Neurocognitive Decline Unrelated to Mild Cognitive Impairment in Type 1 Diabetes

Written by John Otrompke

Patients with type 1 diabetes (T1D) experienced a gradual decline in certain cognitive functions, but the decline was not comparable to mild cognitive impairment, which is a precursor of dementia. The decline in brain volume loss was associated with higher baseline systolic blood pressure (SBP), while a decline in executive function was associated with baseline elevated HbA1C in patients with T1D, according to Eelco van Duinkerken, PhD, Vrije Universiteit Medical Center, Amsterdam, The Netherlands, who presented the 4-year follow-up data.

The study of cognitive decline compared the brain function of 25 patients with T1D and 25 matched controls. All participants had to be free of diseases affecting the brain and psychiatric comorbidities, and had to be right-handed. To explore the theory that microangiopathy is related to cognitive decline, all diabetic patients had proliferative retinopathy as a marker of angiopathy, and diabetes duration of at least 10 years.

At baseline, the mean age for all was ~45 years (range, 18 to 56 years), and the mean duration of diabetes was 35 years. The SBP was 133.9 mm Hg in the diabetes group, compared with 126.9 mm Hg in the control group (p=0.045). The baseline HbA1C values were 7.9% and 5.4% (p<0.001) in the diabetes and control groups, respectively.

There was no difference in general cognitive ability, information processing speed, or attention at follow-up. The researchers noted a slight increase in performance over time in patients with diabetes, but not in the control group; however, this lacked statistical significance.

However, an accelerated decrease in executive function was found in T1D patients relative to the controls, which was ascertained by asking the subjects to identify the color of ink or state how many animals they could think of in 2 minutes.

The changes in brain volume from baseline to follow-up (mean, 4.28 years T1D group; 4.73 years control group) are measured by MRI. The decrease in brain volume was 1.34% in the patients with T1D compared with 0.68% in the control patients (p=0.036).

The brain volume loss was most notable in the frontal and central areas of the right hemisphere, which are associated with executive function performance (p=0.021).

While the baseline SBP was found to correlate with brain volume loss and baseline elevated HbA1C was found to correlate with executive function loss, there was no correlation with severe hypoglycemic events. The change in brain volume was not seen in speed-related domains, as some researchers had theorized.

T1D patients with angiopathy face the possibility of progressive cognitive decline, which is unrelated to mild cognitive impairment.

Metformin/Pioglitazone/Exenatide Triple Therapy Superior to Stepwise Add-On Conventional Therapy in Newly Diagnosed Type 2 Diabetes

Written by Muriel Cunningham

Muhammad Abdul-Ghani, MD, PhD, University of Texas Health Science Center, San Antonio, Texas, USA, presented the results of the Durability of Combination Therapy With Exenatide/Metformin Versus Conventional Therapy in New Onset T2DM study [NCT01107717] that evaluated the effects of a triple-therapy regimen versus stepwise add-on conventional therapy in patients with newly diagnosed type 2 diabetes. In this open-label study, 155 patients were randomized to triple therapy or stepwise add-on conventional therapy, with a goal of achieving an HbA1C of <6.5%. "We hypothesized that starting people with new-onset diabetes on agents that correct core defects known to be present in subjects with type 2 diabetes will produce a greater, more durable, and safer reduction in HbA1C," explained Dr. Abdul-Ghani.

Triple therapy comprised metformin 1000 mg/day, pioglitazone 15 mg/day, and exenatide 5 μg BID. At Month 1, dosages were increased to metformin 2000 mg/day, pioglitazone 30 mg/day, and exenatide 10 μg/day. Pioglitazone was increased to 45 mg/day at Month 3 if glycemic targets (fasting plasma glucose [FPG] <100 mg/dL and HbA1C <6.5%) were unmet. Patients randomized to conventional therapy started with metformin 1000 mg/day. Medication adjustments were made at specific time points if glycemic targets (FPG <100 mg/day and HbA1C <6.5%) were not met: Month 1—metformin increased to 2000 mg/day and glyburide initiated at 5 mg/day; Month 2—glyburide increased to 10 mg/day; Month 3—glargine insulin initiated at 10 units/day. Glargine dosage was increased each week by 10 units/day if FPG remained >100 mg/dL.

Patients were followed every 3 months after the first 3 months. Changes could be made to medications if FPG was <60 mg/dL or in cases of hypoglycemia. Patients were considered treatment failures if they had HbA1C levels >6.5% on two consecutive visits 3 months apart despite maximum therapy. The primary endpoint was the difference in HbA1C between the triple-therapy and conventional-therapy groups.