

Hyperbaric Chamber May Aid Post-CABG Cognition

BY BRUCE JANCIN
Denver Bureau

NEW ORLEANS — Spending a few hours in a hyperbaric chamber before undergoing on-pump coronary artery bypass graft surgery markedly reduces postoperative neurocognitive dysfunction, according to the findings of a randomized double-blind trial.

Sixty-four patients scheduled for on-pump CABG surgery spent three sessions inside a hyperbaric chamber at 24, 12, and 4 hours prior to their surgery. During each session, they were exposed to 60 minutes of 100% oxygen at either 2.4 atm of pressure or normobaric room air. Surgeons, patients, and the neuropsychologist were blinded to which treatment the patient received, Joseph Alex, M.D., reported at the annual scientific sessions of the American Heart Association.

A battery of neuropsychological tests

was administered 1 week before and again 4 months following CABG surgery. Significant neurocognitive dysfunction—a decline of at least 1 standard deviation on any two tests in the battery—was documented in 55% of control subjects and 30% of patients who underwent hyperbaric oxygenation before surgery, according to Dr. Alex of Castle Hill Hospital, Cottingham, and the University of Hull, England.

The patients were similar in time spent on a ventilator or in ICU, blood transfusion, renal dysfunction, and cardiac arrhythmias.

The neuropsychologic test battery included trail-making A and B and the adult memory and information processing table A, among other measures.

Patients who underwent preoperative hyperoxygenation not only had less neurocognitive impairment; they also showed significantly less postoperative anxiety and depression symptoms, Dr. Alex added. ■

Dispensing Confusion Prompts Name Change for Reminyl

BY ELIZABETH MECHCATIE
Senior Writer

Janssen Pharmaceutica has agreed to change the name of its Alzheimer's drug Reminyl in response to inadvertent dispensing of the oral blood glucose-lowering drug Amaryl in its place with resulting cases of severe hypoglycemia and other serious adverse events, including one fatality.

In a Dec. 22, 2004, letter, the FDA acknowledged Janssen's intention to change the name of all Reminyl products. At press time, the new name had not been announced. Amaryl has been the trade name for glimepiride, which is approved for treating type 2 diabetes and is marketed by Aventis. Reminyl is the trade name for galantamine, which is approved for mild to moderate dementia of the Alzheimer's type and is marketed by Janssen Pharmaceutica.

Spontaneous reports submitted to the

FDA and the U.S. Pharmacopeia have described prescriptions that have been "incorrectly written, interpreted, labeled, and/or filled due to the similarity" between the two trade names, according to a "Dear Health Care Provider" letter issued by Janssen. The letter was posted on the FDA's MedWatch Web site (www.fda.gov/medwatch). The starting dose of Reminyl is 4 mg b.i.d., while the starting dose of Amaryl is 1-2 mg b.i.d., with a maximal starting dosage of 2 mg, the letter states. Physicians should spell out the medication name when prescribing over the phone, and clearly print when writing the script.

Errors should be reported by calling the USP Medication Errors Reporting Program, at 800-23ERROR or 800-FAIL-SAF; or the FDA's MedWatch Adverse Event Reporting Program at 800-FDA-1088. Errors also can be reported to the manufacturers: 800-526-7736 (Janssen) or 800-633-1610 (Aventis). ■

Chemotherapy's Cognitive Link Prevalent, but Poorly Understood

BY NORRA MACREADY
Los Angeles Bureau

LOS ANGELES — Cancer patients call it "chemobrain"—a soggy mental state that seems to be a frequent side effect of chemotherapy.

It is rarely studied and poorly understood, but as the number of cancer survivors grows, the impact of chemotherapy on cognitive function will become an increasingly important concern, Curley Bonds, M.D., said at a review of psychiatry and psychopharmacology update sponsored by the University of California, Los Angeles.

Chemotherapy has been reported to affect several aspects of neuropsychological function. The components most commonly affected are focus and concentration, verbal and executive function, and motor activity, said Dr. Bonds of the university.

Several issues complicate research in this area. One is sorting out the impact of chemotherapy from the effect of the cancer itself and that of other forms of therapy. Fatigue, anxiety, and depression commonly accompany cancer and may have an independent effect on higher-order function.

