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Adverse Obstetrical Events are Associated with Significant Risk of Cerebral Palsy

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Abstract

OBJECTIVE—To examine adverse birth events on the development of cerebral palsy (CP) in California.

STUDY DESIGN—A retrospective population-based study of children with CP (as of 11/31/2006), matched to their maternal/infant delivery records (1/1/1991 to 12/31/2001) was performed. Demographic data and intrapartum events were examined. Six adverse birth related events were chosen. Children without CP were controls.

RESULTS—7242 children had CP (59% term) and 31.3% had one or more of the six adverse intrapartum events (12.9% in controls P< 0.0001). This held for both term (28.3% v. 12.7% controls) and preterm (36.8% v. 15.9%, controls) neonates (both P< 0.0001). Maternal (15.1% v. 6.6%) and neonatal (0.9% v, 0.1%) infection were increased in CP cases (P< 0.0001).

CONCLUSION—Almost 1/3 of children with CP had at least one adverse birth- related event. Higher rates in the preterm group may partially explain the higher rates of CP in this group.

Keywords

cerebral palsy; birth asphyxia; uterine rupture

INTRODUCTION

Cerebral palsy (CP) refers to multiple non-progressive, 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. While 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

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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 and very low birth weight infants over the last half of the century (6). However, in a population-based study of CP in the United States, Winter at al. noted only an increase in infant survivors of normal birth weight, with no change in prevalence among low (LBW) and very low birth (VLBW) weight infants (2).

The American College of Obstetricians and Gynecologists (ACOG) 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 or not acute intrapartum hypoxic events are responsible for the development of CP. In the report, they identified four events which when all were present, were sufficient to cause CP. The four events were: 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; 4) exclusion of other identifiable etiologies, 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 State Planning and Development (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 two sources are linked by 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 birth weight, gestational age, and length of stay and who report to OSHPD (98% of all deliveries). These three databases however do not contain certain information which 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 conformation of each case can not be performed. The linkage between these two databases has been studied previously and has been found to be 97.8% accurate for linkage of the three databases (8,9, 10).

The third data source, CDER, consists of data collected by twenty-one non-profit regional centers which–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 three and above. In order to be eligible for DDS services, a person has to be professionally diagnosed with mental retardation, autism, epilepsy, cerebral palsy 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 to 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 11/30/2006 to clients with birth dates on or after 01/01/1990. 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 birth weight, gestational ages, and neonatal complications. The data were analyzed by determining odds ratios (ORs) and 95% confidence intervals 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, birth weight, obstetrical and neonatal co-morbidities. 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 January 1, 1991 until December 31, 2001. Of these, 8,946 cases (Table 1) of CP were identified for analysis (1.45 per 1000 live births) with 7,242 (Table 2) having CP of the spastic quadriplegic or dyskinetic type, and only these were included in our current study. 4,274 were delivered at term; 2,465 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 Tables 1. Amongst 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 pre-gestational 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 to 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% v. 10.25, control, P< 0.0001) than in the preterm cases of CP (9.0% v. 6.2%, control, P< 0.0001) while neonatal infection (771.7, 774.1) was still significantly different but much less frequent (term 1.9% v. 0.3% control, P<0.0001, preterm 0.3% v. 0.05& control, P< 0.0001)

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 which we felt 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 which had one or more is these 6 diagnoses and compared them to the population of patients without CP (Table 2). All children

with CP had a significantly greater rate of adverse events: 31.3% compared to 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 7,242 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 at factors surrounding the birthing process, we identified 6 diagnoses which have been associated with CP in the past (7) and compared those children with CP to those without, for all gestational ages (Table 2). We purposely examined only those children with the spastic quadriplegic or dyskinetic type of CP because these types are the only ones which are caused by birth related neonatal encephalopathy (7). In total, almost one third of children with CP had at least one adverse perinatal event associated with their delivery, which was a value significantly higher than our control group (13%) or reports in the literature (7). One can look at these figures in at least two ways. Our population based study identified that birth related events are a greater cause of future development of CP than previously reported (10–15%), which may not be well received by the obstetrical community due to medical legal issues (7). On the other hand, the majority of children with CP did not have an adverse perinatal event associated with their delivery process to explain their development of CP. This later point continues to reaffirm that the majority of children with CP must have other, non-birth related causes for their CP.

The frequency of CP within our population was 1.4/1000 deliveries which is only slightly less than the 1.7 – 2/1000 previously reported by Winter et al. over a prolonged period (1975–1991) in their study examining children with CP in the Atlanta area (2). We examined the entire state of California and they only examined the Atlanta metropolitan area which could explain the difference. It is intuitive that families with children with CP would probably want to live near larger metropolitan areas which would tend to have better resources for their children and thus could explain the slightly higher rate.

