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The effect of prenatal docosahexaenoic acid supplementation on infant outcomes in African American women living in low-income environments: A randomized, controlled trial

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ABSTRACT

Importance: African American women living in urban, low-income environments are at high risk for poor nutrition during pregnancy and birth complications.
Objective: To test the effectiveness of prenatal docosahexaenoic acid (DHA) supplementation on birth outcomes and infant development in a sample of African American women with Medicaid insurance and living in the city of Pittsburgh.
Design: The Nutrition and Pregnancy Study (NAPS) is a double-blind, randomized controlled trial of prenatal DHA supplementation conducted between 2012 and 2014.
Setting: Participants were recruited from obstetric clinics at the University of Pittsburgh Medical Center.
Participants: Sixty-four pregnant, African American women were enrolled at 16–21 weeks of gestation and randomized to either 450 mg/day of DHA (22:6n-3)(n = 43) or a soybean placebo (n = 21). Four women (6.3%) withdrew from the study: two participants from each study arm; complete data were obtained for 49 infants (76.5%) at the 3-month assessment.
Interventions: Supplementation with DHA or placebo continued from the beginning of enrollment through delivery.
Main outcome and measures: Data on birth outcomes were collected from medical records. At approximately 3 months post-partum, mothers brought their infants to the laboratory where the Bayley Scales of Infant Development (BSID-III) were administered and cortisol response to the Face-to-Face Still-Face (FFSF) paradigm was assessed.
Results: Infants of mothers who received DHA supplementation had higher birth weight (3.174 g versus 2.890 g) than infants of mothers receiving placebo (F [2.40] = 6.09, p = 0.018, *eta* = 0.36), and were more likely to have a 1-min Apgar score greater than 8 (*OR* = 5.99 [95% *CI* = 1.25–28.75], p = 0.025). Infants of mothers who received DHA compared with infants of mothers receiving placebo had lower levels of cortisol in response to the FFSF paradigm (F [1.32] = 5.36, p = 0.018, *eta* = 0.36). None of the scores on the BSID-III differed as a function of active supplement versus placebo.
Conclusions: Infants of women living in urban, low-income environments who received DHA supplementation had more optimal birth outcomes and more modulated cortisol response to a stressor. DHA supplementation may be effective in attenuating the negative effects of prenatal stress on offspring development.

1. Introduction

In the U.S., high levels of acute and chronic stress are found among families living in low-income environments; neighborhood disorder, lack of safety and exposure to violence are all significantly higher in areas with lower per capita income (Evans, 2003; Ewart and Suchday, 2002). More than a quarter of African Americans live in poverty (DeNavas-Walt and Proctor, 2015), and pregnant women living in poverty are at higher risk for poor nutrition (Fowles and Gabrielson, 2005), and are more likely to experience pregnancy and birth complications (Noble et al., 2007; Giscombé and Lobel, 2005).

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Maternal and child health disparities among African Americans in the U.S. may emerge in part from differences in maternal psychosocial stress during pregnancy. According to the prenatal programming hypothesis (Weinstock, 2008; Seckl and Holmes, 2007), chronic exposure to stress leads to suboptimal modulation of maternal stress response and consequently, exposure of the fetus to high levels of glucocorticoids released by the mother. This exposure affects the development of the fetal stress architecture in part by adjusting the threshold at which a stress response is activated, and interfering with the feedback mechanisms involved in maintaining homeostasis. Although the postpartum environment continues to affect brain development, for a substantial number of children this initial insult may set the stage for a developmental trajectory that begins with a poorly modulated response to stress during infancy. Identifying factors that can potentially interrupt this cycle has significant implications for public health.

Growing evidence from animal studies indicates that supplementation with polyunsaturated fatty acids (PUFAs), and with docosahexaenoic acid (DHA) specifically, improves maternal stress reactivity during pregnancy and protects neurodevelopment of the offspring, especially in the context of high levels of stress exposure (e.g., Feng et al., 2012; Pudell et al., 2014). DHA levels in human pregnancy are associated with immediate birth outcomes including birth weight, infant head circumference, and length of gestation (Carlson et al., 2013). An association between DHA consumption during pregnancy and later child developmental functioning also has been observed (Hibbeln et al., 2007; Kohlboeck et al., 2011). Among the few double-blinded, randomized controlled studies of DHA supplementation during pregnancy in humans, the results on offspring neurodevelopment have ranged from modest (Helland et al., 2003) to no effects (Makrides et al., 2010). One possible reason for the lack of consistent findings is that the effects of DHA supplementation may be most evident among vulnerable populations in terms high levels of stress exposure, and/or in terms of offspring functioning under conditions of stress. In the majority of experimental animal studies, effects of DHA supplementation on offspring functioning were observed under conditions of manipulated prenatal stress and/or manipulated stress exposure in the offspring as opposed to typical functioning (Keenan and Hipwell, 2015).

