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SYNOPSIS

Review of "Fluoride exposure and thyroid function among adults living in Canada: Effect modification by iodine status"

Article citation: Malin AJ, Riddell J, McCague H, Till C. Fluoride exposure and thyroid function among adults living in Canada: effect modification by iodine status. Environ Int. 2018;121(Part 1):667-74. Available from: www.sciencedirect.com/science/article/pii/S016041201830833X

Synopses are brief descriptions of original research articles and reviews such as those that appear in the evidence-based abstraction journals. Synopses may be evaluative, and are generally not written by the authors of the original work.

Key messages

- This article adds to knowledge about the relationship between thyroid stimulating hormone (TSH) levels, urinary iodine and urinary fluoride as found in a representative sample of Canadians from the Canadian Health Measures Survey (CHMS).
- This study, by Malin et al. specifically determined if urinary iodine status modifies the effect of fluoride exposure on thyroid stimulating hormone (TSH) levels among moderately to severely iodine deficient adults. Authors state that 1 mg/L increase in specific gravity adjusted urinary fluoride (UFSG) was associated with a 0.35 mIU/L increase in TSH (95% CI: 0.06, 0.64) among adults with iodine deficiency. These results are not clinically significant. The normal range for TSH, as given by the authors, is 0.55 – 4.78 mlU/L. An increase of 0.35 mIU/L in the average or 90th percentile would still be within the normal range.
- This study has some weaknesses in exposure assessment; for example, there is no information on other forms of fluoride exposure apart from water. Tap water fluoride concentrations for those in the study had a mean of 0.22 mg/L, the 10th percentile was 0.00 mg/L and the 90th percentile was 0.6 mg/L. Assessment of iodine exposure is not addressed.
- Single tailed p values were used for the interaction between urinary iodine and urinary fluoride. The use of 2 tail p-value is more justifiable. Additional studies that address these weaknesses would be helpful in clarifying interactions between iodine and fluoride on thyroid function.

Background

- Malin et al.'s article, based on Canadian data, was published online on October 10th 2018; the same day two other papers related to fluoride, one from Canada and one from Mexico were released. There were a number of media releases following these publications. Community water fluoridation has been a source of controversy in some communities. Health units have requested that Public Health Ontario provide a review of these studies to assist in addressing inquiries from the public, media and others.

Appraisal

Study Design

- This cross-sectional study used data from Cycle 3 (2012-2013) of the Canadian Health Measures Survey to assess whether the relationship between fluoride exposure and thyroid function is modified by iodine status among adults, age 18 and above. Fluoride and iodine levels were measured in urine samples. Thyroid gland functioning was assessed by serum levels of Thyroid Stimulating Hormone (TSH). (Reference range provided by the authors was 0.55 – 4.78 mIU/L.)

- The study population (2,671) was divided into two groups, one with moderate/severe iodine deficiency (urinary iodine levels ≤ 0.38 µmol/L) and the other without deficiency (urinary iodine levels > 0.38 and ≤ 2.37 µmol/L). Based on WHO criteria, authors appear to have grouped iodine more than adequate, adequate and mildly iodine deficient individuals together and contrasted them with those who have moderate and severe iodine deficiency.[1] The authors excluded individuals who were iodine excess.

Main findings

- The mean TSH among all individuals in the study was 1.79 mIU/L, 10th percentile, 0.79 mIU/L ; and 90th percentile, 2.87 mIU/L. Among iodine deficient adults, the mean TSH level was 1.66 mIU/L, the 10th percentile was 0.83 mIU/L and the 90th percentile, 2.41 mIU/L.

- The authors state that 1 mg/L increase in urinary fluoride corrected for specific gravity (UFSG)was associated with a 0.35 mIU/L increase in TSH (95% CI: 0.06, 0.64) among adults in the iodine deficiency group. No relationship was found between UFSG and TSH in adults in the non-iodine deficient group. These results do not seem to be clinically significant. The reference or normal range for TSH, as given by the authors, is 0.55 – 4.78 mIU/L. An increase of 0.35 mIU/L in the average or 90th percentile would still be within the normal range.

- Among adults in the iodine deficient group, mean urinary iodine was 0.25 µmol/L, the UFSG was 1.06 mg/L and tap water fluoride was 0.12 mg/L. Among adults in the non-iodine deficient group, mean urinary iodine was 0.99 µmol/L, the UFSG was 0.91 mg/L and tap water fluoride was 0.25 mg/L. It is evident that water is not the only source of fluoride exposure and iodine deficient adults might have been exposed to other sources of fluoride; however, information on other fluoride exposures, such as tooth paste, black tea, sea food, fluoride varnish, have not been collected or adjusted for. Sources of iodine exposure are not addressed. This is a major shortcoming as dietary sources including dairy products would be expected to be major

contributors. Consumers of dairy products (e.g. milk) may consume less tap water and vice versa producing an inverse relationship between urinary fluoride and urinary iodine.

