

In 2015, the Juvenile Diabetes Research Foundation (JDRF), the Endocrine Society, and the American Diabetes Association (ADA) recommended a new classification of prediabetes that integrated aspects of beta cell mass destruction and clinical aspects of T1D progression. In this sense, there are 3 stages in the progression of T1D. In the first presymptomatic stage, in genetically predisposed individuals exposed to a triggering event, an autoimmune response cascade is triggered and the destruction of the mass of beta cells begins, while the level of glycemia is normal. In the second presymptomatic phase, the autoimmune destruction of beta cells occurs in a series of waves, marked by cycles of relapse and remission. These fluctuations lead to gradual changes in the beta cell mass, initially subtle and then progressively pronounced. Consequently, glycemic levels oscillate, initially remaining within the normal range. However, as the immune response escalates and extends, there is a sharp decline in beta cell mass, causing a sudden surge in glycemia beyond normal limits. This transition heralds the onset of the third symptomatic phase, marking the clinical manifestation of the disease (13,14).

In this context, the course of T1D was defined through stages. Stage 0 includes subjects with genetic/familiar predisposition for T1D. Stage 1 is defined by the presence of two or more islet autoantibodies and euglycemia, stage 2 is marked with multiple islet autoantibodies and dysglycemia, and stage 3 is clinically manifested T1D (15).

PREVENTION STUDIES IN TYPE 1 DIABETES UNTIL NOW: FRUSTRATION

In the prediabetes phase, which can last for months or even years, it is possible to detect immunological markers of T1D prediction, in peripheral circulation, in the form of 5 autoantibodies, but also disorders of cellular immunity, as well as in metabolic disturbances that reflect impaired insulin secretion and sensitivity (15,16). In that sense, it is possible to identify people with at risk of developing T1D, due to genetic, immunogenic, and metabolic risk markers.

However, individuals with a lifetime risk exceeding 75% for developing type 1 diabetes (T1D) account for less than 0.01% of the population. This means that for every 10,000 individuals screened within the general population, only one person with an exceptionally high risk for T1D would likely be identified (17).

On the other hand, first-degree relatives (FDRs) of patients with T1D are the largest healthy subpopulation with a familial risk of developing T1D and have 10-20 times higher relative risk of T1D compared to the general population (18).

Simultaneously, last year's ADA recommendations for T1D suggest screening for prediabetes using tests that detect autoantibodies to insulin, glutamic acid decarboxylase (GAD), islet antigen 2, or zinc transporter 8. However, the ADA suggests that screening for T1D should be performed only in FDRs of patients with T1D or for research purposes (19).

Nevertheless, the long-standing strategy of involving predominantly FDRs in interventional studies of T1D prevention has not been successful. Completed T1D prevention studies have been ineffective so far, and the fact is that 85% of T1D patients have no relatives with T1D (17). Immunotherapy interventions have been focused on multiple levels and have included virtually all participants in the activation of autoimmune response, including both cellular and humoral response, i.e. diabetogenic pro-inflammatory T cells, regulatory or anti-inflammatory T cells, B cells, and dendritic cells (20,21). Overall, preventive interventions are divided into studies of primary, secondary, and tertiary prevention. Primary prevention studies focus on intervening in individuals with genetic risk only, to prevent the onset of an autoimmune response. Moreover, secondary prevention studies are done in individuals with additional immunological risk (one or more antibodies to β cell antigens), to slow or block activated autoimmune process. Finally, tertiary prevention studies are conducted in patients with recent-onset T1D (RT1D), aiming to preserve impaired endogenous insulin reserve (14).

Generally, primary prevention trials evaluated the effect of different environmental risk factors on islet autoimmunity. The study BABYDIET showed no benefit from delaying exposure to gluten in early childhood in 150 at-risk children (22). The FINDIA study, including more than 1000 babies with genetic risk of T1D, showed that cow milk formula free of bovine insulin did not reduce the cumulative incidence of islet autoantibodies by the age of 3 (23). TRIGR was a randomized, placebo-controlled study, that included 2160 genetic-risk children and showed no benefit of using highly hydrolyzed milk instead of conventional milk formula on the development of islet antibodies by 6 years of age nor the development of T1D by 11 years of age (24). Studies of primary prevention are ongoing: INGR1D2 study in Belgium, Germany, UK, Poland, and Sweden, where newborns can be tested for an increased genetic risk of T1D. The SINT1A study (**S**upplementation with B. **IN**fantis for Mitigation of **T**ype **1** Diabetes **A**utoimmunity) is a study for infants up to the age of six weeks with an increased genetic risk of T1D, aiming to evaluate whether giving the probiotic B. infantis might modulate immune response (25). The Freder1k study includes newborns up to seven days old in Germany, and the risk of T1D developing is determined by testing a few drops of blood obtained from the umbilical cord. The last 3 studies are under the auspices of the GPPAD (Global Platform for the Prevention of autoimmune diabetes) platform, which brings together experts from Europe and America, to prevent T1D. They calculate genetic risk score (GRS) from blood to identify children at 10% risk for multiple autoantibodies by 6 years of age. They offer those 4–7-month-old children to be included in a primary prevention study Primary Oral Insulin Trial (POInT), in 5 European countries. They will be treated with oral insulin as immunomodulator, until the age of 3 and followed for 7 years (26).

