Exposure to Di-2-ethylhexyl phthalate (DEHP) and Infertility in Women, NHANES 2013-2016

Brittany Trnka, BS; Maya Polan, BS; Victoria Zigmont, MPH PhD

INTRODUCTION

Di-2-ethylhexyl phthalate (DEHP) exposure is widespread in the general population and previous research has suggested that it contains endocrine-disrupting properties that can adversely affect the reproductive health system. The objective of this study was to use the 2013-2016 National Health and Nutrition Examination Survey (NHANES) data to assess the potential association between DEHP exposure and infertility in women.

METHODS

Using a nationally representative, cross-sectional study design, we used multiple logistic regression to measure the association of urinary metabolites of DEHP with self-reported history of infertility among women. Four metabolites of DEHP were examined: mono(2-ethylhexyl)phthalate (MEHP), mono(2-ethyl-5-hydroxy-hexyl)phthalate (MEHHP), mono(2-ethyl-5-oxy-hexyl) phthalate (MEOH), and mono(2-ethyl-5-carboxy-pentyl)phthalate (MECPP). These metabolites were calculated into a molar sum of DEHP (∑DEHP) and split into quartiles for analysis.

RESULTS

After adjusting for age and race, ∑DEHP was associated with increased odds of infertility for the second quartile (AOR=2.35, 95%CI [1.24,4.44], p<0.01) and third quartile (AOR=2.83, 95%CI [1.57, 5.10], p<0.01) when compared to the first quartile (reference). The adjusted OR for the highest quartile of ∑DEHP found no association and it was not statistically significant (AOR=0.99, 95%CI [0.57, 1.73], p=0.98).

<table>
<thead>
<tr>
<th>Model</th>
<th>Infertility</th>
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<tbody>
<tr>
<td></td>
<td>Crude Model OR (95% CI)</td>
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<tr>
<td>Lowest Quartile</td>
<td>1.00 (Ref.)</td>
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<tr>
<td>Second Quartile</td>
<td>2.232 (1.211, 4.414)*</td>
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<tr>
<td>Third Quartile</td>
<td>2.861 (1.70, 4.875)*</td>
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<tr>
<td>Highest Quartile</td>
<td>1.011 (0.576, 1.775)</td>
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<td>Three Highest Quartiles vs. Lowest Quartile</td>
<td>2.045 (1.22, 3.409)*</td>
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</tbody>
</table>

*Adjusted for age and race/ethnicity.  
* Indicates significant p < 0.05.

DISCUSSION

- Due to the temporality of our phthalate exposure and the complexity of infertility, research on this topic is scarce and findings are conflicting.
- There are biological sound explanations for the weaker association with infertility in the highest quartile of ∑DEHP, such as receptor desensitization and metabolic modulation. However, the examination of these biological phenomena are beyond the scope of this analysis.
- Moreover, participants in the highest quartile of ∑DEHP may have extremely high levels of DEHP exposure due to outlier events that are not reflective of their daily exposure (such as exposure to medical devices containing DEHP due to a recent medical procedure) and therefore skew the data.

Strengths

- Large sample size and representativeness of women ages 20-44 living in the United States.
- To our knowledge, this study is one of the first population-based studies to examine the relationship of DEHP exposure and infertility.

CONCLUSIONS

Although there were observed positive associations for the second and third quartiles of ∑DEHP in relation to self-reported history of infertility, the highest quartile was found to have no statistically significant association with infertility. This is not strong evidence for an association between DEHP and infertility. The inconclusive findings of this study add to the already complex existing literature on phthalate exposure and infertility. These findings warrant further population-based cohort studies on phthalate exposure and their relationship to infertility in humans.