Strengths

- The first Canadian study to assess if urinary iodine status modifies the effect of fluoride exposure on thyroid functioning.
- The study sample of 2,671 from the Canadian Health Measures Survey was population based and representative of Canadian population.
- The study used biomarkers for measuring both the exposure and the effect: urinary fluoride; urinary iodine; and serum TSH.
- Urinary fluoride concentrations were adjusted for specific gravity to account for variations in urine dilution.
- The inclusion and exclusion criteria were applied uniformly to all study participants.

Limitations

- Fluoride exposures apart from tap water were not considered in the study. Sources of iodine exposure and their potential effect on fluoride exposure were not considered.
- According to WHO guidelines, the authors appear to have grouped participants with mild iodine deficiency with those having adequate and more than adequate iodine intakes. Those with excess iodine intakes were excluded from the study.
- The interaction between UFSG and urinary iodine was significant (p=0.03, one tailed). A two tailed test of significance for the interaction may be more appropriate. The p values are influenced by the choice of a two tailed vs one tailed test.
- In the overall analysis UFSG was not a predictor of TSH. The increase in TSH associated with UFSG was confined to the group defined as iodine deficient by the authors.
- While some of the findings attain statistical significance, none of the findings appear to be of clinical significance.

Reliability

- The authors are from Mount Sinai, New York; and York University, Toronto.
- The 2016 impact factor for the Environmental International was 7.08.
- Authors reported that they had no conflicts of interest.
- This research was supported by funds to the Canadian Research Data Centre Network (CRDCN) from the Social Sciences and Humanities Research Council (SSHRC), the Canadian Institutes of Health Research (CIHR), the Canadian Foundation for Innovation (CFI), and Statistics Canada.
- Reporting issues:

- Iodine excess individuals were excluded from the study. According to WHO criteria, the authors appear to have grouped iodine more than adequate, adequate and mildly iodine deficient individuals together and contrasted them with those who have moderate and severe iodine deficiency.

Relevancy

None of the associations reported in the study appear to be clinically significant.

Ontario Applicability

The study was based on Canadian data, including study participants who resided in Ontario.

References

1. World Health Organization. Urinary iodine concentrations for determining iodine status in populations [Internet]. Geneva, Switzerland: World Health Organization; 2013 [cited 2019 Feb 8]. Available from: https://apps.who.int/iris/bitstream/handle/10665/85972/WHO_NMH_NHD_EPG_13.1_eng.pdf;jsessionid=44BC436B01A6BF89CF8359592A455CA4?sequence=1

Appendix A

Quality assessment tool sourced from: NIH National Heart Lung and Blood Institute. Study quality assessment tools: Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies [Internet]. Bethesda, MD: National Heart Lung and Blood Institute; 2018 [cited 2018 Oct 18]. Available from: www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools

Malin - Respones to criteria	**Yes**	**No**	**Other (CD, NR, NA)***
1. Was the research question or objective in this paper clearly stated?	X		
2. Was the study population clearly specified and defined?	X		
3. Was the participation rate of eligible persons at least 50%? (2950 of total surveyed were asked to provide sample, and 2671 provided sample = 90.5%)	X		
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	X		
5. Was a sample size justification, power description, or variance and effect estimates provided?	X		
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?		X	
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	X		
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	X		
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	X		
10. Was the exposure(s) assessed more than once over time?		X	
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	X		
12. Were the outcome assessors blinded to the exposure status of participants?			X – can't tell, no description

Malin - Respones to criteria	Yes	No	Other (CD, NR, NA)*
13. Was loss to follow-up after baseline 20% or less?			X – NA; cross-sectional
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		X	

Authors

Sonica Singhal, Scientist, Oral Health, Health Promotion Chronic Disease and Injury Prevention, Public Health Ontario

Elaina MacIntyre, Epidemiologist Specialist, Environmental and Occupational Health, Public Health Ontario

Contributors

Lennon Li, Biostatistical Specialist, Knowledge Services, Public Health Ontario.

Justin Thielman, Epidemiologist Lead, Health Promotion, Chronic Disease and Injury Prevention, Public Health Ontario.

Kara Watson, Senior Product Development Advisor, Health Promotion, Chronic Disease and Injury Prevention, Public Health Ontario.

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