Perhaps the most comprehensive analysis of chemotherapy and cognitive function is a meta-analysis of 30 studies of 29 populations comprising a total of 838 adult patients. The studies included three research designs that compared patients post treatment with control patients who had not undergone chemotherapy, with test scores obtained from normative controls, or with the patients' own baseline scores taken before starting treatment. The cognitive domains tested included attention, verbal and visuospatial memory, visuospatial skill, executive function, psychomotor skill, and information processing speed.

For each domain, the investigators calculated a weighted Cohen's d score, which measures effect size. The scores ranged from 0 (no effect) to +2 (improvement in function) or -2 (deterioration of function), with a score greater than .8 in either direction considered a significant effect. The patients who underwent chemotherapy showed the greatest treat-

ment effects in executive function and verbal memory when compared with the normative controls, with scores of -.93 and -.91, respectively. A significant effect on motor function was also seen (*J. Int. Neuropsychol. Soc.* 2003;9:967-82).

In other controlled research, conducted mostly on women with breast cancer, the rate of cognitive impairment associated with chemotherapy has ranged from 16% to 50% and has persisted for as long as 10 years. Combination chemotherapy with methotrexate, cyclophosphamide, and 5-fluorouracil has been most frequently associated with cognitive problems. (See table.) On the other hand, anthracycline-based agents seem to be associated less frequently with neurotoxicity, Dr. Bonds said. ■

Cancer Drugs Carry Neurotoxic Effects

Chemotherapy Agents Associated With Neurotoxicity

Combination of methotrexate,* cyclophosphamide, and fluorouracil*
Vinca alkaloids
Cytarabine
Platinum analogues
Ifosfamide
Taxol
Taxotere
Fludarabine
Suramin

Agents Associated With Occasional Reports Of Cognitive or Motor Impairment

L-asparagine
Busulfan
Hexamethylmelamine
Procarbazine
Thiotepa

*Also associated with cognitive impairment individually
Source: Dr. Bonds

Treatable Autoimmunity Presented as Dementia

BUDAPEST, HUNGARY — Autoimmune striatal dysfunction may be the underlying cause of dementia-like presentations, in rare cases.

This was the case for a 48-year-old woman, who presented with a 1-year history of progressive difficulties with attention and memory, said Gabriel C. Léger, M.D., speaking at the 4th International Congress on Autoimmunity.

Her husband noted a profound change in her personality. She had become uninhibited and exhaustingly hypersexual and had progressive difficulties functioning at home and at work—finally losing her job.

Her medical history included an episode of self-limiting, ballistic-like movements of the right side of her body during her early 20s. Exhaustive testing turned up no cause. The condition resolved spontaneously after a few months. She had no history of rheumatic fever or childhood chorea. However, at the age of 17 years her mother had Sydenham's chorea, which lasted about 1 year.

Cognitive testing also revealed attention and memory (acquisition) deficits. Additionally, the patient displayed frontal network dysfunction, which psychologic testing confirmed.

Her physical exam was unremarkable, except for mild psychomotor activity of the right hand and right side of the face, said Dr. Léger, a neurologist at the University of Montreal.

The clinicians initially diagnosed frontotemporal dementia, but "the presence of a very mild focal examination bothered us just a little bit," said Dr. Léger. An FDG-PET scan revealed a dramatic increase in metabolism in the left striatum—70% more metabolic activity than in the right striatum.

Hypermetabolic lesions have traditionally been associated with diseases of autoimmunity, he noted. They treated her with a 3-day course of pulsed methylprednisolone sodium succinate, followed by a 2-week prednisone taper period.

Within weeks, the woman noted a resolution of her attention deficits. Neurocognitive assessments also indicated improvement. FDG-PET imaging demonstrated a fairly substantial resolution of the asymmetry of the striatum.

Based on the suspicion that autoimmunity against the basal ganglia was involved, the researchers sent pre- and post-therapy plasma to the laboratory for analysis. High titers of antibodies to the striatum—the antibodies found in Sydenham's chorea—were found in the pretreatment sample and reduced titers were found in the posttreatment sample.

Unlike this case, previously published studies involving hypermetabolic lesions have also involved previously diagnosed disorders, such as Sydenham's chorea, Dr. Léger said.

—Kerri Wachter