Marketing and Health Effects of Electronic Cigarette Use on Pregnancy

OBJECTIVES

1. To define the types of media exposure that impact future use of electronic cigarettes
2. To explain differences in media response when comparing pregnant and nonpregnant women
3. To describe behaviors, perceptions and beliefs regarding the use of e-cigs among pregnant women and women of childbearing age.
4. The describe the impact of prenatal tobacco and electronic cigarettes use on the immune response and level of dependency.

A Little Person sparked my research interest?

United States had one of the highest rates ranked 131st out of 184 countries

SIGNIFICANCE

- No use of nicotine is safe during pregnancy
- The ever use of ecigs was found to correlate with reported exposure to ecig advertising
- Uncontrolled ecig advertising has the ability to cause individual and population level harm

METHODS

- A secondary data analysis of a cross sectional survey including 201 women of childbearing age was used (Figure 1)
- Parent study was a multisite study conducted at two university affiliated clinics (rural and urban), that used quota sampling to ensure an appropriate sample of pregnant (101) and nonpregnant (100) women
- Inclusion criteria included women, ages 18-44 and recent or current use (within 3 months) of tobacco (conventional or ecigs)

Survey of media and marketing practices

- [Image of survey chart]

United States had one of the highest rates ranked 131st out of 184 countries

EXPOSURE TO MEDIA AND INTENTION TO USE ELECTRIC CIGARETTES

RESULTS

There is a significant relationship between media exposure and the influence of future intention to use ecigs among women of childbearing age. Significant correlations exist between type of media exposure and future intent to use ecigs including:

- magazine (p=0.018)
- social media (p=0.039)
- internet blogs (p=0.014)
- internet news (p=0.014)

No differences existed in media responses when comparing pregnant and nonpregnant women, nor when comparing women living in rural and urban sites.

DISCUSSION - CLINICAL IMPLICATIONS

Media and marketing exposures of ecigs to women of childbearing age influence future intention to use.

- magazines, social media, internet blogs, internet news, TV had the highest amount of exposure.

These data support the need for further assessment of how ecig advertising and targeting strategies influence use patterns.

These results highlight the need for counter media campaigns to report the direct and indirect health effects of prenatal nicotine exposure via electronic cigarettes.

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Provides need to assess for tobacco use, including novel products, at each healthcare visits while enforcing the message: no safe amount of tobacco during pregnancy.

SIGNIFICANCE

- Limited federal regulations
- Use and sales are growing at alarming rates among women of childbearing age, including pregnant women
- Perceptions of e-cig safety may increase use and/or promote dual use
- May be perceived as smoking cessation aid
- E-cigs contain nicotine and toxic chemicals posing significant health risk
E-CIG EXHALED CHEMICALS

Table 2 – Concentrations of selected chemicals in captured exhaled vapor

<table>
<thead>
<tr>
<th>Compound</th>
<th>Highest mg/mL</th>
<th>Higher mg/mL</th>
<th>Lowest Limit mg/mL</th>
<th>Safety Margin mg/mL</th>
<th>Safety Margin (percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,2-Propanediol (Propylene Glycol)</td>
<td>170.00</td>
<td>17.0</td>
<td>0.00</td>
<td>170</td>
<td></td>
</tr>
<tr>
<td>1,2-Propanol</td>
<td>4.57</td>
<td>0.47</td>
<td>0.05</td>
<td>4.58</td>
<td></td>
</tr>
<tr>
<td>Isopropyl alcohol (isopropyl acetate)</td>
<td>36</td>
<td>3.35</td>
<td>0.00</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Dihydroxyacetone</td>
<td>7</td>
<td>0.02</td>
<td>0.00</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Traces</td>
<td>&lt;</td>
<td>0.00003</td>
<td>0.00</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Nicotine</td>
<td>7</td>
<td>0.07</td>
<td>0.03</td>
<td>99.93</td>
<td></td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>&lt;</td>
<td>0.00009</td>
<td>0.00</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>&lt;</td>
<td>0.00009</td>
<td>0.00</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Propene</td>
<td>&lt;</td>
<td>0.00009</td>
<td>0.00</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