When the cases are separated into term and preterm groups, several interesting differences occur. The incidence of adverse birth related events (Table 2) is higher in the preterm group as compared to the term group (36.8% preterm vs. 28.3% term). The biggest difference appears to be in the risk of abruption (2.4% term vs. 10.8% preterm), with slightly lower risks of asphyxia and uterine rupture but higher risks of cord prolapse in the preterm group. Historically, the increased risk of CP in the preterm infant has been felt to be related to the complications of prematurity, especially in the very preterm (or very low birth weight) delivered child (6, 12,13). Neonatal hypoxemia secondary to respiratory distress syndrome (RDS) appears to be one of the leading causes of the future development of CP in the very preterm infant. Difficult or traumatic deliveries are thought to be less of a problem in the preterm infant due to a higher cesarean section rate and less birth trauma at the lower birth weight categories (14). It would appear that adverse intrapartum events contribute more frequently to, or impact to a greater degree upon, the future development of CP in the preterm infant as compared to their term counterparts suggesting that these adverse events could partially explain the higher rate of CP in preterm children.

The choice of one or more of these 6 categories (abruption, uterine rupture, fetal distress, birth trauma, cord prolapse, birth asphyxia) to define a possible birth related event is a choice the authors made because most have been associated with CP (7,15). Two are clearly an obstetrical emergency (uterine rupture, cord prolapse) which requires immediate action if newborn injury is to be prevented. Others are less clearly defined (fetal distress, birth trauma, abruption) and

while associated with CP, they seem to be open to more provider interpretation possibly explaining a significant number of patients in the control population also having these diagnoses (Table 2). Birth asphyxia, while not the preferred terminology in use today to describe neonatal encephalopathy, was widely used during the time period of our deliveries and clearly has been associated with the development of CP (16). Our examination of the newborn discharge records did not find that neonatal encephalopathy nor hypoxic ischemic encephalopathy was used to any extent during our study period and its definition certainly was not clear during that time so we decided not to use it in our analysis.

Infection has been recently shown to be a cause of CP, especially in term infants without other causes for their CP (17). We used an index for maternal infection which included many ICD-9 codes (including amniotic infection). This maternal infection measure supports maternal infection being associated with CP because it was found 2.5 times more often in term infants with CP (compared to controls) as opposed to 1.5 times higher in the preterm group. Clearly much more research in needed in the area of infection and CP and is the subject of another study.

Demographic factors did not seem to play a role in the future development of CP except for an increase in CP with advanced maternal age and increasing parity in the preterm group and a decreasing rate of CP with increasing parity in the term group (Table 1). Increasing parity is usually associated with a more rapid labor and delivery process and it is possible that adverse birth related events are lower with shorter labors and less difficult deliveries in the term group.

To what degree the information from this study can help us prevent adverse birth related event causes of CP is unclear. Several causes like uterine rupture will probably decrease as only hospitals with in house OB/GYN and anesthesia staff will be allowed to perform attempted vaginal births after cesarean (VBAC) deliveries. Patient safety initiatives which focus on provider communication skills and standardized fetal heart rate tracing interpretations, should provide for earlier detection of fetal distress and thus lower the frequency of CP as well.

There are limitations to the use of administrative databases some of which were described above. We utilized ICD-9 CM diagnostic and procedural codes and other demographic information on the CDER, maternal/infant discharge records, and birth/death certificates. Most of the principle diagnoses and procedures have been shown to be adequately sensitive and any errors are primarily acts of omission instead of incorrectly entered data (18,19).

The state CDER database of children in California with CP is run by the Department of Developmental Services and is a MediCal billing database containing diagnostic and billing information. The state provides services for these children with CP and pays for these services through state programs. While not all children with CP are required to receive state funded care, certainly those children with severe disabilities, more likely than not, will be included due to the expenses involved. Children suspected to have CP at younger ages are referred to regional centers for evaluation and thus enter the state system this way. Whether children with adverse birth outcomes are followed more closely than children without these same outcomes can not be determined by our project, however pediatricians, not obstetricians, are the primary referrers to the CDER program. Because of the above factors, the vast majority of children with CP are thought to be in the CDER database.

