American College of Medical Toxicology

ACMT Position Statement: Post-Chelator Challenge Urinary Metal Testing

Heavy metals, such as lead and mercury, are ubiquitous in the environment [1-4]. Exposure in human populations is constantly occurring, and detectable levels of lead and mercury are commonly found in blood and urine of individuals who have no clinical signs or symptoms of toxicity and may be considered background or reference values [1-5]. Although urine testing for various metals in an appropriate clinical context, using proper and validated methods, is common and accepted medical practice, the use of post-challenge (a.k.a., post-provocation) urine metal testing, wherein specimens are typically collected within 48 hours of chelation agent administration, is fraught with many misunderstandings, pitfalls and risks. The American College of Medical Toxicology issues this position statement in disapproval of the use of post-challenge urinary metal testing in clinical practice and the use of such test results as an indication for further administration of chelating agents.

In current evidence-based medical practice, urinary testing is commonly used in the biomonitoring of exposure to certain metals such as arsenic and inorganic mercury and the severity of their associated toxicity. It is accepted practice to conduct such testing, e.g., in exposed individuals with clinical evidence of peripheral neuropathy, as long as validated collection and analytical methods are employed prior to, or after, a sufficiently long time interval (e.g., 3-5 days) following administration of a chelating agent, i.e., applied to non-challenge urine specimens, and the results are compared to appropriate reference values [5, 6]. In some non-evidence-based medical practices, however, assessment of metal poisoning is frequently based on non-validated post-challenge urine metal testing, which invites inappropriate comparison to normal urine reference ranges [4-7].

Chelating agents such as dimercaptosuccinic acid (DMSA), dimercaptopropanesulfonic acid (DMPS), dimercaprol (BAL), and edetate calcium disodium (CaNa2-EDTA) bind metallic and metalloid elements and have been shown to increase their elimination from the body. Chelating agents have been found to mobilize metals in healthy individuals who have a body burden considered normal for a standard reference population, as well as in those who are determined to have a high body burden of the same metallic species [4, 8-11]. More specifically, urine specimens collected in relatively close temporal proximity to administration of chelating agents, i.e., post-challenge specimens, are expected to have increased concentrations of metallic elements. This includes elements, such as zinc, that are essential to normal physiologic functions and maintenance of good health.

Normal reference values for non-challenge urine metal test results vary among and within different populations. Ranges for these values have been established in nationally certified laboratories that meet proficiency standards for urinary metal testing [5]. However, scientifically

acceptable normal reference values for post-challenge urine metal testing have not been established [10]. In addition, scientific investigation to date has failed to establish a valid correlation between prior metal exposure and post-challenge test values [10]. Despite the lack of scientific support to do so, it is also a common practice of some laboratories and care providers to provide or apply non-challenge normal reference values as a comparative means of interpreting results of post-challenge urine metal testing [5]. Currently available scientific data do not provide adequate support for the use of post-challenge urine metal testing as an accurate or reliable means of identifying individuals who would derive therapeutic benefit from chelation.

Unfortunately, the practice of post-challenge urine metal testing and its application to assessment of metal poisoning often leads to unwarranted and prolonged oral and/or intravenous administration of chelating agents, in response to the results of serial post-challenge testing that remain elevated above non-challenge reference values. Chelation therapy based on such laboratory values, in addition to being of no benefit to patient outcome, may actually prove harmful [5, 12]; catastrophic outcomes such as acute fatal hypocalcemia have been reported following the improper use of a chelating agent, edetate disodium (Na2-EDTA) [13]. In addition, the safer formulation of this agent, CaNa2-EDTA, has been demonstrated to increase urinary excretion of essential minerals such as iron, copper and zinc [8, 14]. There is published experimental evidence that deleterious effects may occur when chelation is applied in the absence of prior lead exposure. [15] Other chelating agents such as DMSA and DMPS may also increase the elimination of certain essential elements, as well as promote target organ redistribution of metallic elements of concern such as mercury [16-18].

It is, therefore, the position of the American College of Medical Toxicology that post-challenge urinary metal testing has not been scientifically validated, has no demonstrated benefit, and may be harmful when applied in the assessment and treatment of patients in whom there is concern for metal poisoning.

References

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