METHODS

• Eligibility criteria
  - Women age 18-44 years
  - English speaking
  - Self-report tobacco/ecig use in the past 12 months
  - Cross sectional study using quota sampling to recruit participants
  - Pregnant, n=101
  - Nonpregnant, n=99
  - 30 item survey
  - Likert scale

RESULTS

Total Sample Demographics (n=194)

<table>
<thead>
<tr>
<th>Age (n=200)</th>
<th>25.8 [5.8 R]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race/Ethnicity (n=180)</td>
<td></td>
</tr>
<tr>
<td>White/non-Hispanic</td>
<td>143 (78%)</td>
</tr>
<tr>
<td>Other</td>
<td>60 (32%)</td>
</tr>
<tr>
<td>Education (n=194)</td>
<td></td>
</tr>
<tr>
<td>College graduate</td>
<td>31 (16%)</td>
</tr>
<tr>
<td>Less than college graduate</td>
<td>163 (84%)</td>
</tr>
<tr>
<td>Pregnant (n=194)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>101 (52%)</td>
</tr>
<tr>
<td>No</td>
<td>93 (48%)</td>
</tr>
</tbody>
</table>

E-cig Ever Use and Current Use

Results Specific to Pregnancy Status

• Pregnant women are 64% less likely to be current e-cig users compared to non-pregnant women (p=0.02).

• Only 15% of pregnant women are current e-cig users, compared to 27% non-pregnant women.

• Pregnant women are more likely to perceive e-cigs as a greater health hazard.

• E-cig use was unrelated to race, education, income, employment or partner status.

CONCLUSIONS

• E-cig use is growing despite concerns about safety and dual use.

• Nearly all pregnant and non-pregnant e-cig users also smoke conventional cigarettes (dual users).

• Younger tobacco-using women were more likely to be current or ever e-cig users.
UK Focus Group Study of E-cigs

- Demographics (n=12)
  - 8 pregnant, 4 postpartum
  - 75% Caucasian
  - 58% single
  - Average household income <$9,999

- Methods:
  - Qualitative, descriptive study
  - Smoking in 3 months of pregnancy
  - Semi-structured interviews
  - Transcripts coded and analyzed with MAXQDA

Four Overarching Themes

1. Attraction to e-cigarette as a harm reduction strategy

2. Uncertainty about health effects of e-cigs

3. Ambivalence regarding product novelty

4. Behaviors reflected dual use and often complete relapse

1. Harm Reduction Strategy

According to one participant, “At the beginning of my pregnancy, I would only smoke like maybe 3 cigarettes at the most…and I went to Marlboro Lights…and then I completely just quit and picked up the e-cig.”

Perceptions:
- Not as threatening
- Cleaner
- Benefit of being just vapor

2. Uncertainty of Health Effects

“And now there’s like studies out that they’re [e-cigs] not as safe as they once thought so I just don’t even chance it anymore.”

Mixed messaging from healthcare providers:

“My sister did [use e-cigs] and her doctor told her not to use it at all. He said he would rather her smoke like a couple of cigarettes a day than use the e-cig.”

3. Ambivalence regarding Product Novelty

PROS:
- Flavors
- Ability to select nicotine dose
- Can conceal illicit substance use

CONS:
- Frustration with equipment
- Frustration with ‘not strong enough’
- Discomfort with use

4. Dual Use and Relapse

“I just lost the taste for e-cigs and stayed with the cigarette.”

“It made me quit for like a month or two but then I got to where I wanted an actual cigarette, and so I was like, just forget this and I’ll go back to a cigarette.”

“It [electric cigarettes] helped with the cravings…but after I had him [her son], I picked it [traditional cigarettes] right back up.”
CONCLUSIONS AND CLINICAL IMPLICATIONS

• Initially drawn to e-cigs as smoking cessation aid or healthier alternative
• Uncertainty of health implications complicated by inconsistent healthcare messaging
• Switching may occur during pregnancy, but participants report relapse in postpartum
• Clear messaging of effects of nicotine and evidence-based methods to prevent relapse are needed.
• Current NIDA R01 study to explore the impact of electronic cigarettes (e-cigs) on perinatal immune responsiveness and birth outcomes.

