Effect of Vitamin D3 Supplementation During Pregnancy on Risk of Persistent Wheeze in the Offspring: A Randomized Clinical Trial

IMPORTANCE: Observational studies have suggested that increased dietary vitamin D intake during pregnancy may protect against wheezing in the offspring, but the preventive effect of vitamin D supplementation to pregnant women is unknown. OBJECTIVE: To determine whether supplementation of vitamin D3 during the third trimester of pregnancy reduces the risk of persistent wheeze in the offspring. DESIGN, SETTING, AND PARTICIPANTS: A double-blind, single-center, randomized clinical trial conducted within the Copenhagen Prospective Studies on Asthma in Childhood 2010 cohort. Enrollment began March 2009 with a goal of 708 participants, but due to delayed ethical approval, only 623 women were recruited at 24 weeks of pregnancy. Follow-up of the children (N = 581) was completed when the youngest child reached age 3 years in March 2014. INTERVENTIONS Vitamin D3 (2400 IU/d; n = 315) or matching placebo tablets (n = 308) from pregnancy week 24 to 1 week postpartum. All women received 400 IU/d of vitamin D3 as part of usual pregnancy care. MAIN OUTCOMES AND MEASURES: Age at onset of persistent wheeze in the first 3 years of life. Secondary outcomes included number of episodes of troublesome lung symptoms, asthma, respiratory tract infections, and neonatal airway immunology. Adverse events were assessed. RESULTS: Of the 581 children, persistent wheeze was diagnosed during the first 3 years of life in 47 children (16%) in the vitamin D3 group and 57 children (20%) in the control group. Vitamin D3 supplementation was not associated with the risk of persistent wheeze, but the number of episodes of troublesome lung symptoms was reduced, and the airway immune profile was up-regulated (principal component analysis, P=.04). There was no effect on additional end points. Intrauterine death was observed in 1 fetus (<1%) in the vitamin D3 group vs 3 fetuses (1%) in the control group and congenital malformations in 17 neonates (5%) in the vitamin D3 group vs 23 neonates (8%) in the control group. CONCLUSIONS AND RELEVANCE: The use of 2800 IU/d of vitamin D3 during the third trimester of pregnancy compared with 400 IU/d did not result in a statistically significant reduced risk of persistent wheeze in the offspring through age 3 years. However, interpretation of the study is limited by a wide CI that includes a clinically important protective effect.