OBSTETRICS

Adverse obstetric events are associated with significant risk of cerebral palsy

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OBJECTIVE: To examine adverse birth events on the development of cerebral palsy in California.

STUDY DESIGN: A retrospective population-based study of children with cerebral palsy (as of Nov. 30, 2006), matched to their maternal/infant delivery records (Jan. 1, 1991 to Dec. 31, 2001) was performed. Demographic data and intrapartum events were examined. Six adverse birth-related events were chosen. Children without cerebral palsy were controls.

RESULTS: There were 7242 children who had cerebral palsy (59% term) and 31.3% had 1 or more of the 6 adverse intrapartum events (12.9% in controls $P < .0001$). This held for both term (28.3% vs 12.7% controls) and preterm (36.8% vs 15.9%, controls) neonates (both $P < .0001$). Maternal (15.1% vs 6.6%) and neonatal (0.9% vs 0.1%) infection were increased in cerebral palsy cases ($P < .0001$).

CONCLUSION: Almost one-third of children with cerebral palsy had at least 1 adverse birth-related event. Higher rates in the preterm group may partially explain the higher rates of cerebral palsy in this group.

Key words: birth asphyxia, cerebral palsy, uterine rupture

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Cerebral palsy (CP) refers to multiple nonprogressive, heterogeneous syndromes of posture and motor impairment associated with certain lesions of the brain arising early in the neurodevelopment of infants.[1] It is one of the most common motor disabilities in childhood. Although there has been debate as to the changes in rates over time, current studies estimate a prevalence of 2 to 3 per 1000 live births.[2] Initially characterized by William Little in 1860 as being associated with asphyxiation during delivery, Sigmund Freud postulated in 1897 that CP may be the result of intrauterine factors affecting fetal neurodevelopment.[3,4] Findings of the National Institute of Neurological Disorders and Stroke (NINDS) during the 1980s suggested that only a small number of cases of CP are caused by lack of oxygen during birth.[5] Previous studies have attempted to suggest an increased prevalence of CP due to the increased survival of low (LBW) and very low birthweight (VLBW) infants over the last half of the century.[6] However, in a population-based study of CP in the United States, Winter et al noted only an increase in infant survivors of normal birthweight, with no change in prevalence among LBW and VLBW infants.[2]

The American College of Obstetricians and Gynecologists convened a Task Force on neonatal encephalopathy and CP to review the evidence and make recommendations.[7] This extensive report was published in 2003; it represents the largest effort (to date) to examine the causes of CP and whether acute intrapartum hypoxic events are responsible for the development of CP. In the report, they identified 4 events that when all were present, were sufficient to cause CP. The 4 events were as follows: (1) evidence of a metabolic acidosis in fetal umbilical cord arterial blood obtained at delivery (pH <7 and base deficit >12 mmol/L; (2) early onset severe or moderate neonatal encephalopathy in infants born at 34 or more weeks of gestation; (3) CP of the spastic quadriplegic or dyskinetic type; and (4) exclusion of other identifiable causes, such as trauma, coagulation disorders, infectious conditions, or genetic disorders. In our study, we identified those children with CP of the spastic quadriplegic or dyskinetic type and examined adverse-related birth outcomes within the state of California.

Materials and Methods

This project was approved by the California Protection of Human Subjects committee, the Office of Statewide Health Planning and Development (OSHPD), and the University of California, Davis Human subjects committee. The data for this study came from several sources: (1) Patient Discharge Databases of all maternal and newborn/infant discharge data published by the California Office of OSHPD; (2) the Linked Vital Statistics Birth and Infant Death File published by the California Department of Health Services (DHS); and (3) the Client Development Evaluation Report (CDER) compiled by the California Department of Developmental Services (DDS). The first 2 sources are linked by

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the California OSHPD and provide information on all live births in California, including infant demographics, prenatal care, infant survival, delivery, infant and maternal diagnoses and procedures, and outcomes such as birthweight, gestational age, and length of stay and who report to OSHPD (98% of all deliveries). These 3 databases, however, do not contain certain information that may be important in identifying a cause of CP in a particular case such as a low Apgar score. Because these are administrative computerized databases, we were not able to perform a chart review of any of the cases of interest and thus individual confirmation of each case can not be performed. The linkage between these 2 databases has been studied previously and has been found to be 97.8% accurate for linkage of the 3 databases.[8-10]

The third data source, CDER, consists of data collected by 21 nonprofit regional centers that, under contract with the California DDS, provide services to persons with developmental disabilities. The CDER is used by the California DDS to document the diagnostic and functional level of development for the majority of persons with neurologic disability age 3 and above. To be eligible for DDS services, a person has to be professionally diagnosed with mental retardation, autism, epilepsy, CP, and conditions similar to mental retardation. Linking clients in the CDER file to their birth record enabled us to compare the prenatal and delivery experience in infants later diagnosed with CP with those children without a later CP diagnosis. It is important to note that the CEDR is an encounter database that provides a snapshot of the current DDS caseload as of Nov. 30, 2006 to clients with birth dates on or after Jan. 1, 1990. Among the various types of CP, those with the spastic quadriplegic or dyskinetic type were identified and included in our analysis.

