

Status report

PFOA and adult thyroid disease in the mid-Ohio valley

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Background: There are a number of reports of studies of PFOA (or C8) in relation to thyroid hormones or thyroid disease among populations with low PFOA exposure levels or among workers with higher exposures, with contradictory results. There is one report of a significant positive association between PFOA levels and increased self-reported thyroid disease among a representative sample of US adults exposed to low background levels of PFOA. The C8 Science Panel has previously reported an association in a cross-sectional study between PFOA and thyroid disease in children based on a small number of cases in the mid-Ohio valley, but no association with thyroid hormones in children. Researchers at W. Virginia University have studied the same mid-Ohio valley adult population studied here, cross-sectionally, and found a positive association between PFOA blood levels and thyroid hormones. Here we report on thyroid disease incidence in a longitudinal (follow-up) study of a large adult population in the mid-Ohio valley exposed to relatively high levels of PFOA.

Methods: We have studied approximately 32,200 mid-Ohio valley residents exposed to PFOA in drinking water. Approximately 28,500 were community residents who participated a community survey during 2005-2006 (the C8 Health Project), while the remaining 3,700 were workers who worked in the DuPont plant (of whom about 1,800 also participated in the C8 Health Project). All subjects were interviewed during 2008-2011 regarding their medical history, including non-malignant thyroid disease. Participants reporting thyroid disease were asked to classify their thyroid disease by type (hypothyroidism, hyperthyroidism, goiter, Grave's disease, Hashimoto's disease, specified other), and to report their age at diagnosis and whether they had received medication for the disease. The analysis was restricted to subjects born during or after 1920, and thyroid disease occurrence was restricted to age 20 or older.

Self-reported thyroid disease was classified as 'functional' thyroid disease (disease potentially affecting thyroid function) after a review of the interview data. 'Functional' thyroid disease

included goiter, thyroiditis, hyperthyroidism, hypothyroidism, or a thyroid function problem of unknown type, but excluded nodules with no noted functional abnormality, cysts, tumors, thyroidectomy without one of the above listed, congenital thyroid anomalies, or thyroid disease without a reported type. People who reported thyroid disease that was not considered ‘functional’ disease were excluded from the analysis. Any thyroid disease, with data on age at diagnosis, was reported by 3900 subjects (12%), with a median age at diagnosis of 43; 3600 (90% of those reporting disease) were considered to have had ‘functional’ thyroid disease. Of these 3100 had a reported age at diagnosis in the eligible range, including 2000 with an initial functional diagnosis of hypothyroidism, and 700 with an initial functional diagnosis of hyperthyroidism, and 400 with other conditions or both types of conditions reported. There were about 5 times as many cases among women as men.

In addition, we sought medical records for all people who self-reported thyroid disease with medication, and who gave us consent to seek their records. We were able to obtain medical records for 64% of self-reported ‘functional’ thyroid disease, of which 91% were confirmed by the medical record. We conducted supplemental analyses limited to the validated cases. Exposure in our study was each person’s cumulative blood level of PFOA (yearly estimated levels summed over all years of exposure). Past blood levels were estimated based on air and water emission data from the DuPont plant over time, residential histories from subjects, and a model which predicted how much PFOA entered the drinking water and was then taken into the body. Predicted blood levels based on this exposure model were well correlated with observed measurements of PFOA blood levels among C8 Health Project participants in 2005-2006.

Primary analyses were restricted to ‘functional’ thyroid disease (hereafter simply called thyroid disease). We analyzed whether subjects with higher cumulative PFOA blood levels were more likely to report developing thyroid disease, compared with subjects with lower cumulative PFOA levels. Analyses controlled for age, year of birth, race, gender, education, smoking, and alcohol consumption. The average time of follow-up (after age 20) until the end of follow-up was 33 years.

Results

There was a positive trend of increasing thyroid disease with increasing cumulative blood levels that was statistically significant for women, and nearly significant for men and women combined. Analyses by categories of cumulative exposure showed that the ratios of rates for thyroid disease, by increasing decile of cumulative exposure (<42, ng/ml-years, 42-93, 94-127, 128-167, 168-238, 238-400, 401-821, 822-2,226, 2,227-6,028, 6,029+) versus the lowest decile (<42), were 1.00 (lowest) 1.04, 1.44, 1.34, 1.31, 1.26, 1.36, 1.33, 1.42, and 1.47 (highest decile) for women, and 1.00 (lowest decile) 0.89, 2.41, 1.35, 1.35, 1.50, 1.52, 1.72, 1.61, and 1.39 (highest decile) for men. These positive trends were statistically significant for women ($p=0.03$, trend test using the log of cumulative exposure) but not for men; the magnitude of association for men was similar to women, but results were based on smaller numbers of cases. In separating disease types, a significant positive trend was found only for hypothyroidism for women ($p=0.05$, log cumulative exposure).

Analyses restricted to validated cases of thyroid disease (based on medical records) were consistent with, and slightly stronger than, overall results. For women rate ratios for validated thyroid disease by decile of cumulative blood levels were 1.00 (lowest decile), 1.10, 1.46, 1.37, 1.56, 1.35, 1.65, 1.47, 1.65, and 1.65 (highest decile), which was a significant positive trend ($p=0.007$). For men they were 1.00 (lowest decile), 1.46, 3.65, 2.40, 2.32, 2.17, 2.39, 2.55, 2.37, and 2.15 (highest decile), a positive trend which was not statistically significant ($p=0.75$, based on the log of cumulative exposure). Again, a significant positive trend was found for hypothyroidism among women ($p=0.03$, log cumulative exposure), but not men.

Sub-analyses restricted to new thyroid disease occurring after the C8 Health Project in 2005-2006, i.e., in 2006-2008, again considering cumulative blood levels as the measure of exposure, were generally consistent with results of analyses using the entire follow-up period, although the number of cases was smaller and positive trends were not statistically significant.

Conclusions

Our data show a positive association between cumulative blood levels of PFOA and thyroid disease occurrence, using all cases or restricting to validated cases. Positive trends were

statistically significant only for women. The risk of disease increased above the lowest exposure categories, but then did not increase after that.