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Pregnant Smokers May Reduce Harm Done to Baby's Lungs by Taking Vitamin C

ATS 2018, San Diego, CA – Women who are unable to quit [smoking during their pregnancy](#) may reduce the harm smoking does to their baby's lungs by taking vitamin C, according to a new randomized, controlled trial presented at the ATS 2018 International Conference.

In a previous study, the researchers reported that daily supplemental vitamin C in pregnant women who could not quit smoking improved their newborn's pulmonary function as measured by passive respiratory compliance and the time to peak tidal expiratory flow to expiratory time. At one year, the study also found that babies whose mothers took vitamin C were less likely to develop wheeze.

In the newest study, the researchers measured force expiratory flows (FEFs) at 3 and 12 months of babies born to 252 mothers who smoked. FEF measures the speed with which air can be forced out of the lung. The mothers who smoked were randomized to either receive 500 mg of supplemental vitamin C every day or a placebo in addition to the same prenatal vitamin. They were encouraged throughout their pregnancies to quit smoking. On average, the mothers in both arms of the study who could not quit smoked seven cigarettes a day.

“We performed FEFs in this study because they provide a more direct measurement of actual air way function, and are more predictive of future disease,” said lead study author Cynthia McEvoy, MD, professor of pediatrics, Division of Neonatology, at the Oregon Health & Science University School of Medicine and OHSU Doernbecher Children's Hospital. “Because infants are not cooperative at 3 and 12 months of age, we had to use sophisticated testing techniques to get these results, but they are similar to the results you would get when doing a [spirometry test](#).”

The researchers measured FEFs at three intervals defined by the percentage of air remaining in the lung during forced exhalation: FEF₇₅, FEF₂₅₋₇₅ and FEF₅₀. At three months, there was a statistically significant difference in lung function between the babies born to the two groups of women at the FEF₂₅₋₇₅ and FEF₅₀ intervals. At 12 months, there was a statistically significant difference in lung function between the two groups of babies at all three intervals.

The study did not find a significant difference between the two groups of babies in gestational age at delivery, delivery mode, incidence of prematurity or birthweight.

The researchers said that they are not certain why vitamin C has this protective effect on the lungs but are focusing on this question in continuing research. Study co-investigator Eliot Spindel, MD, PhD, professor of neuroscience, OHSU School of Medicine, speculates that it may “block the increased collagen deposition around the airways that has been shown in animal models of babies born after smoke/nicotine exposure during pregnancy, which likely makes the lungs and airways stiffer” and/or “prevent some of the epigenetic changes that contribute to the lifelong effects of in-utero tobacco exposure.”

The study will follow the children until they are six years old to see if vitamin C has a long-term effect on improving childhood respiratory health. The researchers are particularly interested in determining whether children born to mothers who took vitamin C supplements are less likely to develop [asthma](#), which is difficult to diagnose in the first year of life.

Despite the apparent benefits of vitamin C, Dr. McEvoy said, “getting women to quit smoking during pregnancy has to be priority one.” For those roughly 50 percent of pregnant smokers who will not, or cannot quit despite all efforts, quit smoking, vitamin C supplementation may be a simple and safe way to help their babies breathe better, she added.

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Abstract 7248

Improved Forced Expiratory Flows in Infants of Pregnant Smokers Randomized to Daily Vitamin C versus Placebo

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Rationale: We previously reported a randomized controlled trial demonstrating that daily supplemental vitamin C to pregnant smokers significantly improved their offspring's newborn pulmonary function tests (PFTs) (passive respiratory compliance and the time to peak tidal expiratory flow to expiratory time) and decreased the incidence of wheeze through 1 year of age (JAMA 2014; 311:2074-2081). In this subsequent trial, we hypothesized that infants of pregnant smokers randomized to vitamin C would have significantly increased infant forced expiratory flows (FEFs) as compared to placebo.

Methods: Women < 23 weeks of gestation with a singleton pregnancy unable to quit smoking were randomized to daily vitamin C (500 mg) or placebo through delivery. Both groups received the same prenatal vitamin. Smoking cessation was discussed throughout gestation. Fasting ascorbic acid and urine cotinine levels were measured. The primary outcome was FEFs at 3 months of age performed with the raised volume rapid thoracic compression technique (Viasys Jaeger BabyBody). Secondary outcomes included FEFs at 12 months of age. Analyses of the FEFs were done on intention to treat using mixed model analysis of covariance adjusting for design factors (site, gestational age [GA] at randomization) and covariates (length, race, age, sex).

Results: We randomized 252 pregnant smokers. Randomization balanced relevant covariates including: cigarettes/day at randomization (7 versus 7); GA at randomization (18.3 weeks in placebo vs 18.5 weeks in treated group). Both groups had comparable urine cotinine and ascorbic acid levels at randomization. At mid and late gestation, the vitamin C group had higher levels of ascorbic acid than the placebo group. Of the 243 infants at delivery, there was no significant effect of the intervention on delivery mode, birthweight, GA at delivery, or incidence

of prematurity. We completed FEFs in 225 infants at 3 months of age and 213 FEFs at 12 months. Infants of pregnant smokers randomized to vitamin C had higher FEFs (FEF₇₅, FEF₂₅₋₇₅, FEF₅₀) at 3 and 12 months of age compared to placebo. (Table).

Conclusion: These results expand our previous findings in newborns to demonstrate improved FEFs through 12 months of age after vitamin C supplementation to pregnant smokers. We speculate that vitamin C supplementation in pregnant women who cannot quit smoking may improve the pulmonary function *trajectory* of their offspring by blocking some of the effects of in- utero smoke on lung development. This cohort is in active follow-up through 5-6 years of age to study their PFT trajectory and development of asthma.

| Infant Pulmonary Function Tests | | | |
|--|---------------------------------------|---|---------|
| | Infants of placebo treated smokers | Infants of vitamin C treated smokers | p-value |
| 3 Month PFTs (n=225) | (n=111) | (n=114) | |
| White (%) | 88 (79.3) | 89 (78.1) | NS |
| Male (%) | 57 (51.4) | 59 (51.8) | NS |
| Age at PFT (wks) | 15.3 ± 3.0 | 15.3 ± 3.2 | NS |
| Length at PFT (cm) | 60.2 ± 2.9 | 60.2 ± 3.2 | NS |
| FEF ₇₅ (mL/sec) | 188.7 ± 66.4 | 200.7 ± 71.1 | 0.10 |
| FEF ₂₅₋₇₅ (mL/sec) | 365.8 ± 93.8 | 387.4 ± 98.1 | 0.04 |
| FEF ₅₀ (mL/sec) | 408.5 ± 94 | 436.7 ± 101.5 | 0.02 |
| 12 Month PFTS (n=213) | (n=105) | (n=108) | |
| Age at PFT (wks) | 51.5 ± 5.5 | 52.7 ± 5.7 | NS |
| Length at PFT (cm) | 73.9 ± 3.3 | 74.4 ± 3.2 | NS |
| FEF ₇₅ (mL/sec) | 324.0 ± 84.1 | 351.6 ± 71.7 | 0.03 |
| FEF ₂₅₋₇₅ (mL/sec) | 567.1 ± 117.1 | 609.0 ± 114.3 | 0.02 |
| FEF ₅₀ (mL/sec) | 616.1 ± 123.7 | 654.5 ± 128.3 | 0.05 |

Values are Mean ± SD.