SIGNIFICANCE

• E-cigarettes use among pregnant women has increased
  • perceptions of e-cigs as a safer and healthier alternative
  • aid for smoking cessation
• Inflammation/infection is the primary biological risk factor for adverse perinatal outcome
• Pregnancy is an unique immunological state---a balance in immune response is needed to protect the fetus
• Deregulation of cytokines can lead to pregnancy complications, and unfavorable perinatal outcomes including preterm labor.

The Impact of Electronic Cigarette and Dual Use on Perinatal Immune Response in First Trimester

The objective of this study is to examine first trimester immune response of serum cytokines among pregnant women who use electronic cigarettes.

Concentrations of Cytokines in First Trimester by Smoking Status

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>NonSmoking (&lt;10/day)</th>
<th>Smoking &gt;10/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytokine</td>
<td>Interquartile Range</td>
<td>Interquartile Range</td>
</tr>
<tr>
<td>IL-10</td>
<td>2.12 (3.01)</td>
<td>1.40 (3.89)</td>
</tr>
<tr>
<td>IL-1α</td>
<td>765 (2682)</td>
<td>438.50 (1194)</td>
</tr>
<tr>
<td>IL-1β</td>
<td>11.80 (60.89)</td>
<td>23.65 (57.92)</td>
</tr>
<tr>
<td>IL-6</td>
<td>12.10 (74.20)</td>
<td>23.65 (57.92)</td>
</tr>
<tr>
<td>IL-8</td>
<td>12.10 (74.20)</td>
<td>23.65 (57.92)</td>
</tr>
<tr>
<td>TNFα</td>
<td>1.05 (3.98)</td>
<td>0.97 (1.17)</td>
</tr>
<tr>
<td>CRP</td>
<td>4.46 (18.83)</td>
<td>0.67 (32.63)</td>
</tr>
</tbody>
</table>

*Kruskal Wallis, p <.05

Linear Regression of Cervical IL-10 Concentration Among Women by Urine Cotinine

**SERUM IL-10 Results (n=115)**

Smoking status and obesity were significant predictors of first trimester IL-10.

Table 2: Multivariable regression model for first trimester serum IL-10 concentrations

<table>
<thead>
<tr>
<th>Model</th>
<th>df</th>
<th>F value</th>
<th>p value</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking Status</td>
<td>1</td>
<td>21.9</td>
<td>0.012</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>1</td>
<td>13.17</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>1</td>
<td>3.23</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1</td>
<td>1.31</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>1</td>
<td>0.25</td>
<td>0.61</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.001

*Second Trimester Serum IL-10 was significantly associated with Preterm Birth (p<.02)
CURRENT STUDY: METHODS

Design
- This was a preliminary analysis using quota sampling of an ongoing, prospective multi-center study of pregnant women.
- Participant eligibility included pregnant women in their first trimester, ages 18-44, who currently use e-cigarettes, conventional cigarettes, or both (dual use).
- Maternal serum was collected during the first trimester to measure the following cytokine levels: IL-1α, IL-1β, IL-2, IL-6, IL-8, IL-10, TNFα, CRP and MMP-8.

Sample Collection
- Blood was allowed to coagulate for 30 minutes, then spun at 1300xg for 10 minutes.
- Serum was transferred to 0.5mL cryotubes and stored at -80°C.
- Prior to analysis, samples were:
  - Thawed, vortexed, spun at 1300xg for 10 minutes,
  - Diluted 100-fold for CRP, 20-fold for MMP8, and 2-fold for cytokines.

