CORRESPONDENCE

Semaglutide in Early Type 1 Diabetes

TO THE EDITOR: Most patients with new-onset type 1 diabetes have substantial intact beta-cell reserve.[1] Thus, we analyzed the efficacy of semaglutide, an agonist of glucagon-like peptide 1 (GLP-1), in patients with a new diagnosis of type 1 diabetes.

From 2020 through 2022 at our center, we included 10 patients between the ages of 21 and 39 years who had initiated semaglutide treatment within 3 months after a diagnosis of type 1 diabetes in a retrospective analysis of metabolic outcomes at 1 year. At the time of diagnosis, 4 of the 10 patients presented with diabetic ketoacidosis, whereas the others had polyuria, polydipsia, and weight loss. Nine patients had antibodies against glutamic acid decarboxylase, and one had autoantibodies against islet antigen 2. At the time of diagnosis, the mean (±SD) glycated hemoglobin level was 11.7±2.1% and the fasting C-peptide level was 0.65±0.33 ng per milliliter. All the patients were receiving standard basal and prandial insulin.

Semaglutide was started at a weekly dose of 0.125 mg to monitor side effects and avoid hypoglycemia. Subsequently, the dose of prandial insulin was adjusted down, whereas the semaglutide dose was adjusted up to a maximum of 0.5 mg weekly. The basal insulin dose was reduced according to data from continuous glucose monitoring. Carbohydrate intake was restricted in all the patients.

Prandial insulin was eliminated in all the patients within 3 months, and basal insulin was eliminated in 7 patients within 6 months. These doses were maintained until the end of the 12-month follow-up period. The mean glycated hemoglobin level fell to 5.9±0.3% at 6 months and to 5.7±0.4% at 12 months. The fasting C-peptide level increased in all the patients to a mean of 1.05±0.40 ng per milliliter, and the time-in-range was 89±3% according to continuous glucose monitoring. Mild hypoglycemia was recorded during the period in which the semaglutide dose was increased. After dose stabilization, no episodes of hypoglycemia were reported, along with no reports of diabetic ketoacidosis or other serious side effects.

Since we did not have our own control data in this retrospective analysis, we reviewed data from patients who were receiving insulin therapy in control groups in four studies involving patients with early type 1 diabetes (Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org).[2-5] Those patients showed initial improvement in glycated hemoglobin levels during the first 6 months. Thereafter, they all showed an increase in the glycated hemoglobin level, a finding that was consistent with the end of the so-called "honeymoon period" in the treatment of early type 1 diabetes (Fig. 1). It is possible that differences between the populations may have had an effect on such outcomes.

In all, our preliminary observations support the need for prospective, randomized clinical trials with larger numbers of patients to investigate this approach further. In this small case series,

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we found that the initiation of semaglutide soon after the diagnosis of type 1 diabetes was associated with the elimination of prandial insulin in all 10 patients and basal insulin in most of the patients, along with increased C-peptide levels and better glycemic control during the year of observation.

Paresh Dandona, M.D., Ph.D.
Ajay Chaudhuri, M.D.
Husam Ghanim, Ph.D.
State University of New York at Buffalo
Williamsville, NY
dandona@buffalo.edu

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

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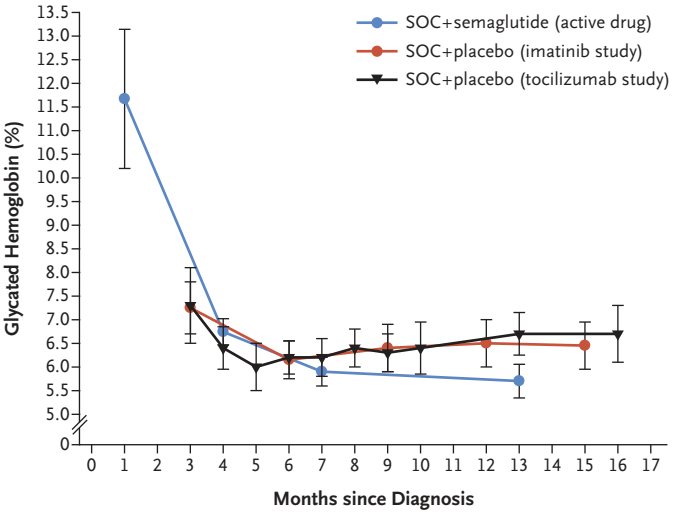

Figure 1. Glycated Hemoglobin Levels in Patients with Recently Diagnosed Type 1 Diabetes.

Shown are glycated hemoglobin levels after the initiation of semaglutide treatment in 10 adult patients who had recently received a diagnosis of type 1 diabetes at a single center, as compared with historical data from adult control groups in two trials with available point estimates and variability ranges from referenced articles.[3,4] Patients in the control groups were receiving standard-of-care (SOC) therapy consisting of education regarding type 1 diabetes, insulin treatment with or without continuous glucose monitoring, and placebo. All the patients in the semaglutide group were receiving SOC with basal and prandial insulin therapy before starting semaglutide.

Ketamine versus ECT for Nonpsychotic Treatment-Resistant Major Depression

TO THE EDITOR: The article by Anand et al. (June 22 issue)[1] concerns an important issue — the therapeutic approach that should be used for patients with treatment-resistant depression. However, the article has some drawbacks.

First, bilateral electroconvulsive therapy (ECT) is standard care for treatment-resistant depression. Bilateral ECT has a faster onset and is more efficacious than unilateral ECT.[2] The patients in this trial who ultimately underwent ECT started with unilateral ECT, which may be an indication that the authors were biased toward the ketamine group. It is awkward that after a median of four sessions, 38.8% of the patients in the ECT group had switched from unilateral to bilateral treatment. Why was bilateral ECT not used from the start? Second, in the ECT group, 51 and 63 patients were taking anticonvulsant and benzodiazepine therapies, respectively. How could ECT be effective in these patients? Third, the authors note that 71 patients in the trial were using augmentation medications. Unfortunately, the authors did not specify which medications they were referring to. Did the medications include lithium, which is widely used for treatment-resistant depression?[3,4]

Sérgio A. Souza, Jr., M.D.
Tainá R. Josino, M.D.
Luisa W. Bisol, M.D., Ph.D.
University Hospital Walter Cantidio
Fortaleza, Brazil
lwbisol@ufc.br