Screens Fail to Find Diabetic Neuropathy

Noninvasive tests are not as sensitive as nerve conduction and should not be used for screening.

BY KATE JOHNSON
Montreal Bureau

QUEBEC CITY — Noninvasive methods for identifying pediatric diabetic neuropathy are not as sensitive as conventional nerve conduction studies and should not be considered for screening purposes, Danièle Pacaud, M.D., said at the joint annual meeting of the Canadian Diabetes Association and the Canadian Society of Endocrinology and Metabolism.

"[Noninvasive methods are] fast, less painful, and they don't require a neurology referral, but unfortunately they are also not as good," she reported regarding new research.

Long-standing diabetic neuropathy can be associated with serious complications such as foot ulcerations, amputations, nephropathy, myocardial infarction, and stroke, said lead investigator Dr. Pacaud, a pediatric endocrinologist at the Alberta Children's Hospital and the University of Calgary in Calgary, Alberta.

Early detection could reduce or delay such complications, but this condition can often exist subclinically, she said.

In adults, two inexpensive, rapid screening tests—the vibration perception thresholds (VPT), and the tactile perception thresholds (TPT)—have been recommended for detecting subclinical neuropathies. However, these tests have not been well assessed in children, she said.

The study compared VPT and TPT with the standard nerve conduction studies (NCS) in 73 children (mean age 13 years) with type 1 diabetes.

The NCS measures median and peroneal motor nerve conduction, as well as sural sensory nerve response. Two abnormalities on this test indicate diabetic neuropathy.

In VPT testing, subjects are asked to touch a box with their big toe and indicate whether it is vibrating. The amplitude of the vibrations is steadily decreased until the subjects cannot feel them.

In TPT, subjects are asked to indicate when they feel microfilaments that are applied to the plantar surface of the foot.

All children in the study were administered a neurological questionnaire by a research coordinator. They also underwent NCS and received a neurological exam by a neurologist. In addition, the children were given both the VPT and TPT by a research nurse. Finally, a research assistant performed a chart review to obtain information on hemoglobin A_{1c} levels and duration of diabetes. All four investigators were blinded to the results obtained by the others.

The study found that, according to the standard NCS, diabetic neuropathy was common. Of the 73 subjects, 42 (57%) had two abnormalities on NCS, indicating diabetic neuropathy.

Of those abnormalities, 37 were picked up by VPT, 26 by neurological exam, and 19 by TPT.

"Compared to the gold standard NCS, neither the VPT, TPT, nor neurological exam was found to be acceptable as [a screening test]," Dr. Pacaud said.

Consistent with other reports, significant variables found to be related to the presence of neuropathy included age, height, degree of metabolic control, and an abnormal neurological exam.

Dr. Pacaud said the neurological symptoms questionnaire was not useful, because few patients experienced regular symptoms.

Although at present, early detection of subclinical diabetic neuropathy would not change a patient's treatment, there may soon be treatments available for this indication, Dr. Pacaud noted.

"At this point, the only treatment we would offer would be to reinforce the importance of metabolic control, which we are already trying to do. However, there are some specific therapies that are being tested, and once they become available it would be important to be able to use screening to identify which individuals would be able to benefit," she told this newspaper, including aldose reductase inhibitors, certain nutritional supplements, and antioxidant therapies. ■

Diabetics' Memory Deficits Localized in Brain

BY KATE JOHNSON
Montreal Bureau

QUEBEC CITY — Magnetic resonance imagery and spectroscopy of the brain show decreased hippocampal volume in children with type 1 diabetes, and evidence of neuronal damage in a subgroup of those children who have hypoglycemic seizures, according to a new study.

These findings coincide with another study of children with type 1 diabetes, showing deficits in memory that are specifically tied to the hippocampal region, reported researchers from York University in Toronto.

"The hippocampus is quite sensitive to fluctuations in glucose, and also has a high number of insulin receptors—so if there is too much insulin, this can have an impact on functioning," said Mary Desrochers, Ph.D., who supervised both studies. The results were presented as posters at the joint annual meeting of the Canadian Diabetes Association and the Canadian Society of Endocrinology and Metabolism.

The first study included 10 children with type 1 diabetes (aged 10-14 years, with an age of onset of less than 5 years), half of whom had severe hypoglycemic episodes. They were age-matched to 10 healthy controls.