Secondary prevention trials include intervention at stages 1 and 2 of T1D, and some of them used insulin for immunomodulation and induction of anti-inflammatory Th2 or regulatory immune response, which might protect β-cells. The National Institute of Health Diabetes Prevention Trials (DPT-1) consisted of two clinical trials and demonstrated that low-dose subcutaneous or oral insulin therapy did not prevent T1D in FDRs irrespective of prediabetes stage. However, post-hoc analysis of subgroups of FDRs with high IAA titers reported delayed progression to T1D with oral insulin (27,28). The European Nicotinamide Diabetes Intervention Trial (ENDIT) showed that nicotinamide previously demonstrated a protective effect on β-cells in animal models, and did not delay or prevent T1D in high-risk FDRs (29).

Finally, tertiary prevention trials include interventions in stage 3, clinically manifested T1D, aiming to preserve β-cell function and mass to achieve better metabolic control of T1D (lower incidence of hypoglycemia, lower HbA1c) and delay microvascular complications (30). Historically, cyclosporin transiently preserved β- cell function, but it was related to renal toxicity (31). Later on, several immunomodulatory drugs did not succeed in protecting β-cells in the long term, did not induce insulin independence, and were associated with adverse events. Along this line, trials used anti-CD3 monoclonal antibodies teplizumab (32) and otelixizumab, abatacept (CTLA4-Ig) (33), alefacept (34), anti-CD20 monoclonal antibody, rituximab (35), as well as anti-inflammatory agents (36) and mycophenolate mofetil with or without daclizumab (37).

NOVELTIES IN TYPE 1 DIABETES THERAPY: PREVENTION IN FOCUS

Recently, there was a turning point in this investigational area when it was shown that it is possible to delay T1D with immunotherapy in people with a high risk for T1D, in stage 2 of prediabetes (38). In that context, in November 2022, teplizumab was approved in the USA to delay the onset of overt T1D in adults and children ≥ 8 years of age with stage 2 T1D. It can be said that this event was the most important for the community of T1D patients in the last 100 years and since the discovery of insulin: a drug that can slow the progression of T1D, appeared on the market under the tradename Tzield®.

Teplizumab, a humanized IgG1 kappa CD3-directed monoclonal antibody (Anti-CD3 mAb) modifies disease progression from stage 2 to stage 3 T1D by preserving β-cell function. The effect of teplizumab is based on blocking Th 1 proinflammatory autoimmune response, and inducing T regulatory, protective, anti-inflammatory response (38). Research in this field has been published

in the last 20 years, first in patients with RT1D (32). In this multinational, randomized, placebo-controlled 2-year trial, in a large sample of RT1D up to 12 weeks from diagnosis, a 14-day treatment with different doses of teplizumab was implemented. The primary outcome was composite, the percentage of patients on insulin therapy <0.5 U/kg per day and $HbA_{1C<}$ 6.5% at 1 year, and it was not achieved. Despite this, post-hock analyses suggest that teplizumab could protect β-cells and might lower the daily insulin dose (32). Subsequently, recognizing the partial success achieved in certain cases along with the limited duration of response, further investigations including teplizumab are undertaken. ABATE study aimed to evaluate the efficiency and safety of two doses of teplizumab, to slow the decline in C-peptide levels in patients with RT1D within 2 weeks of diagnosis, and to identify characteristics of responders on the study drug (39). The results pointed out that patients on teplizumab had a higher level of C-peptide at 2 years, which was a 75% improvement. It has been reported that subjects on teplizumab have a delay of decline in C-peptide by 15.9 months, but responses to the drug varied, and the authors identified responders and nonresponders to the drug. Moreover, responders to the drug were identified by metabolic (lower HbA_{1c} levels of and insulin use at baseline) and immunologic (lower level of Th1-like IFN-γ-producing CD8+ T cells) features (39). The most frequent adverse events were rash, transient upper respiratory infections, headache, and nausea.

