OBSTETRICS

Racial and ethnic disparities in use of 17-alpha hydroxyprogesterone caproate for prevention of preterm birth

Lynn M. Yee, MD, MPH; Lilly Y. Liu, BA; Allie Sakowicz; Janelle R. Bolden, MD; Emily S. Miller, MD, MPH

BACKGROUND: Racial/ethnic disparities in preterm birth remain a major public health challenge in the United States. While 17-alpha hydroxyprogesterone caproate (17OHP-C) is recommended for preterm birth prevention in women with a prior preterm birth, non-Hispanic black women continue to experience higher rates of recurrent preterm birth than white women receiving the same treatment. Further investigation of disparities in 17OHP-C use and adherence is warranted.

OBJECTIVE: We sought to evaluate whether racial and ethnic disparities exist in the use of and adherence to 17OHP-C within a population of eligible women.

STUDY DESIGN: This was a retrospective cohort study of women with a prior spontaneous, singleton preterm birth who were eligible for 17OHP-C for preterm birth prevention and received care at a single institution from 2010 through 2014. Associations between self-identified race/ethnicity (non-Hispanic black vs women in all other racial/ethnic groups) and documented counseling about 17OHP-C, receipt of any 17OHP-C, and adherence to 17OHP-C administration were each estimated by bivariable analysis and multivariable logistic regression. Adherence to 17OHP-C was defined as not >1 missed dose, initiation <20 weeks' gestational age, and continuation until 37 weeks or delivery.

RESULTS: Of 472 women who were clinically eligible for 17OHP-C, 72% (N = 296) had documented 17OHP-C counseling and 48.9% (N = 229) received 17OHP-C. There were no differences in likelihood of 17OHP-C counseling or receipt of 17OHP-C based on race/ethnicity. While overall 83% (N = 176) of women were adherent to 17OHP-C, only 70% (N = 58) of non-Hispanic black women were adherent, compared to 91% (N = 118) of all other women ($P < .001$). Non-Hispanic black women had more missed doses (2.4 vs 0.4 doses, $P < .001$) and later initiation of care (12.0 vs 10.2 weeks, $P < .001$) than women in other racial/ethnic groups. After adjustment for potential confounders, non-Hispanic black women were significantly less likely to be adherent to 17OHP-C (adjusted odds ratio, 0.16; 95% confidence interval, 0.04—0.65). A significant interaction between non-Hispanic black race/ethnicity and public insurance was identified (adjusted odds ratio, 0.16; 95% confidence interval, 0.05—0.52).

CONCLUSION: In a diverse cohort of women eligible for preterm birth prevention, non-Hispanic black women are at an increased risk of nonadherence to 17OHP-C. Non-Hispanic black women with public insurance are at a particularly increased risk of nonadherence.

Key words: 17-alpha hydroxyprogesterone caproate, adherence, disparities, health services, preterm birth, preterm birth prevention, racial disparities

Introduction

Reducing racial/ethnic disparities in rates of preterm birth in the United States has been a major public health challenge. In the United States, non-Hispanic black women face disproportionately greater rates of preterm birth than women in other racial and ethnic groups, with rates as high as 16-18% compared to 5-9% in a white population.[1,2] Moreover, non-Hispanic black women are significantly more likely to experience recurrent or very early preterm birth than women in other groups.[2] This cycle of reproductive disadvantage has contributed to widening disparities in health outcomes between racial/ethnic minority and majority groups in the United States.

The use of 17-alpha hydroxyprogesterone caproate (17OHP-C) has become a hallmark of preterm birth prevention in contemporary obstetrics.[3] The American College of Obstetricians and Gynecologists (ACOG) guidelines on prevention of preterm birth recommend initiation of progesterone between 16 0/7 and 20 6/7 weeks for women with a prior preterm birth.[1] However, not all eligible women receive 17OHP-C; early data suggested <60% of eligible women were offered 17OHP-C.[4] More recently, Turitz et al[5] demonstrated that in a population of women eligible for 17OHP-C, women who additionally had prior term births, for example, were less likely to utilize 17OHP-C, whereas women with prior second-trimester losses were more likely to initiate 17OHP-C. Reasons for failure to appropriately utilize 17OHP-C are myriad and have been hypothesized to include patient-, provider-, and systems-level barriers.[5]

Beyond initial uptake of 17OHP-C, adherence to recommended therapy is clinically challenged by the need for weekly intramuscular injections. The 17OHP-C protocol requires either frequent visits to a health care setting or training for and insurance coverage of a home-based injection delivery process. These requirements have been hypothesized to be reasons for nonadherence to 17OHP-C therapy.[6,7] Prior work in community settings and managed care patients suggests this limitation both interferes with initiation

