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Aamir Al-Mosawi*

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Opinion Article

New Therapies for Type 1 Diabetes Mellitus: An Educational Article an Expert Opinion

Aamir Al-Mosawi *

Advisor doctor and expert trainer, The National Center of Training and Development and Baghdad Medical City Baghdad, Iraq

***Correspondence Author:** Aamir Al-Mosawi, Advisor doctor and expert trainer, The National Center of Training and Development and Baghdad Medical City, Iraq.

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Abstract

Diabetes mellitus type 1 is a lifelong condition resulting from failure of the production of insulin because of loss of pancreatic islet beta-cells because of autoimmune damage. Patients with this diabetes type 1 need lifelong treatment with insulin to remain alive. Demands for changing this dire situation of lifelong dependence on insulin have been increasing. The aim of this paper is to provide an overview of diabetes type 1 cure research progress.

Conclusion and expert opinion: Emphasis has been increasingly made that treatment of diabetes type 1 with immunotherapeutic agents such as rituximab can slow the decline in C-peptide, but do not affect the underlying pathophysiology of the condition. Experimental studies have suggested the use of multi-factorial therapies that aim at increasing pancreatic islet beta-cells islets mass and proliferation through stimulating neogenesis, decreasing cell apoptosis and enhancing cell regeneration. The current evidence-based expert opinion suggests that the use of multi-factorial safe therapies including sitagliptin, γ-aminobutyric acid (GABA), vitamin D3, and lansoprazole in patients with recent development of diabetes type 1 can improve pancreatic function and reduce insulin requirement and can possibly lead to partial remission. Verapamil can be safely used for the same purpose in patients with high blood pressure.

Keywords: diabetes type 1cure research progress; sitagliptin; γ-aminobutyric acid (GABA); vitamin D3; and lansoprazole; verapamil

Introduction

Diabetes mellitus type 1 is a lifelong condition resulting from failure of the production of insulin because of loss of pancreatic islet beta-cells because of autoimmune damage. Patients with this type 1 diabetes need lifelong treatment with insulin to remain alive. Demands for changing this dire situation of lifelong dependence on insulin have been increasing.

Experimental studies have suggested the use of multi-factorial therapies that aim at increasing pancreatic islet beta-cells islets mass and proliferation through stimulating neogenesis, decreasing cell apoptosis and enhancing cell regeneration [1-5].

In 2017, Wenjuan Liu from Canada and her research group reported an experimental study on male mice with streptozotocin-induced pancreatic beta cell damage. One week before streptozotocin injection, the animals received no treatment, γ-aminobutyric acid (GABA), sitagliptin, or GABA+sitagliptin for six weeks. GABA and sitagliptin alone increased plasma insulin, decreased plasma glucagon levels, and reduced blood glucose. Treatment with GABA plus sitagliptin markedly augmented the anti-diabetic effects. Immuno-histochemical exams showed that treatment with GABA plus sitagliptin resulted in more increase pancreatic beta cell proliferation, in beta cell mass, and more increase in small-size islet numbers. Treatment with GABA plus sitagliptin also decreased apoptosis [4].

In 2018, Fernando Ovalle from the United States and his research team reported a placebo-controlled study (Phase-2) which included patients with recent development of diabetes type 1 treated with insulin plus oral verapamil (Calcium-channel blocker) once-daily for one year. Compared with placebo, the addition of verapamil treatment was associated with an improvement in pancreatic beta cell function. Verapamil treatment also resulted in less increase in insulin requirements, less hypoglycemic attacks. The use of verapamil was considered effective and safe. The beneficial effect of verapamil was attributed to a decrease in the expression of thioredoxin-interacting protein, and thus augmenting the survival of pancreatic beta cells [6].

In 2022, Guanlan Xu from the United States and his research group reported a placebo-controlled study which included patients with type 1 diabetes

treated with verapamil. Verapamil reduced the increased circulating pro-inflammatory T-follicular-helper cells markers. RNA-sequencing. Verapamil also helped in regulating the thioredoxin system and decreased apoptosis. Verapamil treatment slowed the progression of diabetes, improved pancreatic beta-cell function and thus contributed to decreasing insulin requirements for 2 years. The beneficial effect of verapamil disappeared when the treatment was stopped [7].