Surprisingly, after 7 years of follow-up, interesting findings have been published, suggesting there is still a slower decline in C-peptide and sustained beneficial immunological responses up to 7 years after diagnosis of T1D in drug responders, although they did not differ significantly according to insulin use and HbA1c level (40).

Finally, the results from the most successful prevention study in the area of T1D prevention in the last 50 years were reported in 2019. This was a phase 2, randomized, placebo-controlled, double-blind trial of teplizumab involving FDRs of patients with T1D who were nondiabetics but had a high risk for T1D, stage 2 of prediabetes (2 autoantibodies and dysglycemia). Patients were randomized to a single 14-day course of teplizumab or placebo, and follow-up for progression to overt T1D with the use of OGTT every 6 months (38).

The study included 76 participants, mainly children and adolescents, and there were 44 on teplizumab and 32 on placebo. It was reported that the average time to the diagnosis of T1D was 48.4 months in subjects on teplizumab and 24.4 months on placebo. Moreover, in overt T1D progressed 43% of subjects on teplizumab and 72% of subjects on placebo.

Furthermore, a sustainable effect on the progression of T1D was detected after 923 days of follow-up. In that sense, the average time to overt T1D was 27.1 months in placebo and 59.6 months in the teplizumab group. After this period, 22% and 50% respectively were not diagnosed with T1D (41). Moreover, besides metabolic changes (increased C peptide level), immunological changes in responders were detected. In that sense, a higher percentage of just one subset of T cells, $KLRG1^{+-}$ $TIGIT^{+}EOMES^{+}CD8^{+}$ T cells, associated with T-cell unresponsiveness, was reported, suggesting selectivity in the effect of teplizumab (41). Simultaneously, changes in T cells correlate with improved metabolic function β cells, and the frequency of T cells that produce proinflammatory cytokines IFNγ and TNFα, was reduced in subjects on teplizumab (41).

NOVELTIES IN TYPE 1 DIABETES DIAGNOSIS: SCREENING IN FOCUS

The great success achieved within this study breathed new life into research in this area. It is suggested that limitations in prevention studies relate mainly to the study population: dominantly FDRs in stage 2, a small number of subjects, and age, because so far teplizumab has been adminitered only to children over 8 years of age.

So, the idea of screening for T1D in the general population, and not only in the population of FDRs, has arisen and become popular. In that context, it has been shown that children who progress from stage 2 to stage 3 T1D, make this progress at the same rate (50% risk by 2 years), regardless of whether they are children-FDRs of patients with T1D or children from the general population (42). Furthermore, the advantages of screening for T1D in the general population are identifying children at risk, offering them education and metabolic monitoring, and lowering the rate of diabetic ketoacidosis (DKA) at the clinical manifestation of T1D. Simultaneously, it was reported that children identified with prediabetes in public health screening compared to children with incident T1D, had a lower prevalence of DKA, lower rates of hospitalization in emergency departments, and higher levels of residual β cell function (43).

In that context, in 2015, the Fr1da study was initiated in Bavaria, Germany, designed to evaluate screening in the general population for multiple islet autoantibodies for early detection of T1D in children (44,45). The study was conducted in collaboration with primary care physicians and included over 165,000 children until now. The authors also created a predictive score that took into account the level of HbA1c, the level of glycemia in the 90^{th} minute of 2h OGTT, and the titter of IA2 antibodies, by which it is possible to identify the normoglycemic group of children, in stage 1, which rapidly, with a high risk of 50% over 2 years, progress to clinically manifest T1D (stage 1b children). The main findings of this study were: that screening in the general population is feasible, public health screening for islet autoantibodies detected 0.027% of children with undiagnosed overt T1D and 0.038% with

undiagnosed stage 2 or stage 1b T1D, with 50% risk to develop clinical T1D within 2 years. Moreover, identifying people in stage 1b prediabetes will double the number of people who may benefit from disease-modifying drugs, and there is a huge social benefit (lower DKA rate, better course of T1D, education, less distress) (42).

Ongoing screening programs in FDRs of patients with T1D – TrialNet (a U.S.-based consortium) and INNODIA (a European private/public partnership) – began by screening FDRs to increase efficiency for enrolment in preventive clinical studies. The Type 1 Diabetes TrialNet Pathway to Prevention Study, started in 2004, has screened more than 220,000 FDRs. Initially, assays for ICA, IAA, IA2A, and GADA (by RBA) were performed, and from 2019, screening was modified to GADA and IAA only, and then they might undergo testing for other available antibodies. Generally, TrialNet identified 5% of FDRs with at least one autoantibody, and half of these had multiple autoantibodies. INNODIA screens for four autoantibodies by RBA and has screened more than 4,400 FDRs, with similar results regarding the detection of FDRs with prediabetes (46).

