LETTERS TO THE EDITOR

Chelation Therapy for Kidney Transplant Recipients With Lead Exposure

To the Editor:

We read with interest the article of Sotomayor et al. According to the researchers, pretransplant plasma lead concentrations, which decrease after kidney transplantation, are associated with increased risk of late kidney allograft failure. The finding is useful and stimulating, as it carries the implication of potential chelation therapy for kidney transplant recipients with lead exposure. Nevertheless, there are several untapped issues associated with this observational study.

First, plasma specimens were used in the study for evaluation of body exposure to lead, cadmium, and arsenic. Plasma samples are suboptimal, and instead whole blood samples should be collected for analysis. A previous study confirmed that lead level in whole blood is the ideal marker to distinguish between patients with different mean levels. Sommar et al found that plasma lead performed well in those with high exposure, such as lead workers, but at low exposures plasma lead was inaccurate. Second, apart from lead, cadmium, and arsenic, the body burden of mercury should also be examined, as excess of mercury is also correlated with poorer kidney outcomes. Third, it is suggested newer hydrophilic dithiol chelators—for example, meso-2,3-dimercaptosuccinic acid (DMSA) or 2,3-dimercapto-propanesulphonate (DMPS)—be considered for kidney transplant recipients with confirmed lead exposure. In this regard, although a blood lead reference value of 10 μg/dL is commonly used in adults, no safe blood lead level has been recognized. Therefore, the harmful effects of lead at any detectible level should not be ignored.

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Article Information

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References


In Reply to "Chelation Therapy for Kidney Transplant Recipients With Lead Exposure"

We are grateful to Drs Ju-Shao Yen and Tzung-Hai Yen for their appraisal of our article. The authors suggest that plasma samples are suboptimal for body exposure evaluation compared to whole-blood samples, based on a study in which within- and between-variation of various lead biomarkers were compared using inductively coupled plasma mass spectrometry equipment introduced in 2001. Given the tremendous and still ongoing improvements in this field, the only valid conclusion of the study from Sommar et al is that total variance in whole-blood lead concentrations is largely attributable to inter-individual differences; in terms of plasma concentrations, the equipment that was used does not allow for valid conclusions that can be extended to more recent equipment. An equipment-independent way to judge between the use of plasma or whole-blood lead samples for body exposure evaluation would be to assess the longitudinal association of exposure with different health effects, but the work by Sommar et al did not address this question. Importantly, previous studies suggest a stronger correlation for plasma rather than whole-blood specimens, advocating for the use of the former. We previously argued that plasma concentrations of heavy metals reflect the fraction most freely available to form the ultrafiltrate to which kidney tubular epithelial cells are exposed, and which would be the source of toxicity. We now applied the same line of reasoning to lead exposure, like others did before. It should furthermore be underlined that we studied kidney transplant recipients rather than the general population. Our article discusses how the postransplant osteodystrophy common to transplant recipients may argue for use of plasma samples. Despite these considerations, we acknowledge that the question of which biomarker can best...
assess the prospective association with graft function decline still needs to be delineated and would be an interesting one to address.

Finally, while we previously found no evidence for a cross-sectional association between plasma mercury and kidney function, a potential prospective association cannot be excluded and likewise warrants further studies.

Camilo G. Sotomayor, MD, PhD, Daan J. Touw, PhD, and Stephan J.L. Bakker, MD, PhD, on behalf of the TransplantLines Investigators

**Article Information**

TransplantLines Investigators: A list of the members of this investigator group is provided in Sotomayor et al.2

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**References**


3. Sommar JN, Hedmer M, Lundh T, et al. Investigation of lead investigator group is provided in Sotomayor et al.2


**RESEARCH LETTERS**

**Clinical Factors and Adverse Kidney Outcomes in Children With Antineutrophil Cytoplasmic Antibody–Associated Glomerulonephritis**

To the Editor:

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides are rare disorders in childhood with a variable clinical presentation. Given ANCA vasculitides’ rarity, data informing clinical practice and treatment are mainly based on adult data. The purpose of this study was to characterize clinical characteristics of ANCA-associated glomerulonephritis (AAGN) in childhood to determine factors associated with adverse renal outcome and the requirement for kidney replacement therapy (KRT) across a global study population.

This was a retrospective cross-sectional international survey distributed through professional pediatric nephrology organizations from December 2019 to March 2020 intended to create a registry of children with AAGN to understand clinical practices. Through an online form, pediatric nephrologists entered demographic and clinical information on all children with AAGN in their center in a de-identified fashion. All centers were required to obtain their own institutional ethics or governance approval. Inclusion criteria were patients under 20 years at presentation who were diagnosed with AAGN in 2000-2019 and had kidney involvement. Data elements that were collected included baseline demographic data, clinical features at presentation, treatment received (maintenance and induction), and data on 3 clinical outcomes: requirement for KRT, serum creatinine concentration (Scr), and death. Specifically, nephrologists were asked to report the peak Scr and any requirement for KRT in the first 3 months after presentation during the induction treatment period. Nephrologists were also asked to report on the need for KRT and vital status at last known follow-up. Further methodological details are in Item S1.

Based on responses from 114 different clinicians, 337 children from 41 different countries were included in the final analysis. Median duration between initial presentation and last known follow-up was 26 (IQR, 11-57) months. Table S1 details baseline characteristics of included children. Table S2 shows the organ involvement at presentation across different clinical phenotypes. Table 1 shows the most frequent induction and maintenance treatments used in the entire cohort. A total of 113 children (34%) received plasma exchange at induction. Sixteen deaths were reported in this cohort (5% mortality), with a mean age at death of 13.7 ±5.7 years.

Table 2 characterizes the clinical factors and treatment according to KRT requirements at initial presentation and at last known follow-up. We found a high prevalence of adverse renal outcomes, with 40% of children requiring KRT at last known follow-up, slightly higher than previously published data.1-4 Children who did (vs did not)