The inhibition of mercury absorption by dietary ethanol in humans: cross-sectional and case-control studies

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Background: Since the ingestion of mercury absorption by ethanol was serendipitously discovered in 1965, a limited number of small number studies with both animal and human subjects have reported results consistent with this finding.

Aims: To investigate this phenomenon in a large scale human study with low level Hg exposed dentists.

Methods: Data were collected for a sample of 1171 dentists, and both cross sectional and case-control methods were utilised to examine the data.

Results: Abstainers (n = 345) had significantly higher urinary mercury concentrations (HgU) than drinkers (n = 826): 5.4 µg/l v. 4.8 µg/l. Multiple linear regression showed a significant effect of ethanol dose on HgU after adjusting for potential confounders. A case-control analysis in which cases were defined as those individuals with urinary Hg concentrations of ≥15 µg/l (top 5%), and controls as those with concentrations of <1.0 µg/l (bottom 5%), showed a clear protective dose-response relation; there was a decreasing risk of being a “case” (having an HgU ≥15 µg/l) with increasing ethanol consumption. The significance of the adjusted model is p < 0.001, and the χ² test for trend across ethanol consumption categories in the adjusted model is p < 0.05, confirming the dose-response relation.

Conclusion: We believe that this straightforward investigation provides the first specific confirmation in a large scale human study of the inhibitory effect of ethanol on urinary mercury concentration, and by inference, on mercury absorption.

A larger scale human study comparing mercury exposed chloralkali workers (n = 89) to controls (n = 75) found no significant relation between between self reported alcohol intake and mercury levels in blood or urine. Alternatively, a study among Faroe Island residents which examined umbilical cord blood and the effect of maternal seafood diet on fetal exposure to lead, mercury, and selenium found a significant difference in cord blood mercury concentration between abstainers and ethanol drinkers, with abstainers having higher concentrations than alcohol users. This finding was considered by the authors to be epidemiological confirmation of the phenomenon of the previously described inhibition of mercury absorption by ethanol. A recent study of long term low level mercury exposed humans (n = 14) found that dosing with ethanol increased the mercury concentration in exhaled air, and that higher doses of ethanol resulted in higher mercury levels in exhaled air as well as a longer time to return to background levels.

Magos et al suggested from animal studies that the mechanism by which ingested ethanol inhibits the absorption of mercury vapour is most probably the inhibition of the oxidation of mercury, and that the site of this inhibition is not necessarily restricted to the blood. No significant alternative theories have been published to date, although a number of subsequent animal studies have presented the same conclusion.

The purpose of the current study was to examine the relation of self reported ethanol intake to recent mercury exposure as measured by urinary mercury concentration (HgU) among a large sample of low level occupationally exposed dentists.

METHODS

Subjects were recruited at a large dental professional meeting. Dentists are well known to experience low level mercury exposure through their use of elemental Hg in preparing and
placing dental amalgam. Unadjusted spot urine samples, which have been shown to provide reasonable estimates of 24 hour HgU concentrations for cross sectional studies10 11 as well as questionnaire data concerning practice, personal, and office characteristics were collected from 1171 dentists over a three day period. Urinary mercury concentrations were one of several laboratory tests offered to dentists attending a national professional dental meeting. The sample was comprised of all dentists at the meeting who electively chose to have a urinary mercury concentration performed. This sample did not significantly differ from all dentists nationally in age, gender, or duration of practice. Urinary mercury concentrations were determined on-site with a portable laboratory, using atomic absorption technique methods reported elsewhere.12 Samples are analysed within minutes of being collected. The detection limit is $\sim 0.3$ μg/l. Standards and recalibration of the process are run frequently throughout the assessment period. Mercury concentration results were immediately reported to the dentists, stored on a portable computer, and later entered into an SPSS database for subsequent analysis. Ethanol ingestion was self reported as average number of alcohol units (equivalent of 1 ounce of spirits) per week during the past year. Because certain vitamins may have an antioxidant effect, vitamin usage was surveyed, and included as a covariate in the analyses. Questionnaire data were entered by a data entry service at the University of Washington using double entry techniques to reduce error. Analyses were conducted using SPSS statistical software.

Subjects were initially categorised bivariately as either drinkers or abstainers, as in the above referenced Faroe Island study7 for analyses utilising the entire subject population. To further investigate the effects of ethanol on urinary Hg concentration, simple and multivariate linear regression analyses were performed on the total study population, and case-control (logistic regression) analyses were performed on a subset of the study population in which the cases were defined as those individuals with urinary Hg concentrations of $>15$ μg/l (= top 5%, n = 43), and controls as those with concentrations of $<1.0$ μg/l (= bottom 5%, n = 112).