MRI showed that all patients with diabetes had smaller hippocampal volumes than did controls. And MRI spectroscopy showed elevated levels of inositol and glutamate, suggestive of neuronal damage, in children with a history of hypoglycemic seizures.

"This tells us that overcontrol of hyperglycemia is possibly an issue," Dr. Desrochers told this newspaper. "All of the children in this study had excellent glycemic control and some of the parents told us that they sometimes give their children extra injections of insulin. So that would be something to look into—whether overcontrol is playing a role in the incidence of hypoglycemic seizures."

The study also looked at the neuropsychological functioning of the children and found a trend toward long-term (explicit) memory deficits associated with type 1 diabetes specifically in the areas of verbal and visual memory, functions that are controlled by the hippocampus. However, more conclusive evidence for memory deficits came from a separate study.

In that study, conducted by Ph.D. candidate Lila Elkhadem, explicit and implicit memory skills were compared in 15 children with type 1 diabetes and 17 healthy controls (mean age between 11 and 12 years).

Explicit memory is actively learned whereas implicit memory is information that is more passively absorbed, explained Dr. Desrochers.

"Implicit memory develops earlier and remains robust throughout life. It is what is learned every day, whereas explicit memory is involved when you tell someone they need to remember something," she said.

The study found that in children with diabetes, implicit memory did not differ from controls, but explicit memory was affected.

"They remembered fewer words and fewer themes in stories, as well as fewer numbers in a digit span test," Dr. Desrochers said. She added that there were some less significant problems with visual memory.

The study also examined the relationship between memory and both blood glucose fluctuations during the day and duration of diabetes. It found that children with more variation in their blood glucose levels performed worse on almost all types of memory tests, compared with children with more stable blood glucose levels. And longer duration of diabetes was associated with poorer performance.

Finally, the study also found that memory in children with diabetes was also affected by time of day—with significantly better performances noted in the morning.

The findings have implications for how children with type 1 diabetes should be scheduled and taught in school. ■

In Gestational Diabetes, Metformin Matches Insulin

BY TIMOTHY F. KIRN
Sacramento Bureau

RENO, NEV. — Metformin controlled blood glucose levels as well as insulin in patients with class A2 gestational diabetes, and was not associated with any adverse maternal or neonatal outcomes, according to a randomized trial with 63 patients.

"We found that metformin appears to be an acceptable way to achieve glucose homeostasis in the A2 diabetes patient," Christian Briery, M.D., said at the annual meeting of the Society for Maternal-Fetal Medicine.

The study enrolled pregnant patients who were at greater than 11 weeks' gestation but less than 35 weeks' gestation.

'We found that metformin appears to be an acceptable way to achieve glucose homeostasis in the A2 diabetes patient.'

The women received a starting dose of insulin of 0.7 U/kg daily, in three doses (31 patients) or 500 mg metformin twice daily (32 patients). The patients were then monitored weekly to see that they achieved a postprandial blood glucose level of less than 120 mg/dL and a fasting glucose level of 60-90 mg/dL, said Dr. Briery of the University of Mississippi Medical Center, Jackson.

In blood glucose measurements taken by the patients at home, the mean fasting glucose level was 96.8 mg/dL in the insulin-treated patients and 92.6 mg/dL in the metformin group.

Similarly, the mean postprandial glucose levels ranged in the insulin group from 104.4 mg/dL 2 hours after breakfast to 112.5 mg/dL 2 hours after lunch, while they ranged in the metformin group from 104.6 mg/dL 2 hours after breakfast to 108.1 mg/dL 2 hours after dinner.

The maternal and delivery measures considered included abdominal delivery, gestational age at delivery, shoulder dystocia, and postpartum hemorrhage. There was no difference in those measures between the groups. There was one intrauterine fetal death in the metformin group from a "cord problem" that was determined not to be related to treatment because the mother's glucose levels were consistently normal, Dr. Briery said.

Neonatal outcomes that were considered include birth weight, 5-minute Apgar score, respiratory distress syndrome, neonatal hypoglycemia, and neonatal ICU admission. Again, there was no difference in the groups.

A previous study of metformin use in pregnancy looked specifically at patients with polycystic ovary syndrome, who conceived while on the drug, and it likewise found no indication of any adverse effects that might be associated with the agent. ■