Steroids Fail to Aid Survival In Bacterial Meningitis Study

BY MARY ANN MOON
Contributing Writer

Adjuvant corticosteroid therapy did not improve survival or shorten hospitalization in the largest observational study of its kind ever conducted in children, researchers reported.

These findings held true across all pediatric age groups and regardless of whether the infecting organism was pneumococcal or meningococcal, according to Jillian Mongelluzzo of the division of infectious diseases, Children's Hospital of Philadelphia, and her associates.

Adjuvant corticosteroid therapy does reduce hearing loss in children with meningitis caused by *Haemophilus influenzae* type b (Hib), but since the widespread use of vaccines against Hib in 1985 and *Streptococcus pneumoniae* in 2000, the epidemiology of bacterial meningitis has changed dramatically, they said.

Nonetheless, the use of adjuvant corticosteroid therapy appears to be increasing, so "a randomized trial is warranted to explore the possible benefit … before such corticosteroid use becomes routine," the investigators noted (JAMA 2008;299:2048-55).

In this retrospective cohort study, the investigators used data from the Pediatric Health Information System, a database that covers 27 tertiary care children's hospitals across the country, to track meningitis trends from 2001 through 2006 in areas where Hib meningitis is no longer prevalent.

In all, 2,780 cases of bacterial meningitis in children younger than 18 years were assessed.

Adjuvant corticosteroids, most often dexamethasone, were given to 248 children (9%). The use of these agents increased steadily over time, from 5.8% of patients in 2001 to 12.2% in 2006.

Use varied greatly by hospital, with some centers never giving adjuvant corticosteroids and one giving them in 37% of cases, Ms. Mongelluzzo and her associates said.

There were 15 deaths among children who received corticosteroids (6% mortality) and 102 among the 2,532 children who did not (4% mortality), a difference that was not statistically significant.

The treatment did not improve survival when the data were analyzed by age group, nor did it affect the length of the interval between admission and death, Dr. Mongelluzzo and her associates said.

The median length of stay for children who received corticosteroids was 12 days (range 7-21 days), while the median for children who did not receive corticosteroids was 10 days (range 6-20 days)—a difference that also was not statistically significant.

Length of stay is important to consider because "longer hospitalizations increase the risk of hospital-acquired complications," the investigators said.

These results did not change when the data were analyzed by type of infecting organism, including Hib, *S. pneumoniae*, and *Neisseria meningitidis*, and others.

It is not yet clear why corticosteroids do not improve survival in children as they do in adults.

Adults may have different predisposing factors for meningitis or a different inflammatory response, which could change their course of disease in comparison with children, Ms. Mongelluzzo and her associates noted.

They added that this study did not address the possible benefits of adjuvant corticosteroid therapy on hearing loss or neurologic morbidity in children. ■

Neonatal GBS Incidence Falls; Stricter Guidelines Credited

BY MARY ANN MOON
Contributing Writer

The incidence of invasive group B streptococcal disease declined among infants aged 0-6 days after stricter measures for perinatal prevention were widely adopted across the country in 2002, federal scientists have reported.

However, there was a significant increase in the disease among black infants during this period, a finding that is "particularly concerning and requires investigation," said Christina R. Phares, Ph.D., of the Centers for Disease Control and Prevention (CDC) and her associates.

However, there was a significant increase in GBS disease among black infants in 2004 and 2005, which is 'particularly concerning and requires investigation.'

The revised guidelines recommended antenatal culture-based screening as the optimal method for identifying candidates for intrapartum chemoprophylaxis.

The CDC investigators assessed epidemiologic trends among 14,573 cases of invasive group B streptococcal (GBS) disease identified by a national surveillance program between 1999 and 2005, the most recent year for which data are available.

In 2005, there were an estimated 21,500 cases of invasive GBS in the United States, including 1,700 fatalities (JAMA 2008; 299:2056-65).

The overall incidence of invasive GBS disease among adults and children in 2005 was 12.8 per 100,000 population in blacks, 6.5 per 100,000 in whites, and 5.1 per 100,000 in all other races combined.

Mortality also was significantly higher for black neonates and black adults aged 45 years and older than for other racial groups.

Early-onset GBS (before 1 week of age) decreased by 27%, from 0.47 per 1,000 live births before the revised guidelines to 0.34 per 1,000 live births in 2003-2005. This is "very close" to the impact that the stricter guidelines were predicted to have, the researchers said. However, there were small increases in incidence in 2004 and 2005, almost all of which occurred among black infants.