The *International Classification of Diseases, 9th revision, Clinical Modification* (ICD-9-CM)[11] diagnostic and procedural codes were used to identify various diagnoses and outcomes. All infants were grouped and analyzed according to birthweight, gestational ages, and neonatal complications. The data were analyzed by determining odds ratios (ORs) and 95% confidence intervals (CIs) for adverse outcomes for each group where appropriate. The ORs were adjusted for maternal age, parity, maternal education, payer source, race/ethnicity, timing of initiation of prenatal care, number of prenatal visits, gestational age, birthweight, obstetric, and neonatal comorbidities. Logistic regression was used to control for the presence of a variety of risk factors. The control group consisted of infants delivered who did not receive the diagnosis of CP within the specified time frame.

The study and control group were examined in total and then broken down into term (≥37 weeks of gestation at delivery) and preterm (<37 weeks of gestation at delivery).

RESULTS

A total of 6,145,357 deliveries were reviewed over the study period from Jan. 1, 1991, until Dec. 31, 2001. Of these, 8946 cases (Table 1) of CP were identified for analysis (1.45 per 1000 live births) with 7242 (Table 2) having CP of the spastic quadriplegic or dyskinetic type, and only these were included in our current study. A total of 4274 were delivered at term; 2465 were delivered preterm with 6% not having gestational age classified and thus were not included in the group. The demographic data for the mothers who delivered during this time period are displayed in Table 1. Among all patients, there were very few significant increased risks among any of the studied demographic characteristics for either term or preterm pregnancies, except for advanced maternal age (>40 years of age), increasing parity, and higher rates in non-Hispanic whites in the preterm group (Table 1). There were no consistent differences in the demographic factors in the term group. Children delivered from multiple gestations, after correcting for gestational age at delivery and other factors, had significant increases in risk of CP in both term and preterm deliveries.

Pregnancy risk factors including chronic hypertension, preeclampsia, and pregestational diabetes were not associated with any increase risk of CP in either term or preterm delivered infants. Gestational diabetes in the term (but not preterm) population was associated with a 19% increase risk of CP as compared with controls (OR, 1.19; 95% CI, 1.03–1.37) after adjustment. Maternal infection (ICD-9 CM codes 670, 672, 647, 646.6, 658.4, 659.2, and 659.3) was seen more frequently in the term cases of CP (25.6% vs 10.25; control, $P < .0001$) than in the preterm cases of CP (9.0% vs 6.2%; control, $P < .0001$); whereas, neonatal infection (771.7, 774.1) was still significantly different but much less frequent (term 1.9% vs 0.3%; control, $P < .0001$, preterm 0.3% vs 0.05; control, $P < .0001$)

In an effort to determine what effect adverse events surrounding the labor and delivery process itself could have on the subsequent development of CP, we identified 6 diagnoses that we believed were likely to be associated with CP and they include, placental abruption (ICD-9 CM 641.2), uterine rupture during labor (ICD-9 CM 665.1), fetal distress (ICD-9 CM 656.3, 768.2-4), birth trauma (ICD-9 CM 767), cord prolapse (ICD-9 CM 663.0, 762.4), and asphyxia (ICD-9 CM 768.5-9). The more up-to-date term for birth asphyxia, hypoxic ischemic encephalopathy, was not in common use during our study period and was not reported significantly to be of use in our study. We examined the database for those cases that had 1 or more is these 6 diagnoses and compared them with the population of patients without CP (Table 2). All children with CP had a significantly greater rate of adverse events: 31.3% compared with 12.9% for those children without CP. Both term and preterm infants demonstrated greater rates of adverse events, with preterm cases being higher than term cases (Table 2).

COMMENT

Our population based study of 7242 children with spastic quadripalegic or dyskinetic CP, matched to their maternal and infant delivery records, provides the largest study of children with CP and the opportunity to examine their adverse birth-related events. In this effort to look