Gender dependent accumulation of dioxins in smokers

S Fierens, G Eppe, E De Pauw, A Bernard

Aims: To evaluate the contribution of tobacco smoking to dioxin accumulation.

Methods: Dioxin (17 PCDD/F) concentrations in fasting blood from 251 subjects (161 never smokers, 54 past smokers, and 36 current smokers) were quantified.

Results: Whereas serum dioxin concentrations of male smokers were on average 40% higher than those of non-smokers, in women, smoking was associated with significantly lower serum dioxin levels. A synergistic potentiation of dioxin metabolism by tobacco smoke in women is postulated to explain these paradoxical findings.

Conclusions: Current smoking is associated with gender dependent effects on dioxin body burden and is a potential source of confounding in human studies using blood dioxins as indicators of exposure.

Tobacco smoke contains a variety of polycyclic hydrocarbons, including dioxins (polychlorinated dibenzodioxins/dibenzo-furans). It has been estimated that smoking 20 cigarettes per day should lead to a dioxin intake almost equivalent to that from food (1–3 pg TEQ/kg bw/day), the major source of human exposure. However, studies that have measured dioxins in smokers did not find higher levels; some studies on breast milk even reported significantly lower values than in non-smokers. We show here that dioxin concentrations are affected by a gender-smoking interaction that could exert a confounding effect.

METHODS

Volunteers were recruited during a study conducted in order to estimate the environmental exposure to dioxins in different areas of Wallonia, Belgium. A total of 251 non-occupationally exposed participants, aged 21–80 years, were examined, including 36 current smokers, 54 past smokers (13 years on average since smoking cessation), and 161 never smokers. The proportions of subjects living within 2 km of an incinerator, the only environmental source found to affect dioxin body burden in this study, were not significantly different between the three smoking categories (33%, 37%, and 30% respectively; \( \chi^2 = 0.82; p = 0.66 \)). Information about smoking habits, dietary habits, anthropometric characteristics, residential history, and health status was obtained from a self-administered questionnaire. The volunteers provided approximately 200 ml of blood under fasting conditions in order to evaluate the body burden of dioxins. The seventeen 2,3,7,8-substituted polychlorinated dibenzodioxin/dibenzo-furan (PCDD/Fs) and four “dioxin-like” coplanar polychlorinated biphenyls (cPCBs no. 77, 81, 126, 169) congeners were quantified by gas chromatography-high resolution mass spectrometry (GC-HRMS) on the lipid fraction of serum. The results were reported per gram fat and expressed in toxic equivalents (TEQ).

RESULTS

When data from both sexes were combined, serum dioxin concentrations appeared virtually identical between current smokers, past smokers, and never smokers (geometric mean: 25.6, 25.6, and 25.7 pg TEQ/g fat, respectively; ANOVA: F = 0; p = 1). The analysis by gender, however, revealed that dioxin levels were significantly higher in male current smokers but lower in female current smokers (table 1). The same pattern of effects was observed with coplanar PCBs. Current smokers did not present any difference in age, body mass index (BMI), or animal fat intake, compared with never smokers, that could explain these discrepant variations, the decrease of dioxin levels observed in female smokers being on average associated with a higher animal fat intake. A stepwise multiple linear regression analysis testing possible predictors (smoking status, age, BMI, animal fat intake, residence around incinerator, fish or alcohol consumption, menopause, contraceptive pills, lactation) confirmed the increase of serum dioxin levels in male current smokers (partial \( r^2 = 0.038 \), slope = 0.14, \( p = 0.013 \)) and the decrease in female current smokers (\( r^2 = 0.043 \), slope = –0.14, \( p = 0.006 \)). As illustrated in fig 1, serum dioxin levels adjusted for age and other covariates were on average 39.4% higher in male current smokers and 27.5% lower in female current smokers than in the respective control groups of never smokers. A two way ANOVA on adjusted dioxin values showed a highly significant interaction between gender and smoking status (current smokers or not) (model: \( F = 5.81, p = 0.0008 \); interaction: \( F = 17.09, p < 0.0001 \)).

DISCUSSION

The increase in dioxin body burden observed in male current smokers is in accordance with their higher intake of dioxins as predicted from their smoking habits. That past smokers of both sexes present normal levels is not really surprising since they have stopped smoking on average 13 years ago, a time

Main messages

- Male smokers have higher serum dioxin levels than non-smokers, whereas female smokers have lower serum dioxin levels than non-smokers.
- Current smoking is a potential source of confounding in human studies using blood dioxins as indicator of exposure.

Policy implications

- When measuring blood dioxins as indicator of exposure in populations including current smokers, data from male and female smokers should be analysed separately.
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