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of 17OHP-C within the recommended time period and contributes to injections discontinued prematurely for reasons other than delivery or reaching term.[6,7] Women who discontinued 17OHP-C prior to delivery or 37 weeks were more likely to be older and non-Hispanic black, suggesting nonmedical factors may be underlying explanations for reported adherence challenges.[7] Differences in adherence to 17OHP-C appear to be associated with clinical outcomes, such as differences in rates of recurrent preterm birth and neonatal intensive care unit admission.[8,9]

Importantly, non-Hispanic black women prescribed 17OHP-C continue to experience higher rates of recurrent preterm birth than white women receiving the same treatment.[10] Yet, these racial/ethnic differences have not been fully explored in diverse US populations, and a number of questions about prematurity-related health disparities remain. Thus, the objective was to examine 17OHP-C use from a health services perspective, and to identify if race/ethnicity was independently associated with counseling about, receipt of, or adherence to a 17OHP-C regimen for preterm birth prevention.

Materials and Methods

This is a single-institution, retrospective cohort study of women eligible for 17OHP-C for preterm birth prevention. Women age $\geq$18 years with a current singleton gestation and prior spontaneous preterm birth (<37 weeks' gestational age) of a singleton gestation who delivered at our institution and had available medical records were included. Women were included regardless of timing of entry to prenatal care. Standard practice at our institution during the study period was to recommend weekly 17OHP-C for any woman with a current singleton gestation and a prior spontaneous preterm birth of a singleton between 20-37 weeks' gestational age. At our institution, women in 3 large practices had complete electronic medical records, including details of 17OHP-C administration, available for comprehensive review. All women eligible for 17OHP-C, including those who received 17OHP-C via home administration, were included in the analyses of 17OHP-C counseling and receipt. Women were excluded from the analysis of adherence if they were known to have received 17OHP-C but did not have medication administration records available for review, such as those who may have received home 17OHP-C administration with unobtainable records. Institutional review board approval from Northwestern University was obtained prior to initiation of the study.

After identification of eligible records from an institutional electronic database, all deliveries meeting criteria from January 2010 through November 2014 were reviewed. This time period was chosen to include the complete time period in which the 3 major practices with available records had been comprehensively recording 17OHP-C use in the electronic medical record. The sample size was fixed and included all women eligible for 17OHP-C use in our institutional system in the complete time period for which records were available.

Three main aspects of 17OHP-C use were each investigated separately: documented counseling about 17OHP-C, receipt of 17OHP-C, and adherence to 17OHP-C. Patients were considered to have been counseled if the medical record contained written documentation of a discussion about 17OHP-C use, regardless of whether initiation of 17OHP-C occurred. Receipt of 17OHP-C was considered to have occurred if the patient was prescribed 17OHP-C and received at least 1 injection documented in the medical record. For adherence, an a priori adherence definition that incorporated the original Meis et al[3] trial protocol and the Society for Maternal-Fetal Medicine (SMFM) recommendations[11] for 17OHP-C initiation and continuation was chosen, requiring initiation <20 completed weeks gestation and continuation until 37 weeks gestation or delivery. Adherence to 17OHP-C protocols additionally required not more than 1 missed dose to allow for near-perfect adherence scenarios in which 1 missed dose may not represent a pattern of nonadherence; a sensitivity analysis was additionally performed in which women who missed any doses were considered nonadherent.

Maternal demographic and clinical characteristics were abstracted from the medical record. Race/ethnicity was self-reported and recorded in the medical record; race/ethnicity data were collected in as much detail as was in the record but were dichotomized as non-Hispanic black vs women in all other racial/ethnic groups due to small cell sizes. Other maternal demographic characteristics investigated included maternal age and insurance status. Clinical factors investigated included the intendedness of the pregnancy, number of prior preterm births (1 vs >1 prior preterm birth), presence of a prior term birth, gestational age at presentation to care, and gestational age at earliest preterm birth. Pregnancy intendedness was identified from the record of the prenatal intake visit at the initiation of prenatal care; if the record did not explicitly state that the pregnancy was intended or unintended, this information was considered missing.

We described patient characteristics stratified by 17OHP-C counseling, receipt, and adherence using χ^2 tests and Mann-Whitney U tests. Multivariable logistic regressions were used to investigate independent factors associated with 17OHP-C counseling, receipt, and adherence. The regression models accounted for factors with a P value $<.1$ in the bivariable analysis. In addition, given the overlapping domains of each of the outcome variables, each regression model accounted for factors with a P value $<.1$ in any of the bivariable analyses. Additional regression models were created to include the provider group as a random effect to account for any differences based on care provider group. Finally, based on the findings regarding non-Hispanic black race/ethnicity and insurance status, a post hoc decision was made to perform an analysis with an interaction term created to explore potential effect modification between non-Hispanic black race/ethnicity and public insurance. The regression models for 17OHP-C