Letter and Reply

Lead and CKD

Sir,

We have read with interest the article by Spector et al. [1] which showed that higher blood levels of lead were associated with lower estimated glomerular filtration rate (eGFR) levels and impaired kidney function (eGFR < 60 mL/min/1.73m²) in 3941 US adults participating in National Health and Nutrition Examination Survey (NHANES). This effect was particularly observed in subjects >60 years of age. We have recently performed an analysis to assess the relationship between exposure to background environmental lead concentrations and kidney function. To that end, data of individuals who participated in the Prevention of Renal and Vascular Endstage Disease (PREVEND) study, a prospective community-based cohort study, were used [2]. Topsoil lead concentration in the area of residence was used as a marker of environmental lead exposure. Measurement of topsoil lead was commissioned by the Groningen municipal council and performed prior to this study [3]. The end points for kidney function were estimated glomerular filtration rate (eGFR) [4] and decline of eGFR. The relationships between environmental lead exposure (expressed as milligram per kilogram topsoil) and eGFR (in mL/min/1.73m²) and kidney function decline were assessed using linear regression analyses and adjusted for age, sex, smoking habits and baseline eGFR.

All topsoil lead concentrations were well below the Dutch soil concentration limit (intervention value) for lead [mean (SD) lead 38.5 (28.5) mg/kg topsoil]. Lead concentrations were available for 8549 of the 8592 participants of the PREVEND study [49.9% male, mean (SD) age 49.8 (12.7) years, 95.5% Caucasian]. Mean eGFR at baseline was 80.6 mL/min/1.73m²/year. After adjustment, lead in environmental topsoil was not associated with level of eGFR [an hazard ratio (HR) 0.00 (~0.011 to 0.012)]. The association between environmental lead exposure and yearly decline in kidney function was not clinically relevant, although statistically significant [an HR 0.003 (0.002 to 0.005)]. Similar conclusions were reached when we confined our analyses to subjects >60 years of age. Therefore, we conclude that environmental exposure to background concentrations of lead is not a risk factor for reduced eGFR or accelerated decline in eGFR. These data, in combination with the NHANES data, may indicate that other environmental sources of lead, such as cigarette smoke, lead paint and industrial exposure, may be more important contributors to high-blood levels of lead, leading to reduced glomerular filtration rate [1].

CONFLICT OF INTEREST STATEMENT

None declared.

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Letter and Reply

Reply

Sir,

We thank the authors for their interest in our manuscript [1] and for considering the impact of exposure to environmental toxicants on kidney function. Studies with prospective data in large populations, such as the PREVEND study, are uncommon in nephrotoxicant research but of great value.

As their lead dose metric, Grootendorst et al. have utilized data on soil lead levels in the community in which study participants reside. Use of these existing data provides a cost-effective means to explore the impact of lead exposure on kidney function. In addition, an external exposure metric also avoids concerns regarding reverse causality which are often raised in kidney research using toxicants in blood or urine.

The proportion of overall lead exposure derived from soil is important in interpreting their results. As ambient lead levels have declined with leaded gasoline bans, soil lead has become a larger contributor to total lead exposure in the general population [2]. Lead in soil is absorbed across the gastrointestinal tract, although at low rates when ingested with food (<5%) [3]. The surface of vegetables can be contaminated by lead-containing soil; lead taken up into leafy plants or edible roots is another exposure pathway from lead in soil [4]. Studies in children have shown that soil lead contributes to blood lead levels [5, 6]. Although soil is a less important source of lead in adults, increased blood lead levels through soil contamination of house dust [7] and homegrown produce have been reported in adults [8]. A recent evaluation of lead in food identified cereals, vegetables and tap water as the most important current contributors to lead exposure in the general European population [9].

In considering the potential for residential soil to be a substantial source of lead in PREVEND participants, who are adults, a number of factors must be considered. These include mobility of the population, timing of lead measurements in topsoil compared to estimated glomerular filtration rate (eGFR) assessments and the extent to which the population utilizes small garden plots to grow produce, such as potatoes and leafy vegetables [9]. Interestingly, although soil lead was not associated with eGFR in a cross section, after adjustment, a 1 SD higher soil lead (28.5 mg/kg) was associated with an increase in eGFR of 0.09 mL/min/1.73 m²/year in a study in which the mean yearly change in eGFR was a decline of −0.45 mL/min/1.73 m²/year. Whether this finding is due to residual confounding, a biological mechanism, such as lead-related hyperfiltration [10, 11], or chance, is unknown. Ideally, the combination of measures of topsoil lead with established lead biomarkers, such as blood or bone lead, would have allowed for an evaluation of the contribution of soil lead to internal dose in the study population. Analysis of alternative outcome measures, such as the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) eGFR or glomerular filtration rate estimated with cystatin C, would also be of interest in this population with mean baseline eGFR well above 60 mL/min/1.73 m². Overall, we encourage researchers with access to high-quality datasets that include kidney outcomes to consider the impact of nephrotoxicants, such as lead, cadmium and arsenic, in their work.

CONFLICT OF INTEREST STATEMENT

None declared.

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