E-cigarette use in reproductive-aged women and pregnancy: a rising health concern

As of December 2019, the Centers for Disease Control and Prevention and media have highlighted the sudden spike in cases of EVALI, a newly coined acronym meaning electronic-cigarette (e-cigarette) or vaping-associated lung injury, with >2,500 cases requiring hospitalization and >50 fatalities in the United States. These new data are concerning as e-cigarette use among reproductive-aged women appears to be steadily increasing. In addition, although 18%–25% of women quit once pregnant, many supplement or replace tobacco products with e-cigarette use. This has not proven to be effective.

Much is known regarding the adverse effects of smoking during pregnancy. This consists of increased obstetric and perinatal complications including preterm birth, premature rupture of membranes, placental abruption, and placenta previa (1), as well as a higher risk of intrauterine growth restriction. Each pack of cigarettes smoked during pregnancy decreases birth weight by an average of 2.8 g. Neonates also have an increased risk of necrotizing enterocolitis, sudden infant death syndrome, and an increased incidence of orofacial clefts, heart defects, limb reduction defects, clubfoot, craniosynostosis, gastroschisis, anal atresia, hernia, and cryptorchidism. In addition, abnormal behavioral and neurodevelopmental outcomes (i.e., global intelligence/academic performance, attention deficit/ hyperactivity disorder, externalizing behaviors, and future substance abuse) have been reported (2).

Less is known regarding reproductive function. However, an association between cigarette smoking and infertility has been established (3). Evidence suggests that smoking by women, even at one-half pack/day use, is linked with impaired fecundity, increased risk of spontaneous abortion and ectopic pregnancy, accelerated loss of reproductive function, advancement in the time until menopause by 1–4 years, risk of multiple gestation, and trisomy 21. Smokers have a higher mean basal follicle-stimulating hormone level and a lower antimüllerian hormone level. They also require nearly twice the number of in vitro fertilization attempts to conceive as nonsmokers. In addition, there is fair evidence that semen parameters are adversely impacted in smokers with men and women smokers displaying genetic alterations in sperm and oocytes, respectively. The effects are dose-dependent; although smoking has yet to be conclusively shown to reduce male factor fertility. The adverse effects of passive smoking have also been established with evidence that nonsmokers with excessive exposure to tobacco smoke may have reproductive consequences as important as those observed in smokers.

Despite the declining prevalence, almost 18% of all adults in the United States continue to smoke cigarettes while ignoring the known deleterious health and perinatal effects of smoking. Many are unfamiliar with the reproductive risks (3). As healthcare professionals offer various interventions, including behavior modification, group counseling, feedback, advice, and weaning nicotine with patches and gum, each have proven to be of limited effectiveness. Two nonnicotine Food and Drug Administration-approved smoking cessation agents are currently available—varenicline (pregnancy category C) and bupropion-sustained release (pregnancy category B). Each are considered first-line therapies for smoking cessation (3).

Alternatively, many smokers use e-cigarettes to supplement or replace tobacco products with the intention of quitting or reducing their smoking habit. This has not proven to be effective. E-cigarettes are battery-operated devices that vaporize nicotine for inhalation. Developed in 2004, they have become increasing popular due to advertising claims that market them as a safer alternative to tobacco cigarettes. From 2004 to 2016, e-cigarettes were not tested or approved by regulatory agencies (e.g., U.S. Food and Drug Administration, UK Medicines and Healthcare Products Regulatory Agency). As such, they were not federally required to display warning messages about possible smoking-related pregnancy complications.

Awareness of e-cigarettes among adults in the United States doubled between 2009 and 2010. The number of people who currently use e-cigarettes has increased from 0.3% (2010) to 6.8% (2013). In a recent online survey, nearly 65% of respondents view e-cigarettes as being safer than tobacco cigarettes, with approximately 75% switching to e-cigarettes when women learned that they were pregnant. Furthermore, some indicate that use has come at the direction of their healthcare provider (4).

At present evidence does not offer any assurance that e-cigarettes are less harmful than tobacco cigarettes during pregnancy (2). E-cigarette refill flavor fluids have been found to be cytotoxic to human embryonic stem cells (1). Trace levels of toxicants, including formaldehyde, acetaldehyde, nickel, and lead, are still present, albeit one to two orders of magnitude lower than in combustible tobacco products. Studies show that 21%–85% of nicotine present in cartridges can be vaporized by e-cigarettes, demonstrating significant amounts of nicotine delivery, which increases with user experience and is exacerbated by longer puff durations. In studies conducted on saliva cotinine (a nicotine metabolite) in e-cigarette users, where median use was 150 puffs/day, the mean cotinine level was 373 ng/mL (for reference, users of a 21-mg/day nicotine patch have cotinine levels of 167 ng/mL, whereas cigarette smokers have cotinine levels of 310 ng/mL). Thus one may argue that e-cigarette users actually may have higher nicotine levels compared with tobacco cigarette users based on their duration of use and experience.

Additional substances are also present in e-cigarette fluids that are untested for human pregnancy. Although research is sparse, there are reports on the effects of e-cigarettes on pregnancy initiation and second-generation fetal reproductive health in mice. Specifically, e-cigarette-exposed uteri exhibited disorganized implantation sites with hemorrhagic blood cells, delayed implantation, time to pregnancy, and fetal survival in comparison with sham-exposed implantation sites (normal morphology with surrounding

decidualized stromal cells). E-cigarette exposure in utero also resulted in decreased weight gain in women, reduced fertility in men, and lower offspring weight and number (5).

As the popularity and use of e-cigarettes steadily increases among reproductive-aged women, we must continue to find more effective ways to modify the smoking patterns of both sexes and encourage overall cessation of smoking, including e-cigarette devices, at least during attempted conception and subsequent pregnancy. Reproductive-aged women may switch to e-cigarettes to quit smoking, but our understanding of their impact on reproductive health and pregnancy remains inconclusive.

Physician awareness and knowledge also continues to be lacking. At present, <50% consistently screen their patients for noncombustible tobacco product use and >10% of obstetrician-gynecologists think that e-cigarettes have no adverse reproductive health effects. In addition to questioning the smoking habits of patients, it should also prompt expansion to include e-cigarette use and that of other non–nicotine-containing products, albeit in a nonjudgmental manner. Furthermore, it is imperative to continue ongoing research on the potential harmful effects of e-cigarettes on fetal, maternal, and paternal reproductive health, as well as to adequately educate patients and create a sense of urgency.

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