

Study Finds Corticosteroids Harmful After Head Injury

BY JANE SALODOF MACNEIL
Southwest Bureau

Findings from the Corticosteroid Randomization After Significant Head Injury Trial that intravenous corticosteroids increased mortality among patients with traumatic brain injury should put to rest once and for all questions about the role of steroids for this indication, Donald Marion, M.D., told this newspaper.

Current guidelines on the management and prognosis of severe head injury do not recommend use of intravenous corticosteroids, said Dr. Marion, a Boston-based senior research fellow at the Brain Trauma Foundation, New York.

Intravenous steroid use for this indication has been on the decline for at least 10 years in the United States. A decade ago, 60%-70% of physicians used steroids in the treatment of traumatic brain injury (TBI); today that has dropped to about 20%.

Negative findings from the unusually large British CRASH trial of more than 10,000 patients should end debate over use of corticosteroids after head injuries, according to Dr. Marion.

Investigators in the United Kingdom randomized 10,008 adult TBI patients to a 48-hour infusion of methylprednisolone or placebo. They reported 25.7% of the corticosteroid group but only 22.3% of the placebo group died within 6 months of entering the CRASH trial.

Although fewer patients developed severe disability on corticosteroids, the combined outcome of death or severe disability still favored the placebo. In the corticosteroid arm of the study, 38.1% were dead or severely disabled at 6 months, compared with 36.3% of the

control group (Lancet 2005;365:1957-9).

"These analyses lend support to the conclusion ... that corticosteroids should not routinely be used in the treatment of head injury," the CRASH trial collaborators stated in a research letter.

The results provide "clear evidence that treatment with corticosteroids following head injury affords no material benefit," according to the investigators. "The absence of evidence of any neurologic benefit from corticosteroid treatment might also have implications

for the use of corticosteroids in spinal cord injury, which should remain an area for debate."

For the trial, investigators randomized patients with a Glasgow Coma Scale score of 14 or less within 8 hours of head injury. All patients received a 48-hour infusion of placebo or methylprednisolone, which Pfizer provided.

The 6-month analysis was based on follow-up data for 9,673 patients (96.7%): 4,854 on corticosteroids and 4,819 patients on placebo. At that point 1,248 corticosteroid patients and 1,075 placebo patients had died.

Conversely, 2,213 placebo patients (45.9%), but only 2,120 corticosteroid patients (43.7%) had made a good recovery. Stratification by severity of head injury and time from injury produced no substantial differences.

Dr. Marion noted in his interview with this newspaper that "the question they [the CRASH researchers] really needed to answer was not whether steroids were bad, but whether steroids improve outcome. They not only proved steroids did not improve outcome but also that people who had steroids had worse outcomes. ... Those people who are following evidence-based medicine are not likely to use steroids." ■

Although fewer patients developed severe disability on corticosteroids, the combined outcome of death or severe disability still favored placebo.

Risk of Death From Brain Cancer Doubled in Certain Gulf War Veterans

Gulf War veterans exposed to chemical munitions destroyed in Iraq were almost twice as likely to die from brain cancer as their unexposed colleagues, Tim A. Bullman and his associates have reported.

In 1991, soldiers destroyed two large Iraqi weapons caches containing sarin and cyclosarin. Almost 100,500 soldiers were exposed to the resultant explosive plume, which drifted for 4 days, said Mr. Bullman, a health statistician with the Department of Veterans Affairs in Washington, D.C., and his associates. They examined causes of death during the first 9 years after the explosion in the

exposed group and almost 225,000 soldiers in the region who were not exposed to the plume (Am. J. Pub. Health 2005;95:1382-8).

Brain cancer was the only disease significantly more common in the exposed group, who had a 1.94 increased risk of dying from the disease. Soldiers exposed for 2 or more days were at a greater risk than those exposed for only 1 day (3.26 vs. 1.72).

The cause of the increased cancers remains unknown since sarin has not been shown to be carcinogenic, the investigators said.

—Michele G. Sullivan

Restless Legs Syndrome Linked To Cardiovascular Disease

BY BRUCE JANCIN
Denver Bureau

DENVER — Restless legs syndrome was associated with a significantly increased prevalence of cardiovascular disease in the Wisconsin Sleep Cohort Study, John W. Winkelman, M.D., reported at the annual meeting of the Associated Professional Sleep Societies.

