PRESENTING AUTHOR'S NAME & RESEARCH TITLE

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Prenatal exposure to fipronil is associated with thyroid dysfunction and miRNA expression

PURPOSE/BACKGROUND

Fipronil is a widely used phenylpyrazole insecticide and has been reported to induce disturbed behavior and endocrine or reproductive dysfunction in animal models. Although the distribution and toxic effects of chronic exposure to fipronil in humans are still unclear, we recently showed that serum fipronil sulfone, a primary fipronil metabolite, placentally transfers to the fetus and causes adverse health outcomes in newborns using a birth cohort of parent-infant triads. However, the underlying mechanisms describing how prenatal fipronil exposure leads to thyroid dysfunction and the role of epigenetics have not yet been identified. Therefore, we (1) determined the effects of prenatal fipronil exposure on the expression of miRNAs in placenta tissues and (2) evaluated epigenetic alterations associated with prenatal fipronil exposure and their relationship to thyroid dysfunction in newborns.

MATERIALS & METHODS

Personal information (demographic, behavioral, clinical, and socioeconomic data), fipronil and fipronil sulfone levels, and biospecimens (placenta tissues) were utilized from the existing birth cohort of parent-infant triads in Korea. For this study, the expression of 800 miRNAs in thirty-nine placenta tissues was profiled using the nCounter Analysis System (Nanostring technologies). The expression of miRNAs relevant to infantile fipronil sulfone and thyroid hormones (T3, T4, free T3, free T4, and TSH) levels in cord blood were analyzed.

RESULTS

Among a total of 800 miRNAs, miR575, miR130a-3p, and miR6721-5p were significantly upregulated, and miR548a-5p, miR585-3p, miR615-3p, and miR370-3p were downregulated in response to fipronil sulfone levels in infantile cord blood after adjustment for maternal age, maternal pre-pregnant BMI, parity, smoking status (indirect smoking status for maternal level), parental education levels, and household income. Of these miRNAs, the downregulation of miR585-3p attributable to prenatal fipronil exposure was associated with a decrease in T3 hormone in newborns. The core functional network from prenatal fipronil exposure to decreased T3 was on the pathway through miR585-3p and its predicted endocrine-related target genes.

DISCUSSION/CONCLUSION

Our results suggest that epigenetic biomarkers for prenatal fipronil exposure and thyroid dysfunction provide mechanistic data to explain the T3 decrease in newborns and critical information for predicting the health effects of early-life fipronil exposure. However, further studies into the potential for miRNAs as informative biomarkers using a larger sample size are warranted.