The incidence of late-onset GBS (age 7-89 days) remained stable, averaging 0.34 cases per 1,000 live births throughout the 7-year study. Similarly, the incidence of childhood disease (90 days–14 years) remained stable at 0.56 per 100,000 population, with 61% of these cases occurring in children aged 3-12 months.

In contrast, the incidence increased significantly among adults—by 48% in people aged 15-64 years and by 20% in people aged 65 and older. This might be in part because of the increase in underlying medical conditions such as diabetes in this age group, Dr. Phares and her associates said.

Serotype data suggested that a pentavalent conjugate vaccine potentially could have prevented "up to 96% of neonatal disease and 88% of pediatric, adult, and pregnancy-associated disease, which translates to approximately 19,000 cases" of the 21,500 estimated to have occurred in 2005.

"Maternal GBS vaccination trials should be a public health priority, followed by expanded vaccine development to target disease among elderly and younger adults with chronic underlying conditions," they concluded. ■

Antiretroviral Therapy Conveys Metabolic Risks in HIV Youth

BY DIANA MAHONEY
New England Bureau

BOSTON — Long-term exposure to antiretroviral therapy appears to convey substantial metabolic risk to adolescents and young adults with HIV infection, according to a National Institutes of Health study.

In a cross-sectional investigation of 40 HIV-infected patients aged 11-27 years who acquired HIV in infancy or childhood and had been exposed to antiretroviral therapy (ART), a majority of study participants had impaired glucose tolerance and other metabolic abnormalities, said Dr. Colleen M. Hadigan of the National Institute of Allergy and Infectious Diseases and her colleagues.

Whereas the medical literature is replete with studies linking such metabolic complications as dyslipidemia, lipodystrophy, and insulin resistance to long-term ART in HIV-infected adults, the pediatric literature is relatively sparse, and comprehensive reviews of metabolic consequences of ART in children are rare, Dr. Hadigan reported at the 15th Conference on Retroviruses and Opportunistic Infections.

The current study was designed to characterize the extent of metabolic abnormalities in a cohort of adolescents who acquired HIV infection perinatally or in childhood, she said.

All study subjects were ART experienced, with a mean treatment duration of 14 years, and all had current or past protease inhibitor and stavudine exposure. At the time of the investigation, 88% of the patients were receiving a protease inhibitor. At enrollment, approximately half of the patients had an HIV RNA of fewer than 50 copies per milliliter; the mean CD4 count was 665.

According to the study protocol, all of the subjects completed oral glucose tolerance testing and fasting insulin and lipid studies, and all underwent anthropometric assessments including whole body dual-energy x-ray absorptiometry (DXA) scans.

An analysis of the results showed impaired glucose tolerance in 20% of the subjects. The mean fasting insulin level for the group was 18 IU/mL, the mean glucose level was 86 mg/dL, and the mean homeostatic model for assessment of insulin resistance (HOMA) was 3.9, Dr. Hadigan reported at the conference, which was sponsored by the Foundation for Retrovirology and Human Health and the Centers for Disease Control and Prevention.

Approximately 38% of the subjects had a HOMA value greater than 4.0, and thus met the criteria for insulin resistance, Dr. Hadigan said. In addition, 50% had elevated triglyceride levels (greater than 150 mg/dL), 53% had low levels of HDL cholesterol (less than 50 mg/dL for females and less than 40 mg/dL for males), and 24% had an elevated total cholesterol level (greater than 200 mg/dL).

With respect to body mass index (BMI) and body fat, the mean BMI was 22 kg/m^2, the mean waist-to-hip ratio was 0.92, and the mean percentage of body fat by DXA was 20. Approximately 15% of the subjects were overweight, with a BMI greater than 25, and one patient was obese, with a BMI greater than 30. Similarly, 16% of the subjects had a waist-to-hip ratio greater than 1.00. Of interest, Dr. Hadigan noted, was the fact that insulin resistance by HOMA was significantly positively correlated with waist-to-hip ratio in this mostly nonobese population.

Although none of the subjects had type 2 diabetes, the results suggest that long-term exposure to ART may substantially increase their risk for that outcome as well as for cardiovascular disease, Dr. Hadigan warned. As such, "these findings warrant careful monitoring in this population, as well as further research." ■