Child Health Research Institute
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Children's NEBRASKA

Comparative analysis of agrichemical mixtures in drinking water and birth defects in Nebraska

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Background: Nebraska residents rely on groundwater for agriculture production and human consumption. Many areas of Nebraska struggle with nitrate contamination but the presence of other agrichemicals in conjunction with nitrate is of growing concern.

Significance of the problem: Nebraska birth defect rates are approximately two times higher than the U.S. rate of 1 in every 33 births. Exposure to pesticides and nitrate in drinking water have been suggested as risk factors for birth defects but study results are inconsistent.

Hypothesis: We hypothesized that exposure to agrichemical mixtures through drinking water has a greater impact on fetal development than the single compounds.

Experimental design: To assess exposure, participants must have lived at the same residence for at least three years prior to conception. We examined maternal exposure to nitrate, nitrite and nitrosatable agrichemicals through household drinking water for 23 infants with birth defects and 19 unaffected control infants born during 2014-2015 and 2018-2019. Using data collected for the Birth Outcomes and Water study (www.bow.unl.edu), we constructed case/control tables for exposure/nonexposure to agricultural compounds, and calculated odds ratios and 95% confidence intervals to estimate the risk of birth defects.

Results: Mothers exposed to nitrite were 3.6 times more likely to have a child with a birth defect (95% CI, 1.1-13.5) than nonexposed mothers. Exposure to co-occurring nitrite and atrazine increased birth defect risk by 4-fold (95% CI, 1.1-16.2). Concurrent exposure to nitrite and alachlor ESA increased risk for birth defects nearly 5-fold (95% CI, 1.2-21.4), and exposure to the combination of nitrite and alachlor OA was associated with a 6.5-fold increased risk for birth defects (95% CI, 1.3-35.1). No significant association was observed between birth defect risk and exposure to nitrate ($p=0.7$) or atrazine as single compounds ($p=0.4$), or nitrate in combination with any nitrosatable agrichemical measured.

Conclusions: Our findings suggest that exposure to drinking water containing nitrite alone and in a mixture with atrazine, alachlor ESA or alachlor OA increases risk for adverse pregnancy outcomes. To our knowledge, this is the first study to evaluate individual exposure to nitrite and agrichemical mixtures in drinking water as risk factors for birth defects. A larger study is required for confirmation and to evaluate relationships between exposure and specific types of birth defects. Future studies should also consider gene-environment interactions by searching for polymorphisms in candidate genes such as N-nitrosamine metabolizers (NQO1, CYP450 2E1) and cytogenetic studies including chromosomal breakage and translocations.