RESULTS

Table 1 presents study population characteristics for the study population. Certain personal, professional, and practice characteristics such as number of years in practice, and number of accidental elemental mercury spills in office during the past year, have been shown to significantly influence urinary mercury concentration among dentists, and therefore were included as covariates in linear and logistic regression analyses.13 Table 1 also shows study population characteristics for the case and control groups in comparison to the overall study population. The substantially smaller percentage of females in this study (~8%) is due to the smaller percentage of females engaged in active dental practice in the USA (~14%). Female dentists are additionally underrepresented at professional meetings such as the one at which subjects were recruited, accounting for the slight underrepresentation of females in this study population.

A t test comparing urinary mercury concentrations between abstainers and drinkers in the total sample showed a significant difference in urinary mercury concentrations (two tailed p<0.05). Drinkers (n = 826) had a mean urinary Hg concentration of 4.8 μg/l (SD 6.3), while the mean for abstainers (n = 345) was 5.4 μg/l (SD 6.8).

We examined the ethanol dose per week for a dose-response relation with urinary Hg concentration using the questionnaire categories for self reported ethanol dose. Table 2 shows the results. Although the mean HgU does not exhibit a clear dose-response relation, the median, which exhibits a more clear relation, may provide more meaningful information as there are several outliers in the HgU data, which skews the distribution. Because of the distribution skew, we have used the log of the HgU for regression analyses in which we investigate the relations of HgU to ethanol dose. Simple linear regression of ethanol dose on HgU provided a model with a significance of p = 0.013, indicating that ethanol dose is an important predictor of HgU, even without adjustment for potential confounders. A multivariate model which also included the covariates previously shown to influence HgU in cross sectional studies of dentists,13 age, gender, number of accidental Hg spills in past year, number of amalgams in the dentist’s own mouth, number of years in practice, and level of vitamin use provided a model with a significance of p<0.001 for ethanol consumption, adjusted for these potential confounders, indicating that these covariates are additionally important in predicting HgU. In this model, after adjusting for the a priori covariates, the dose of ethanol was inversely related to HgU, with a significance of p = 0.02.

Case-control analyses were performed using logistic regression methods to examine the risk of having a urinary mercury concentration in the top of the distribution versus having one in the bottom of the distribution across categories of increasing ethanol consumption. Table 3 shows both the unadjusted and adjusted odds ratios. The reference category was set as that of abstainers, with an odds ratio of 1.0. In both unadjusted and adjusted analyses, a clear protective dose-response relation may be seen, with decreasing risk of being a “case” (having an HgU $>15$ μg/l) with increasing ethanol consumption. Although the relation appears clear in the unadjusted model, it is not statistically significant. The significance of the adjusted model is p<0.001, and the χ2 test for trend across ethanol consumption categories in the adjusted model is p<0.05, confirming the dose-response relation.

DISCUSSION

Prior animal and human studies have indicated that there is an inhibitory effect of ethanol on mercury absorption. To date, the only reported human evidence with a sizeable study population (n = 1023) is that from the Faroe Island study.7 This study, although involving a large study population, was...
only able to provide limited evidence of the relation, reporting that blood mercury levels were slightly lower if the mother had occasionally ingested alcoholic beverages. It should be noted that the primary exposure in this study population was to methyl mercury, which may have contributed to the limited effect detected.

Dentists provide a good study population in which to examine low level mercury exposure. In this case, we were able to obtain information and HgU samples for a large population in a well controlled study situation over a short study period. Although self report was used for many of the variables included in the analyses, the recall period was for only the past year, and the population is a well educated and scientifically motivated one. In our multivariate analyses, even after adjusting for factors known to influence HgU in dentists, we found clear evidence of the effect of ethanol on HgU. Because certain vitamins are antioxidants, we included the use of vitamins as a covariate, even though there is no good evidence to date that the antioxidant effects of certain vitamins produce an ethanol-like effect on mercury absorption. Although an alternative consideration might be the diuretic effect of ethanol producing a dilution of the Hg concentration with increasing ethanol dose, the clear inverse dose-response relation seen at even a small number of alcohol units per week (0–7), at levels where a diuretic effect on urinary concentration of Hg would be insignificant, would indicate that this possibility is not an important factor.

We believe that this straightforward investigation provides the first specific confirmation in a large scale human study of the inhibitory effect of ethanol on urinary mercury concentration, and by inference, on mercury absorption. Further research with human populations may further elucidate this probable antioxidant effect through examining the potential effect of antioxidant vitamin consumption on mercury absorption.

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