DIFFERENCES IN INFLAMMATORY PROFILE

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Total sample</th>
<th>Conventional only</th>
<th>Dual user</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-1β</td>
<td>0.10 (0.09-0.13)</td>
<td>0.10 (0.09-0.13)</td>
<td>0.10 (0.09-0.13)</td>
<td>.00</td>
</tr>
<tr>
<td>IL-2</td>
<td>0.19 (0.14-0.28)</td>
<td>0.16 (0.19-0.26)</td>
<td>0.28 (0.18-0.31)</td>
<td>.10</td>
</tr>
<tr>
<td>IL-6</td>
<td>0.69 (0.51-1.44)</td>
<td>0.67 (0.52-1.36)</td>
<td>0.70 (0.55-1.50)</td>
<td>.07</td>
</tr>
<tr>
<td>IL-8</td>
<td>2.73 (2.23-3.55)</td>
<td>2.74 (2.38-3.96)</td>
<td>2.74 (2.00-2.85)</td>
<td>.80</td>
</tr>
<tr>
<td>TNFα</td>
<td>0.32 (0.26-0.54)</td>
<td>0.29 (0.25-0.54)</td>
<td>0.46 (0.42-0.49)</td>
<td>.05</td>
</tr>
<tr>
<td>CRP</td>
<td>0.32 (1.99-2.91)</td>
<td>0.42 (1.88-3.04)</td>
<td>2.21 (1.92-2.32)</td>
<td>.49</td>
</tr>
<tr>
<td>MMP-8</td>
<td>5.58 (14.65-420.43)</td>
<td>54.10 (17.41-102.28)</td>
<td>86.06 (26.3-134.65)</td>
<td>.32</td>
</tr>
<tr>
<td>CRP</td>
<td>1.18 (0.93-1.82)</td>
<td>0.78 (0.51-1.69)</td>
<td>1.65 (0.58-2.81)</td>
<td>.17</td>
</tr>
</tbody>
</table>

RESULTS

- Significant differences exist between conventional and dual users during the first trimester of pregnancy (p=0.004), yet no difference in the second trimester (p=0.58).
- Dependence score for the conventional-only = 0 vs. dual = 4.
- Some of the conventional cig only users have very little nicotine dependence according to their Fagerstrom scores.

SAMPLE DEMOGRAPHICS (N=43)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Conventional only (n=39)</th>
<th>Dual user (n=4)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>28.8 (5.9)</td>
<td>28.2 (6.7)</td>
<td>.73</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>22 (71.0%)</td>
<td>6 (85.7%)</td>
<td>.61</td>
</tr>
<tr>
<td>Other</td>
<td>9 (29.0%)</td>
<td>3 (14.3%)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>6 (16.6%)</td>
<td>2 (25.0%)</td>
<td>.63</td>
</tr>
<tr>
<td>High school graduate</td>
<td>14 (48.6%)</td>
<td>4 (40.0%)</td>
<td></td>
</tr>
<tr>
<td>At least some college</td>
<td>11 (36.7%)</td>
<td>4 (40.0%)</td>
<td></td>
</tr>
<tr>
<td>Partnered status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partnered</td>
<td>9 (25.6%)</td>
<td>0 (0.0%)</td>
<td>.008</td>
</tr>
<tr>
<td>Non-partnered</td>
<td>21 (70.0%)</td>
<td>4 (100.0%)</td>
<td></td>
</tr>
<tr>
<td>Age started smoking</td>
<td>17.3 (4.1)</td>
<td>15.5 (5.1)</td>
<td>.22</td>
</tr>
</tbody>
</table>

CONCLUSIONS AND CLINICAL IMPLICATIONS

- This study is among the first to examine first trimester immune response and level of dependence in a population of conventional, e-cigarette and dual users.
- Most e-cigarette users in our population are also conventional users, resulting in dual use, and consistent with current literature.
- Pregnant women engaged in dual tobacco use appear to exhibit a heightened inflammatory milieu.
- Level of dependency was significantly higher in dual users when compared to conventional users in the first trimester of pregnancy.
- Further research to measure the impact of e-cigarettes on immune responsive and level of dependency across all trimesters is warranted.
Funding Acknowledgements

- R01DA040949-01, NIH/NIDA - Project: The impact of electronic cigarettes (e-cigs) on perinatal immune responsiveness and birth outcomes in Appalachia

- 5P20GM103538 Center for Biomedical Research Excellence (COBRE) - Project: Chronic Inflammation at Oral, Serum and Cervico-vaginal Mucosa Throughout Pregnancy

- University of Kentucky Office of Vice President of Research - Project: Electronic cigarette use behaviors, prevalence, and perceptions among women of childbearing age in Kentucky

- University of Kentucky Clinical and Translational Research Center KL2TR003171 - CTSA grant number NIH CTSA UL1TR000117

- Anthem Foundation - Project: Giving Infants and Families Tobacco-Free Starts (GIFTS)

QUESTIONS?