On the other hand, screening in the general population might be divided into two categories: birth cohorts or autoantibody-based screening programs. Birth cohorts use genetic screening and those who have higher risk undergo autoantibody screening. The Type 1 Diabetes Prediction and Prevention Study (DIPP) has started in Finland, the country with the highest incidence of T1D in the world, with more than 250,000 infants screened until now. Moreover, the Newborn Screening for Genetic Susceptibility to Type 1 Diabetes and Celiac Disease and Prospective Follow-up Study (BABYSCREEN), in Finland also, screens for genetic risk for T1D and celiac disease. Furthermore, GPPAD screened more than 279,000 infants as of July 2021 and detected 1.1% of those with increased genetic risk. Additionally, in the USA there are further programs: the Combined Antibody Screening for Celiac and Diabetes Evaluation (CASCADE) program, the Sanford Population-Level Estimation of T1D Risk Genes in Children (PLEDGE) project, and the Precision Individualized Medicine for Diabetes (PRiMeD) project, and they also use calculating GRS from blood spots or saliva.

On the other hand, screening in the general population using autoantibodies include the following studies: ASK (Autoimmunity Screening for Kids, Colorado), T1Detect (USA), Early Detection of Type 1 Diabetes (Fr1da), and Early Detection of Type 1 Diabetes and Hypercholesterolemia in Lower Saxony (Fr1dolin) (Germany) (46).

Having all this in mind, with the expectation that screening in the general population will be accepted worldwide, there are some recommendations for clinical practice. In that context, it is suggested that the best time for screening would be the age of 2 and 5–7 years of age. Moreover, monitoring of subjects with immune markers includes discussion of results and implications; and education about the signs and symptoms of diabetes. The recommendations for metabolic monitoring include OGTT, HbA1c levels, random glycemic levels, or continuous glycemic monitoring (46). In that sense, a 10% increase in HbA1c level during 3-12 months or two consecutive values of HbA1c≥5.9% are markers of progression into stage 3 T1D. Moreover, it has been shown that spending ≥10% with glucose levels ≥7.8 mmol/l, the risk for progression to overt T1D is up to 80% within the next 12 months, and if it is more than 5%, the risk for progression will be 40% in the next 2 years (47,48).

YEAR 2023: DISAPPOINTMENTS AND SUCCESSES

Finally, last year began with disappointments in the area of prevention of T1D.

Abatacept, which stops the activation and proliferation of diabetogenic T cells, due to costimulation blockade, given to individuals in stage 1 T1D during 12 months, disappointingly, did not result in a delay from stage 1 to stage 2. However, abatacept preserved C peptide as well as it was previously shown in R T1D and it implies the possibility of modifying the course of T1D (49). Hydroxychloroquine, an immunomodulatory drug acts on alterations in insulin metabolism through cellular receptors (50), but the study in relatives at risk for T1D was stopped in July 2023, due to unsatisfying results at interim analysis.

On the other hand, low doses of anti-thymocyte globulin preserved C peptide and decreased HbA1 in R T1D (51). Furthermore, a randomized, double-blind, placebo-controlled, phase 2 trial used anti-interleukin-21 antibody and liraglutide for the protection of β cells in adults with RT1D, showed that both drugs act synergistically on C peptide and HbA1c levels, and better than each of them alone (52). Furthermore, verapamil has inhibitory effect on β cell apoptosis by inhibiting thioredoxin interacting protein (overexpressed in diabetes, promoting oxidative stress). It was reported that in children with RT1D, verapamil preserved C peptide for 30% more than placebo after 52 weeks of follow-up (53).

Recently, the results of the T1GER study have been published, about the effect of golimumab (a human monoclonal antibody specific for tumor necrosis factor α) in individuals with RT1D. This was phase 2, a multicentre, placebo-controlled, double-blind, parallel-group trial, that included 56 children and young adults with RT1D on subcutaneous golimumab or placebo for 52 weeks. The authors demonstrated that individuals on golimumab had significantly higher levels of C peptide, lower daily doses of insulin, and a higher incidence of partial clinical remission (54). Moreover, the results from the PROTECT study were published. Teplizumab was given to individuals with RT1D in a new study design, two times, at the beginning of the disease and 6 months

