Racial Differences in the Use of Respiratory Medications in Premature Infants after Discharge from the Neonatal Intensive Care Unit

Scott A. Lorch, MD, MSCE, Kelly C. Wade, MD, PhD, Susan Bakewell-Sachs, RN, PhD, Barbara Medoff-Cooper, RN, PhD, Gabriel J. Escobar, MD, and Jeffrey H. Silber, MD, PhD

Objective To determine the effect of race and ethnicity on the use of oral beta-agonists, inhaled beta-agonists, and inhaled corticosteroids to treat respiratory symptoms in former premature infants after controlling for medical conditions, socioeconomic status, and site of outpatient care.

Study design Using a population cohort of infants born at a gestational age ≤34 weeks at 5 Northern California Kaiser Permanente hospitals between 1998 and 2001 (n = 1436), we constructed multivariable models to determine predictive factors for the receipt of respiratory medications during the first year after discharge.

Results After controlling for confounding factors, black infants were more likely to receive oral beta-agonists compared with white infants (OR 4.30, 95% CI 2.33-7.94), and Hispanic infants were less likely to receive inhaled beta-agonists (OR 0.62, 95% CI 0.39-0.99) or inhaled corticosteroids (OR 0.28, 95% CI 0.12-0.67). These findings were not explained by more outpatient visits for respiratory symptoms in black or Hispanic infants, because the observed racial differences persisted when children of similar respiratory symptoms were examined.

Conclusions Even in a high-risk population of insured infants, substantial racial differences persist in the use of respiratory medications that could not be explained by differences in respiratory symptoms. *(J Pediatr 2007;151:604-10)*

Although several studies have shown a 4- to 5-fold increase in the prevalence of reactive airways disease among black infants,[1,2] the role of race in the management of respiratory disease is less certain. Although some studies have found increased hospitalization and mortality rates from reactive airways disease in black adult patients,[2-4] other studies have explained these disparities by differences in socioeconomic status[5] or access to asthma management plans.[6]

Less information is available about racial differences in the management of reactive airways disease in premature infants. Extreme prematurity often results in respiratory complications such as bronchopulmonary dysplasia (BPD), although even moderate prematurity results in the need for supplemental oxygen during the first weeks after delivery. However, there have only been a few studies of premature infants to determine risk factors for asthma within this specific population.[7-10] None of these studies examined racial differences in the management of respiratory symptoms, particularly in the first year of life. Studies in older children have found lower use of inhaled medications, such as $beta_2$-agonists and corticosteroids, in black infants,[11,12] Hispanic infants,[13,14] and children of lower socioeconomic status.[15] However, these studies focus on children with more severe diagnoses of asthma and did not examine the use of oral beta-agonists, which are frequently prescribed to younger children even though there is little supporting evidence for their use in children.[16-19]

The goals of this study were to determine whether premature infants with respiratory symptoms are treated differently by racial or ethnic status, and to assess whether coexisting medical or socioeconomic factors or a higher incidence of respiratory symptoms explain these differences. We hypothesized that medical conditions such as BPD or

BPD	Bronchopulmonary dysplasia	KPMCP	Kaiser Permanente Medical Care Program
CMIS	Cost Management Information System	NEC	Necrotizing enterocolitis
GA	Gestational age	NMDS	Neonatal Minimal Data Set
IFS	Infant Function Status Study	NICU	Neonatal intensive care unit
IVH	Intraventricular hemorrhage	ROP	Retinopathy of prematurity

From the Department of Pediatrics, Division of Neonatology (S.L., K.W.), the Center for Outcomes Research (S.L., J.S.), and the Department of Pediatrics and Anesthesia and Critical Care Medicine (J.S.), The Children's Hospital of Philadelphia, the Leonard Davis Institute (S.L., J.S.) and the School of Nursing (S.B., B.M.), University of Pennsylvania, Philadelphia, PA, the School of Nursing (S.B.), The College of New Jersey, Ewing, NJ, and the Division of Research, Northern California Kaiser Permanente Medical Program (G.E.), Oakland, CA.

Supported through a grant by the Maternal and Child Health Branch of the Health and Human Resources Services Administration (Grant no. 1 R40 MC05474-01-00).

Submitted for publication Oct 20, 2006; last revision received Mar 14, 2007; accepted Apr 20, 2007.

Reprint requests: Scott A. Lorch, MD, MSCE, Center for Outcomes Research, 3535 Market St, Suite 1029 Philadelphia, PA 19104. E-mail: lorch@email.chop.edu.