This is the first report of such a relationship. Dr. Winkelman termed the connection "intriguing" and worthy of further investigation.

Possible explanations for the restless legs syndrome (RLS)/cardiovascular disease association include adverse cardiovascular effects due to the repeated autonomic arousals that accompany the abnormal leg movements. Alternatively, it could be that cardiovascular disease in some undefined way promotes RLS. Or perhaps the two share a common genetic predisposition, speculated Dr. Winkelman of Brigham and Women's Hospital in Boston.

He reported on 2,770 participants aged 40-75 years in the Wisconsin Sleep Cohort Study. The prevalence of RLS among this representative sample of Wisconsinites was 10.6% as defined by at-least-weekly occurrence of all three of the following complaints: a repeated urge to move the legs, disrupted sleep due to strange and uncomfortable feelings in the legs, and improvement upon getting up and walking.

The prevalence of RLS didn't differ significantly by gender. It did, however, in-

crease with age, as has been reported in other studies.

The prevalence of cardiovascular disease was 4.6% among individuals without RLS, 7.4% in those experiencing RLS roughly once per week, and 11.9% among those who experienced RLS on a nightly basis.

In a multiple logistic regression analysis adjusted for potential confounders including age, body mass index, smoking, diabetes, and treatment for obstructive sleep apnea, individuals with RLS on a weekly basis had a 1.37-fold greater rate of known cardiovascular disease than did those without RLS, while those with RLS nightly had a 2.19-fold increased rate.

In addition to being the first study to link RLS and cardiovascular disease, this is also the first to report that RLS is associated with both self-reported poor general health and excessive daytime sleepiness. Moreover, the severity of these two health problems was correlated with the frequency of RLS. Individuals with RLS once per week were 2.14-fold more likely than were those without RLS to characterize their general health as only fair or poor; those with nightly RLS were 3.31-fold more likely to do so, in an adjusted analysis.

Similarly, individuals with weekly RLS were more likely to report excessive daytime sleepiness and had higher Epworth Sleepiness Scale scores than did participants without RLS. Adults with nightly RLS reported more daytime sleepiness and had higher Epworth scores than did those with less frequent RLS. ■

Kentucky Case Shows Potential Health Impact of Mercury Spill

BY JEFF EVANS
Senior Writer

Mercury spills and exposures are seemingly uncommon but occur with enough regularity to consider toxic exposure to the metal in patients who have headaches, rashes, skin desquamation, and behavioral or psychiatric changes, according to a report by the Centers for Disease Control and Prevention.

One of the more than 40 documented mercury spills that occurred in the Southeast during 1999-2005 involved about 30 people in Kentucky in November 2004 (MMWR 2005;54:797-9).

A young girl who was exposed to mercury in that spill experienced symptoms consistent with mercury exposure (unexplained tachycardia, hypertension, desquamation of soles and palms, rashes, diaphoresis, muscle pain, insomnia, vomiting, and behavioral and psychiatric changes). At one point she was hospitalized for 30 days but was not tested for toxicity because the diagnosis was not considered at the time.

In the Kentucky incident, a 15-year-old boy took mercury from an open storage area during visits to his dentist and then

contaminated school buses and a cafeteria. Local, state, federal, and private health and environmental protection officials collaborated in closing, cleaning, and reopening the school and school buses. None of the approximately 15 students who played with the mercury in the cafeteria had concentrations that exceeded background levels.

Blood concentrations of mercury in the boy and seven family members who occupied a mobile home at different periods before the incident ranged from 32 to 72 mcg/L (normal is 0-10 mcg/L), and their 24-hour urine mercury levels ranged from 28 to 496 mcg/L (normal is 0-19 mcg/L).

The 15 or so other people who spent substantial amounts of time in the home or in three contaminated cars had normal levels of mercury.

The concentration of mercury in their urine was directly associated with the amount of time each person spent in the mobile home. The boy and two other children who had lived in the mobile home for 15 months had the highest urinary concentrations (193-496 mcg/L). The lowest levels were found in three children who had lived in the home for only 10 weeks (28-68 mcg/L). ■