Effect of Vitamin D3 Supplementation During Pregnancy on Risk of Persistent Wheeze in the Offspring A Randomized Clinical Trial - DTU Orbit (11/11/2019)

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