0022-3476/$ - see front matter

10.1016/j.jpeds.2007.04.052

younger gestational age would result in smaller racial and ethnic differences in prescription practices than previously reported. We also hypothesized that these differences would persist when we accounted for the number of visits for respiratory symptoms experienced by each child. To answer these questions, we will use inpatient and outpatient data from a large cohort of premature infants born at the Northern California Kaiser Permanente Medical Care Program (KPMCP) between 1998 and 2001.

METHODS

Study Population

The Infant Functional Status Study (IFS) examined premature births at KPMCP, which is a managed care organization with integrated information services whose perinatal outcomes have been described in a number of previous reports.[20-22] The goal of the IFS study was to define a physiological-based tool to assist in the appropriate discharge of an infant from the neonatal intensive care unit. Infants eligible for the IFS study were born at 5 KPMCP hospitals between 1998 and 2001 at a gestational age of 34 weeks or less. All infants had similar insurance coverage and access to care within the KPMCP system. Obstetricians assigned a gestational age (GA) on the basis of available ultrasound data and the date of the last menstrual period. All women with prenatal care in the KPMCP system underwent at least 1 prenatal ultrasound scan for dating. Exclusion criteria included major congenital anomalies, need for mechanical ventilation at home, placement of a ventriculoperitoneal shunt, or loss to follow-up within 1 year of discharge. This last exclusion criterion occurred when families either moved from the Northern California region or changed insurance plans. Approximately 20% of the eligible infants met one of these exclusion criteria. Eligible infants excluded from the IFS study were older and heavier at birth and more likely to be black or Hispanic than infants enrolled in the final IFS cohort. Between the 2 groups, similar percentages of infants required mechanical ventilation, and the average length of stay in the NICU was not statistically different. A total of 1436 infants were enrolled in the final cohort of the study: all 893 infants born at a GA of 32 weeks or less, and 543 randomly selected infants born at a GA between 33 and 34 weeks. The randomly selected infants were representative of all 33- and 34-week GA infants born within the KPMCP system. This project was approved by the Institutional Review Boards of both The Children's Hospital of Philadelphia and KPMCP.

Data Collection

The initial source for our data was the Kaiser Permanente Neonatal Minimum Data Set (NMDS), which tracks all NICU admissions in the KPMCP.[23] Because the KPMCP information systems use a common medical record number, we could link NMDS records to the KPMCP hospitalization database, the outpatient visit database, the pharmacy database, and the Kaiser Permanente Cost Management Information System (CMIS). The CMIS prospectively collects cost information on all KPMCP hospitalizations, outpatient visits, prescriptions, laboratory tests, and radiologic procedures used by each infant. The less than 1% of encounters with the medical system that occurred outside the health plan were also included in our data collection.

Use of oral beta-agonists, inhaled beta-agonists, and inhaled corticosteroids was identified in the CMIS from prescriptions filled by each infant during the first year after discharge from the NICU. There were no set guidelines for the use of respiratory medications in this patient population at KPMCP during the time frame of the study. We identified outpatient and inpatient visits for wheezing, asthma, reactive airway disease, bronchiolitis, or other respiratory symptoms with the following ICD-9-CM codes in the principal or secondary diagnosis list: 493.x and 786.07.

Variable and Outcome Definitions

Predictive factors. We defined BPD as the need for supplemental oxygen support at 36 weeks postmenstrual age,[24] a patent ductus arteriosus from echocardiographic evidence, and retinopathy of prematurity (ROP) by the most severe disease stage by accepted criteria.[25] Necrotizing enterocolitis (NEC) was defined as stage IIA or worse disease by Bell's criteria, and intraventricular hemorrhage (IVH) was defined by the most severe grade on head ultrasonography.[26] Use of home oxygen was included in infants with BPD. We classified race and ethnicity as Asian, black, Hispanic, white, or other/unknown on the basis of maternal information collected in the NMDS. The number of previous children was used as a proxy for the number of siblings currently in the household, because no information was available about the actual number of other children residing in the household during the year after discharge of the premature infant. As household information on income during the year of the study was not available, we used the median household income of the home zip code of the family as a proxy measure.[27]

Designation of outpatient facility. We assigned a primary outpatient facility for each premature infant with the following algorithm. We first assigned any facility that was used for a minimum of 50% of all well-child visits as the outpatient facility of that infant. Well-child visits were defined by use the ICD-9 code of "V201" or "V202" in any diagnosis code. With this rule, we identified the outpatient facility of 1392 infants. Of the remaining 45 patients, we assigned any facility that was used for a minimum of one 1 well-child visit and the majority of sick visits as the outpatient facility of the child. Twenty-three infants were linked with this rule. The remaining infants were assigned to the facility that was used for most sick visits without a well-child visit.

Controlling for ongoing respiratory severity. To help distinguish whether use of a specific medication resulted from more severe ongoing respiratory illness, we performed 2 analyses. First, we defined a separate subgroup of infants for each