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⊗ Vitamin C for Pregnant Smokers to Improve Infant Lung Function An Orange a Day Keeps the Respiriologist Away?

Despite the well-known detrimental health effects of cigarette smoking, rates of consumption remain high. Furthermore, rates of smoking are highest among women of childbearing age (20–24 yr), affecting one in six women. The risks of smoking during pregnancy include increased rates of miscarriage, prematurity, and low birth weight. Furthermore, the risks to the child from prenatal smoking extend well beyond the neonatal period and are known to include an increased risk of sudden infant death syndrome, low lung function, and lower respiratory tract infection (1). Despite these known risks, only one-quarter of women will quit prior to pregnancy and another 20% will quit during pregnancy (2), suggesting that many women are either not aware of the risks or are unable/unwilling to quit smoking.

The literature suggests that the prenatal period is a critical window for lung growth, which if altered has lifelong impacts. There is good evidence that prenatal cigarette smoking, and nicotine in particular, can directly impact the developing lung (1, 3–5) and that the resultant adverse effects last a lifetime (6, 7). Infant lung function studies have found reductions in flows ranging from 7% to 16% associated with prenatal smoking (4, 8, 9). In older children (school age), smoking during pregnancy was associated with a 6% decrease in expiratory flow rates (3). It is also likely that these early insults when compounded with later exposures lead to accelerated loss of lung function and early development of chronic obstructive pulmonary disease (6, 7, 10).

In this issue of the *Journal*, McEvoy and colleagues (pp. 1139–1147) suggest a possible strategy to mitigate the effects of smoking on the developing lung (11). They showed that maternal vitamin C supplementation for smoking mothers during the second and third trimesters improved 3-month infant lung function. Although at first glance the improvement in lung function may seem modest, the 6% improvement in flows is consistent with the expected difference seen due to smoking in previous studies. The authors also showed that infants of mothers who were homozygous for a polymorphism in the gene coding for nAChR (α -5 nicotinic acetylcholine receptor) had a greater response to the intervention when compared with heterozygotes or those who did not have the polymorphism. The precise mechanism of this protective effect of vitamin C is unclear but may be related to increased oxidative stress due to smoking, which may be counterbalanced by antioxidants such as vitamin C, and this relationship may be modified by nAChR. Animal models show that prenatal nicotine exposure increases α -7 nAChR expression, leading to dysanaptic lung growth (12, 13) and decreased elastin levels, and these effects are ameliorated by a prenatal vitamin C intervention.

This group has previously reported that vitamin C given to pregnant, smoking mothers resulted in a 10% improvement in tidal breathing measures (time to reach peak tidal expiratory flow as a proportion of total expiratory time and compliance of the respiratory system) shortly after birth, but by 1 year these differences were no longer sustained (14). In the current study, the lung function parameters reported are from forced expiratory maneuvers performed at 3–4 months of age. Although a possible mechanism may be the “waning” effect of the prenatal intervention, equally plausible is the notion that the methodology used in the current study is more sensitive to early or milder airway obstruction (15). It is tempting to conjecture that if the authors had used forced expiratory flows at 1 year, they may have been able to detect differences between the two groups.

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Whether these early improvements in flow due to the prenatal intervention are sustained or an ongoing postnatal intervention is required is unclear. Ongoing smoke exposure and therefore oxidative stress are likely to be common, and an isolated prenatal intervention may be augmented by continued vitamin C administration. Epidemiologic studies have shown an inverse association between concentrations of antioxidants such as vitamin C and reductions in all-cause mortality among patients with obstructive lung disease, most of whom were smokers (16). This supports the notion that ongoing vitamin C supplementation in individuals with dietary deficiency or genetic risk should be considered.

The Healthy People 2020 initiative articulated a comprehensive set of goals aimed at improving health and reducing disparity through knowledge awareness. However, the data for tobacco use defy the notion that knowledge alone can curb use. Women are taking up smoking in young adulthood at an alarming rate that is higher than that observed in men, and the reasons for smoking are different. Furthermore, addiction sets in quickly after exposure. Vitamin C is a practical, low-cost, and easily available therapeutic option to combat the oxidant effects of cigarette smoke in individuals who are unable to quit. However, the sobering reality is that those individuals who are at greatest risk are also the least likely to benefit. Current data from the CDC suggest that poor, young women have the highest smoking rates, are the least likely to quit during pregnancy, and have the lowest rates of prenatal care. Prenatal interventions in the second trimester are not likely to impact the vulnerable infants in this population. Thus, although this work is very interesting and may lead to an improved mechanistic understanding, more strategies will be needed to translate antenatal interventions into an efficacious therapy. Evidence suggests that the most effective way to curb smoking among young people is to increase legislation banning smoking, curbing advertisements to young people, and increasing the cost of cigarettes. Ultimately, the best way to protect infants from the effects of smoking remains abstinence from cigarettes. ■

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Padmaja Subbarao, M.D., M.Sc.
The Hospital for Sick Children
Toronto, Ontario, Canada

and

Department of Physiology
and
Dalla Lana School of Public Health
University of Toronto
Toronto, Ontario, Canada

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