later, and it protected the C peptide, but it did not decrease significantly daily insulin dose (55). Additionally, baricitinib, a JAK kinase inhibitor, that blocks cytokine signaling, previously used for treatments of autoimmune diseases in rheumatology and dermatology, was investigated in RT1D. The study was a phase 2, double-blind, randomized, placebo-controlled trial, that included 60 children and young adults in RT1D on baricitinib or 30 individuals on placebo, orally for 48 weeks. The results showed a protective effect on C peptide level, with no difference concerning daily insulin dose and HbA1c, compared to placebo. However, baricitinib reduced glucose variability and improved time in range (56). The oral formulation of the drug will certainly improve the adherence of patients to the medication and the safety profile of all of these drugs is acceptable. Finally, this year, the FDA granted fast track to intralymphatic injection of anti-GAD vaccine. A previous trial of intralymphatic injections of aluminum-formulated glutamic acid decarboxylase showed preservation of β-cell function in patients with HLA DR3-DQ2 (57), and a correlation between the C-peptide level and time in the target glucose range (58). In that context, the phase 3 DIAGNODE-3 trial is assessing the safety and efficacy of the therapy among 330 adolescents and young adults up to 29 years with RT1D, and DR3-DQ2 genotype. The co-primary endpoints of DIAGNODE-3 will be the preservation of endogenous insulin-producing capacity and improved HbA1c.

FUTURE THERAPY OF T1D: COMBINED APPROACH OF IMMUNOMODULATION AND β CELL PROTECTION

Finally, a meta-analysis of 21 trials of disease-modifying interventions in RT1D comprising 1315 adults and 1396 children, was published. The results showed that a 24.8% higher C-peptide level was accompanied by a 0.55% lower HbA1c, after 6 months of treatment. Moreover, improvements in HbA1c are proportional to the degree of C-peptide preservation, suggesting the use of C-peptide as a surrogate endpoint in clinical trials (59). In addition, the immune interventions aimed to protect β cell function and/or mass may soon be offered to patients with RT1D but must be proven to be safe in the short as well as long term (60).

At the same time, the future of studies of T1D prevention should include combining immunomodulatory methods through the depletion of diabetogenic cells, strengthening regulatory cells, and islet regeneration, with a focus on the time of start of therapy and the duration of treatment (59,60).

CONCLUSION

In conclusion, T1D is a predictable autoimmune disease, with clearly defined stages preceding the clinical manifestation of the disease. Primary prevention studies should start earlier, and secondary prevention studies should include more people at risk, which implies screening for T1D in the general population. For the first time, it is possible to postpone the clinical manifestation of T1D in individuals at risk for T1D. People with immune markers of risk for T1D can now live without diabetes or with low metabolic risk for many years, which will allow for a reduction in acute and chronic complications of T1D and potentially a final cure.

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Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

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TIP 1 DIJABETESA: PREVENCIJA I SKRINING U FOKUSU

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Sažetak

Poznato je da je broj obolelih od tipa 1 dijabetesa (T1D) u porastu u celom svetu. Istovremeno, utvrđeno je da u pacijenata sa T1D postoji značajno smanjenje očekivanog životnog veka, u poređenju sa vršnjacima bez dijabetesa. U tom smislu, prevencija T1D je goruće pitanje, imajući u vidu više neuspešnih pokušaja u poslednjih 50 godina. Međutim, nedavno je došlo do prekretnice u ovoj naučnoj oblasti, kada je pokazano da je moguće odložiti T1D imunoterapijom kod osoba sa visokim rizikom za T1D, u fazi 2 predijabetesa. Teplizumab, humanizovano IgG1 kappa anti CD3 monoklonsko antitelo modifikuje progresiju bolesti od faze 2 do klinički manifestnog T1D protekcijom β-ćelija. Istovremeno, smatra se da bi u budućnosti, studije prevencije T1D-a trebalo da uključuju kombinovanje imunomodulatornih metoda kroz iscrpljivanje dijabetogenih ćelija, jačanje regulatornih ćelija i regeneraciju β ćelija, sa fokusom na vreme početka terapije i trajanje lečenja. Studije primarne prevencije trebalo bi da počnu ranije, a studije sekundarne prevencije trebalo bi da uključuju više osoba sa visokim rizikom za ispoljavanje T1D, što podrazumeva skrining za T1D u opštoj populaciji. Osobe sa imunološkim markerima rizika za T1D sada mogu da žive bez dijabetesa ili sa niskim metaboličkim rizikom dugi niz godina, što će omogućiti smanjenje akutnih i hroničnih komplikacija T1D i potencijalno konačno izlečenje. Ovaj pregledni članak predstavlja podatke iz nedavno završenih studija primarne, sekundarne i tercijarne prevencije T1D, kao i novitete u dijagnostici, pretežno skriningu, i terapiji T1D.

Ključne reči: tip 1 dijabetesa, prevencija, skrining, terapija

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