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References

1. Mutch L, Alberman E, Hagberg B, et al. Cerebral palsy epidemiology: where are we now and where are we going? Developmental Medicine and Child Neurology 1992;34(6):547–551. [PubMed: 1612216]
2. Winter S, Autry A, Boyle C, Yeargin-Allsopp M. Trends in the Prevalence of Cerebral Palsy in a Population-Based Study. Pediatrics 2002;110:1220–1225. [PubMed: 12456922]
3. Accardo PJ. Freud on diplegia: Commentary and translation. Am J Dis Children 1982;136:452–456. [PubMed: 7044107]
4. Jones MW, Morgan E, Shelton JE, Thorogood C. Cerebral Palsy: Introduction and Diagnosis (Part I). J Ped Health Care 2007;21:146–152.
5. National Institute of Neurological Disorders and Stroke (U.S.). Cerebral Palsy: Hope Through Research. NIH Publication No. 06-159. July;2006
6. Bhushan V, Paneth N, Kiely JL. Impact of improved survival of very low birth weight infants on recent secular trends in the prevalence of cerebral palsy [see comments]. Pediatrics 1993;91:1094–1100. [PubMed: 8502508]
7. American College of Obstetricians and Gynecologists' Task Force on Neonatal Encephalopathy and Cerebral Palsy, American College of Obstetricians and Gynecologists, American Academy of Pediatrics. Neonatal encephalopathy and cerebral palsy: Defining the pathogenesis and pathyophysiology. Washington: American College of Obstetricians and Gynecologists; 2003.
8. Herrchen B, Gould JB, Nesbitt TS. Vital statistics linked birth/infant death and hospital discharge record linkage for epidemiological studies. Comput Biomed Res 1997;30:290–305. [PubMed: 9339323]
9. Gilbert WM, Nesbitt TS, Danielson B. Childbearing beyond age 40: Pregnancy outcome in 24,032 cases. Obstet Gynecol 1999;93:9–14. [PubMed: 9916947]
10. Braverman P, Pearl M, Egerter S, Marchi K, Williams R. Validity of insurance information of California birth certificates. Am J Public Health 1998;88:813–816. [PubMed: 9585754]
11. Practice Management Information Corporation (PMIC). 6. Edition Hospital edition. Vol. 1,2,3. Los Angeles, CA: PMIC, C2005; 2006. ICD-9-CM: international classification of diseases, 9th revision; clinical modification.
12. Grether JK, Nelson KB, Emery ES III, Cummins SK. Prenatal and perinatal factors and cerebral palsy in very low birth weight infants. J Pediatr 1996;128:407–14. [PubMed: 8774515]
13. Hack M, Wilson-Costello D, Friedman H, Taylor GH, Schluchter M, Fanaroff AA. Neurodevelopment and predictors of outcomes of children with birth weights of less than 1000 g. Arch Pediatr Adolesc Med 2000;154:725–731. [PubMed: 10891026]
14. Gilbert WM. Prevention of Birth Injuries. Clin Obstet Gynecol 2007 Sep;50(3):561–2. [PubMed: 17762409]
15. Clark SM, Ghulmiyyah LM, Hankins GD. Antenatal antecedents and the impact of obstetric care in the etiology of cerebral palsy. Clin Obstet Gynecol 2008;51(4):775–86. [PubMed: 18981802]
16. Graham EM, Ruis KA, Hartman AL, Northington FJ, Fox HE. A systematic review of the role of intrapartum hypoxia-ischemia in the causation of neonatal encephalopathy. Am J Obstet Gynecol 2008 Dec;199(6):587–95. [PubMed: 19084096]
17. Wu YW, Escobar GJ, Grether JK, et al. Chorioamnionitis and cerebral palsy in term and near-term infants. JAMA 2003;290:2677–84. [PubMed: 14645309]
18. Yasmeen A, Romano PS, Schembri ME, Keyzer JM, Gilbert WM. Accuracy of obstetric diagnoses and procedures in hospital discharge data. Am J Obstet Gynecol 2006;194:992–1001. [PubMed: 16580288]
19. Romano PS, Yasmeen S, Schembri, Keyzer JM, Gilbert WM. Coding of Perineal Lacerations and Other Complications of Obstetric Care in Hospital Discharge Data. Obstet Gynecol 2005;106:717–25. [PubMed: 16199627]

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Table 1

Maternal and Paternal Demographic Characteristics of Spastic Quadripalegic or Dyskinetic CP cases.

