

# Revascularization Improves Cognitive Function

BY MITCHEL L. ZOLER

PHILADELPHIA — Both carotid artery stenting and carotid endarterectomy produced a roughly 50% increase in overall cognitive function in a study of 46 patients undergoing intervention for asymptomatic severe carotid stenosis.

The change was big enough to significantly improve the patients' quality of life. But both revascularization methods also had a price: Carotid stenting resulted in a clinically significant deterioration in average psychomotor speed, and carotid endarterectomy produced a clinically significant decrease in average memory.

The unexpected finding raised questions about how two methods of carotid revascularization produce two



different sets of cognitive outcomes.

"We were very surprised by the results," Dr. Brajesh K. Lal said at the annual meeting of the Eastern Vascular Society.

"There is a lot to understand about the travel of microparticles, which may selectively affect different parts of the brain." That is just one possible explanation for the finding. Stenting and endarterectomy differ in arterial clamping, balloon placement, stenting, dissection, and hypoperfusion, any of which could play a role. "We hypothesize multiple mechanisms by which carotid endarterectomy and stenting produce cognitive dysfunction," said Dr. Lal, a vascular surgeon at the University of Maryland, Baltimore.

The study administered six cognitive tests to 46 asymptomatic patients with

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DR. LAL

unilateral carotid stenosis of 70% or more who were scheduled to undergo revascularization. Patients took 50 minutes to complete the panel of tests before surgery and again at 4-6 months after treatment. After treatment, the composite score rose by an average of 0.47 for the stented patients, compared with baseline, and by 0.51 for the endarterec-

tomy patients. The cognitive changes, scored on a scale of 0-1.0, showed that the two groups weren't significantly different, but the increases in both groups were very clinically meaningful.

The same panel of tests should be used on similar patients managed medically to gauge the cognitive effect of medical treatment, Dr. Lal said. ■

## Change in Cognitive Function After Carotid Revascularization

Cognitive domain tested	Average change from baseline in carotid artery stenting patients (n = 21)	Average change from baseline in carotid endarterectomy patients (n = 25)
Motor speed/coordination	+0.63	+0.74
Psychomotor speed	-0.32	+0.58*
Attention	+0.59	+0.66
Memory	+0.46	-0.41*
Verbal fluency	+0.69	+0.61
Learning	+0.77	+0.86
Composite of all six tests	+0.47	+0.51

\* Statistically significant difference between groups.

Source: Dr. Lal

## Botulinum Toxin Found to Reduce Migraine Frequency

BY MICHELE G. SULLIVAN

PHILADELPHIA — OnabotulinumtoxinA appears to be a safe, effective, and well-tolerated headache prophylactic for patients with chronic migraine.

Two large randomized controlled trials showed that the toxin reduced migraine frequency and improved headache-related disability over 24 weeks, Dr. David W. Dodick said at the International Headache Congress.

The studies—PREEMPT 1 and 2—were conducted at 22 centers in North America and Europe, and included 1,384 patients (average age 41 years). Each trial consisted of a 4-week baseline period, during which patients kept a daily headache diary, followed by 24 weeks of treatment during which patients received two injection cycles of either placebo or onabotulinumtoxinA (Botox), which has not been approved by the Food and Drug Administration for migraine prophylaxis. For 24-56 weeks, there was an open-label trial consisting of three injection cycles of the study drug, said Dr. Dodick of the Mayo Clinic Arizona, Phoenix.

At baseline, patients reported a mean of 20 headache days per month, 19 of which were considered migraine days, with a mean of 290 cumulative headache hours. The mean score on the Headache Impact Test-6 (HIT-6) survey was 65, indicating severe impact. Most of the patients (93%) also reported severe



headache-related disability, and 65% were overusing acute pain medications.

During the double-blind phase, patients randomized to the treatment group received two injection cycles (one every 12 weeks) of onabotulinumtoxinA 155 U. The medication was injected at 31 sites across seven muscle areas in the head and neck. At the physicians' discretion, an additional 40 units could be injected among three additional muscle groups.

**Patients receiving the study drug experienced a greater decrease in cumulative headache hours per month.**

DR. DODICK

The study's main end point was frequency of headache days; secondary end points were frequency of migraine days, moderate/severe headache days, monthly headache hours, and proportion of patients with a severe HIT-6 score.

At 24 weeks, patients in the active group had a significantly greater reduction in headache days and migraine days than those taking placebo (-8 vs. -6, respectively). The HIT-6 score also declined significantly more among the active group (-5 points vs. -2 points). Patients receiving the study drug experienced a greater decrease in cumulative headache hours per month (-120 vs. -80 hours), Dr. Dodick said at the congress, which was sponsored by the International Headache Society and the American Headache Society.

Adverse events occurred in 62% of those taking the study drug and 52% of those taking placebo—a significant difference. The study was sponsored by Allergan Inc. Dr. Dodick reported having received honoraria from the company. ■

## Sumatriptan, Naratriptan Not Tied to Birth Defects

BY MICHELE G. SULLIVAN

PHILADELPHIA — Sumatriptan and naratriptan do not appear to significantly raise the risk of major congenital malformations in fetuses that are exposed to the drugs in utero, according to the latest analysis of an international pregnancy registry.

Established in 1996, the GlaxoSmithKline registry has accumulated data on 849 pregnancies exposed to the drugs. Birth defects occurred in 4.5% of infants exposed in the first trimester or during all of their gestation, which was not significantly higher than that previously identified for women with migraines. Major congenital malformations are known to occur in the offspring of women with migraines at a slightly higher rate than in the general population (3.4% vs. 2%-3%, respectively), Marianne C. Cunningham, Ph.D., and her colleague Sara A. Ephross, Ph.D., reported in a poster at the International Headache Congress. Both are employees of GlaxoSmithKline.

The registry relies on a voluntary reporting strategy that encourages health care providers to submit information on exposed pregnancies as early as possible. Retrospective case reporting also is accepted. Pregnancy outcome is ascertained by medical records that the provider forwards after birth, or by medical records confirming other outcomes, including fetal demise or abortion.

So far, the registry has amassed information on 761 pregnancies exposed to sumatriptan and 88 exposed to naratriptan. Outcomes are known for 570 of the sumatriptan-exposed pregnancies

and 57 of the naratriptan-exposed pregnancies. Twenty-one sumatriptan-exposed pregnancies and 31 naratriptan-exposed pregnancies are pending delivery. The rest have been lost to follow-up, the investigators noted in their poster at the congress, which was sponsored by the International Headache Society and the American Headache Society.

Among the sumatriptan-exposed pregnancies, there were 23 birth defects, 4 fetal deaths, 32 spontaneous fetal losses, and 11 induced abortions.

The malformations that occurred in infants who were exposed to sumatriptan in the first trimester included abnormal head circumference, single palmar crease, and systolic murmur; moderate craniosynostosis; cerebral abnormality with developmental delay; partial cleft lip; ventricular septal defects (4); biliary atresia; diaphragmatic hernia; pyloric stenosis (3); anterior displacement of anus; hip dysplasia; polydactyly; malformation of left hand; and Down syndrome (3).

No data were available for the three birth defects that occurred in infants who were exposed to sumatriptan after the first trimester.

Among fetuses exposed to naratriptan, there were five spontaneous losses, one induced abortion, and one live infant with a 2.5-mm ventricular septal defect that was expected to close spontaneously.

The pregnancy registry did not contain any data on the exposure to the combination of sumatriptan and naproxen. The full report was published online in *Headache* (doi:10.1111/j.1526-4610.2009.01529.x). ■