We recently completed a randomized controlled study of DHA supplementation in pregnant, African American women living in urban, low-income environments and observed significant differences in self-reported perceived stress and cortisol response to a controlled stressor at 30 weeks gestation (Keenan et al., 2014). In this report we extend those findings by testing the effects of prenatal DHA supplementation on birth outcomes and infant development at approximately 3 months of age in the same sample.

2. Methods

2.1. Study design

We conducted a double blind, randomized controlled trial (NCT01158976) evaluating the effects of prenatal fatty acid supplementation on infant outcomes in a sample of African American women living in urban, low-income environments in Pittsburgh, Pennsylvania from 2010 to 2012.

2.2. Eligibility and recruitment

Only demographically eligible women were approached for screening. Demographic eligibility included: Medicaid insurance or Medicaid eligible, African American race, age between 20 and 30 years, and 16–21 weeks of gestation. Women were recruited using two methods. First, research assistants attended obstetric clinics at the University of Pittsburgh Medical Center between 2010 and 2012 and provided fliers to patients that listed the demographic inclusion criteria, asking those eligible to complete the screening. Second, demographically eligible patients, identified through electronic medical records, were contacted by mail and phone to assess interest in the study. In person or telephone screenings of all demographically eligible patients were then conducted to assess whether sea fish consumption, an index of fatty acid intake, was less than 2 servings per week. Exclusion criteria consisted of known medical complications (gestational diabetes, pre-eclampsia), regular use of steroid medications, regular alcohol use, cigarettes or use of illegal substances (by maternal report), use of blood thinners or anti-coagulants, use of psychotropic medications, body mass index >40, and allergy to iodine and or soy.

2.3. Participants

One hundred forty-six women were screened for eligibility. Of those screened, 26 were ineligible, 64 were eligible and enrolled, 48 were eligible at time of screening but could not be enrolled prior to the enrollment window (i.e., 16–21 weeks of gestation), and 8 refused to participate (see Fig. 1). Participants were reimbursed on an accelerated schedule with $40 for their first visit and an increase in payments of $10 for each subsequent visit. The Institutional Review Board at the University of Chicago and the Human Research Protection Office at the University of Pittsburgh approved all study procedures.

2.4. Randomization

Once enrolled, women were randomly assigned on a 2:1 ratio to receive an omega-3 nutritional supplement (n = 43) or a soybean oil placebo (n = 21) beginning at enrollment and through the end of pregnancy. We expected greater variability in the dependent measures (e.g., stress reactivity) among the experimental participants than the control patients. Thus, in order to optimize power to test the hypotheses, we enrolled a higher number of participants in the experimental group to adequately capture that variability.

The pharmacist at the University of Pittsburgh carried out a computer generated random assignment of identification (ID) numbers to active supplement or placebo in blocks of 18: six ID numbers were assigned to group A (placebo) and the remaining 12 were assigned equally to either group B or C, both of which received identical doses of active supplement. This approach allowed the pharmacist to randomize on a 2:1 ratio without having the unbalanced design break the blind. The pharmacist provided the staff with appropriate dosed bottles labeled with the ID and treatment letter (A, B or C), thus ensuring that participants and investigators were blinded to the groups to which the participants were assigned. Group assignment was not revealed until all data were collected after the 3-month follow-up.

2.5. Intervention and procedures

Women received supplements via two strawberry flavored gel capsules providing: 450 mg of DHA (22:6n-3); 40 mg of DPA (docospentaenoic acid, 22:5n-6 and 22:5n-3) and ETA (eicosatetranoic acid, 20:4n-6); 90 mg EPA (eicosapentaenoic acid, 20:5n-3); and 10 mg Vitamin E (d-alpha tocopherol), supplied by Nordic Naturals. The strawberry flavored placebo contained 990 mg of soybean oil, 16.5 mg Vitamin E (d-alpha tocopherol), and 10 mg of EPA and DHA for flavor matching purposes. The supplement and placebo were identical in size, color, and smell. Each participant received a 6-week supply. Research assistants contacted participants by phone 3 times per week to ask the time of day that the