		Preterm						Term					
Risk Factors		**N (SQD CP)**	**N (No CP)**	**% (SQD CP)**	**OR (adj)**	**95% CI**		**N (SQD CP)**	**N (No CP)**	**% (SQD CP)**	**OR (adj)**	**95% CI**	
Age	20 and under	456	101,931	0.45	1.1	0.9	1.3	766	817,051	0.09	1.1	0.94	1.20
	21–25	511	130,837	0.39	1	reference		1048	1,315,511	0.08	1	ref	
	26–30	609	136,842	0.44	1.1	0.9	1.3	1111	1,450,043	0.08	1.01	0.91	1.11
	30–35	523	113,128	0.46	1.1	0.9	1.3	856	1,099,733	0.08	1.01	0.90	1.14
	35–40	295	57,280	0.51	1.1	0.9	1.3	424	461,261	0.09	1.2	1.02	1.38
	41+	71	12,069	0.58	1.3	1.0	1.7	67	76,307	0.09	1.1	0.85	1.49
Parity	Nulliparous	970	212,033	0.46	1			1737	2,046,667	0.08	1		
	1	654	154,432	0.42	1.1	0.99	1.2	1213	1,640,045	0.07	0.9	0.82	0.97
	2	398	92,935	0.43	1.2	1.02	1.3	690	875,167	0.08	0.9	0.80	0.98
	3 or higher	435	91,607	0.47	1.2	1.02	1.4	627	653,889	0.10	1.01	0.90	1.13
Maternal education	Less than HS	875	200,640	0.43	1.0	0.9	1.2	1569	1,669,840	0.09	1.1	1.01	1.21
	HS	750	162,667	0.46	1	ref		1272	1,513,752	0.08	1	ref	
	Some college, no degree	495	100,231	0.49	1.01	0.93	1.1	750	1,019,259	0.07	0.9	0.82	1.00
	College	316	81,161	0.39	0.8	0.7	0.95	652	966,164	0.07	0.8	0.74	0.93
Payer	MediCal	1,253	285,721	0.44	1	ref		2143	2,393,459	0.09	1	ref	
	Managed care	717	146,451	0.49	1.04	0.9	1.2	1206	1,575,020	0.08	1.0	0.87	1.03
	Private insurance	394	99,073	0.40	0.9	0.8	1.03	770	1,070,160	0.07	0.9	0.84	1.02
	Self pay/uninsured	84	17,484	0.48	1.1	0.9	1.4	126	158,494	0.08	1.0	0.78	1.16
Race	Hispanic	1,106	261,623	0.42	0.9	0.79	0.98	2071	2,407,489	0.09	1.0	0.88	1.04
	African American	343	60,741	0.56	0.8	0.7	0.9	331	344,693	0.10	1.1	0.89	1.40
	Asian	168	54,688	0.31	0.7	0.6	0.8	344	523,109	0.07	0.9	0.72	1.09
	Non-Hispanic White	803	165,582	0.48	1	ref		1457	1,860,138	0.08	1	ref	
Prenatal visits	None	95	12,421	0.76	1.2	0.8	1.5	55	38,943	0.14	1.3	0.90	1.88
	1–3	204	27,506	0.74	1.1	0.9	1.3	88	87,750	0.10	1.1	0.83	1.38
	4–6	638	74,706	0.85	1.3	1.1	1.5	298	289,408	0.10	1.2	1.02	1.34
	7–10	734	185,521	0.39	1.1	0.96	1.2	1227	1,456,811	0.08	1.0	0.96	1.11

		Preterm						Term					
Risk Factors		**N (SQD CP)**	**N (No CP)**	**% (SQD CP)**	**OR (adj)**	**95% CI**		**N (SQD CP)**	**N (No CP)**	**% (SQD CP)**	**OR (adj)**	**95% CI**	
	11 or more	731	238,274	0.31	1	ref		2526	3,257,746	0.08	1	ref	
Multiples	No	2,187	514,184	0.42	1	ref		4228	5,183,422	0.08	1	ref	
	Yes	278	38,189	0.72	2.0	1.7	2.2	46	37,105	0.12	1.6	1.17	2.15

*SQD refers to spastic quadripalegic or dyskinetic CP; Total # of children with SQD CP=7242

Table 2

Adverse Intrapartum Events and Risk of Spastic Quadripalegic or Dyskinetic CP (SQD CP).

	All				Preterm					Term				
	No CP		SQD CP		No CP		SQD CP		P*	No CP		SQD CP		p*
	N	%	N	%	N	%	N	%		N	%	N	%	
Placental abruption	54,009	0.9	410	5.7	20,953	3.8	265	10.8	0.0001	28,149	0.5	101	2.4	0.0001
Uterine rupture during labor	3,855	0.06	54	0.8	398	0.07	6	0.2	0.02	3,217	0.06	44	1.0	0.0001
Fetal distress	471,279	7.7	1,426	19.7	47,214	8.6	507	20.6	0.0001	400,764	7.7	827	19.4	0.0001
Birth trauma	294,425	4.8	565	7.8	22,301	4.0	178	7.2	0.0001	257,164	4.9	348	8.1	0.0001
Cord prolapse	16,675	0.3	110	1.5	3,320	0.6	54	2.2	0.0001	12,184	0.2	49	1.2	0.0001
Mild to severe birth ashyxia	24,458	0.4	409	5.7	4,231	0.8	113	4.6	0.0001	18,598	0.4	269	6.3	0.0001
Any of the above 6 events	793,415	12.9	2,268	31.3	87,852	15.9	907	36.8	0.0001	663,136	12.7	1,208	28.3	0.0001

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