In 2023, Gregory P Forlenza from the United States and his research group emphasized the experimental evidence suggesting that the over-expression of thioredoxin-interacting protein leads apoptosis and death of beta cell in the pancreas. They reported a placebo-controlled multicenter study which included patients with recent development of diabetes mellitus type 1 aged 7 to 17 years, and had weight of 30 kilograms or higher. Forty-seven patients received oral verapamil one times daily, and forty-one patients received placebo. 83 patients completed the study.

Eight patients who received verapamil and 8 patients who received placebo experienced side effects that were not considered serious.

Compared with placebo, verapamil had a protective effect on stimulated C-peptide secretion at one year from the development of diabetes [8].

In 2009, Mark D Pescovitz from the United States and his research group reported a placebo-controlled study which included 87 patients aged 8 to 40 years with recent development of diabetes type 1. The patients received either rituximab infusions (Four doses on days 1, 8, 15, and 22 of the study) or received placebo. Treatment was associated with considerably lower levels of glycosylated hemoglobin and decreased insulin requirement. The rate of decrease in C-peptide levels was considerably less in patients who received rituximab than that in patients who received placebo. Rituximab treatment was associated with reduction of CD19+ B lymphocytes. Rituximab was not associated with increased infections or neutropenia [9].

In 2014, Mark D Pescovitz and his research group emphasized that treatment of diabetes type 1 with rituximab and other immunotherapeutic agents can slow the decline in C-peptide (Deficiency of insulin is associated with deficiency of C-peptide in diabetes type 1 because of the loss of pancreatic beta-cells, reduction of fasting C-peptide level to less than 0.6 ng/ml indicates pancreatic beta-cell depletion and the need for treatment with insulin), but theses therapies do not affect the underlying pathophysiology of the condition [10].

In 2022, Teresa Quattrin and her research group reported a placebo-controlled multicenter study (Phase 2) which included children and young adults aged 6 to 21 years who recently developed diabetes type 1. 56 patients received subcutaneous golimumab (Anti-tumor necrosis factor monoclonal antibody), and 28 received placebo for one year. Patients who received golimumab had lower insulin requirement than patients who received placebo. 43% of the patients who received golimumab, and only 7% of the patients who received placebo experienced partial-remission [11].

In 2012, Mônica A L Gabbay from Brazil and her research group reported an 18-month (placebo-controlled study which included 38 patients with recent development of diabetes type 1 having fasting C-peptide level of 0.6 ng/mL or higher (Deficiency of insulin is associated with deficiency of C-peptide in diabetes type 1 because of the loss of pancreatic beta-cells, reduction of fasting C-peptide level to less than 0.6 ng/ml indicates pancreatic beta-cell depletion and the need for treatment with insulin).

The patients received oral vitamin D, 2000 IU or placebo. The study showed that vitamin D3 could have a protective immunologic role and may help in delaying the loss of residual pancreatic Beta-cell function [12].

In 2022, Raghunatha Reddy from India and his research group reported a controlled study which include children aged 6-12 years who had recent development of diabetes type 1. Patients received either vitamin D3 plus lansoprazole or received no treatment (Controls). Treatment was not associated with adverse effects. Treatment with cholecalciferol plus lansoprazole for six months was associated with less decrease in the function of residual pancreatic β-cell and decreased insulin requirement [13].

In 2023, Josephine Yu from Australia and her research group published a systematic review which included 28 clinical studies, and concluded that it is recommended to use vitamin D3 supplementation in patients with diabetes type 1 and individuals at high risk of developing diabetes type 1 [14].

Conclusion and expert opinion

Emphasis has been increasingly made that treatment of diabetes type 1 with immunotherapeutic agents such as rituximab can slow the decline in C-peptide, but do not affect the underlying pathophysiology of the condition. Experimental studies have suggested the use of multi-factorial therapies that aim at increasing pancreatic islet beta-cells islets mass and proliferation through stimulating neogenesis, decreasing cell apoptosis and enhancing cell regeneration. The current evidence-based expert opinion suggests that the use of multi-factorial safe therapies including sitagliptin, γ-aminobutyric acid (GABA), vitamin D3, and lansoprazole in patients with recent development of diabetes type 1 can improve pancreatic function and reduce insulin requirement and can possibly lead to partial remission. Verapamil can be safely used for the same purpose in patients with high blood pressure.

Conflict of interest: None.

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