Maternal perchlorate levels during pregnancy and offspring cognitive development: Data from the controlled antenatal thyroid screening study

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In relation to this presentation, I declare that there are no conflicts of interest.
Learning Objectives

• Understand why high maternal perchlorate levels might have a negative impact on childhood cognitive development.

• Aware of the nature of our observed relationship between higher perchlorate levels and IQ.

• Understand the implications arising from the impact of maternal iodine status, thyroid function and levothyroxine treatment on the relationship between maternal perchlorate levels on childhood IQ.
Introduction

• Cognitive development is dependent on an adequate supply of thyroid hormones in fetal life and childhood.

• Iodine is an integral component of thyroid hormones.

• Perchlorate decreases thyroidal iodine uptake.

• Exposure at low levels, is ubiquitous. No safe level has been identified.

Introduction

• The fetus and developing infant may be especially vulnerable to the effects of perchlorate due to their high thyroidal iodine turnover.

• We sought to determine if higher maternal perchlorate levels were associated with sub-optimal IQ in offspring.
Study Population

• Subset of 487 mother child pairs.

• Hypothyroid/hypothyroxinemic & mild iodine deficiency (median UIC 72 μg/liter)

• Urinary perchlorate measured at recruitment (12 weeks).

• 45% subsequently treated with levothyroxine.

• Offspring IQ measured at age 3.
Methods

• Logistic regression undertaken to assess the odds of offspring IQ in the lowest 10% (IQ <80) if maternal perchlorate levels were in the highest 10% (>10.89 μg/liter). Analyses were repeated for individuals with the highest tertile of perchlorate (>4.0 μg/liter).

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<thead>
<tr>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
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<tr>
<td>Crude</td>
<td>Maternal age</td>
<td>Model 2+</td>
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<td></td>
<td>Maternal smoking</td>
<td>Maternal TSH</td>
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<td>Maternal FT4</td>
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<td></td>
<td>Received T4</td>
<td>Maternal Iodine</td>
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<td>Age &amp; sex of child at IQ test</td>
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• Generalized ordered logistic estimates were used to identify if a proportional or non-proportional odds model best.
Urine perchlorate was detectable in all women with a median concentration of 2.58 μg/liter (95% CI 0.08 – 38.9 μg/liter).

Total IQ: OR = 3.14 (95% CI 1.37, 7.12) p= 0.006
Verbal IQ: OR = 3.14 (95% CI 1.42, 6.90) p= 0.005

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Total IQ  OR = 1.51 (95%CI 0.80, 2.82) p= 0.20
Verbal IQ OR = 1.82 (95%CI 1.00, 3.30) p= 0.05

Total IQ  OR = 1.36 (95%CI 0.72, 2.59) p= 0.34
Verbal IQ OR = 1.73 (95%CI 0.93, 3.20) p= 0.08
Further Analyses

- Offspring of mothers with perchlorate in the highest 10% were more likely to have IQ scores in the lowest decile. 
  \[ B = -1.80 \ (95\% CI \ -2.92, \ -0.68) \ p=0.002 \]
  Very strong evidence of non proportional odds \( p=<0.001 \).

- No evidence of an association between maternal urinary iodine : perchlorate ratio and odds of offspring IQ in the lowest 10%.
Limitations

• Observational data subject to residual confounding.

• Limited data on social class.

• Did not have neonatal or childhood thyroid function.

• Only spot samples of urinary iodine and perchlorate.
Conclusions

• First study to show higher maternal perchlorate levels were associated with lower offspring IQ using individual-level patient data.

• Negative impact of perchlorate levels more profound on verbal IQ than performance IQ. Greater impact on lower IQ.

• The lack of a protective effect of levothyroxine and lack of a substantial impact after adjusting for maternal thyroid and iodine status is intriguing.
Conclusions

• There may be a direct effect of perchlorate on the fetal thyroid gland which results in a negative impact on cognitive development.

• Alternatively maternal perchlorate exposure may be a proxy for neonatal perchlorate exposure.

• Pressing need for larger studies on the impact of perchlorate from the general pregnant population. Studies also needed to assess the impact of perchlorate levels in childhood on thyroid function and IQ.
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