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Review

Validity of human nails as a biomarker of arsenic and selenium exposure: A review

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Abstract

Human nail clippings have been used in recent epidemiological studies as a routine bioindicator of arsenic and selenium exposure. To ensure sound application of this biomarker, however, it is important to consider properties and scientific knowledge pertaining to validation of this particular tool. In this review, the use of human nails to measure exposure to arsenic and selenium is discussed in the context of the biomarker validation framework. Literature related to both analytical procedures and intrinsic characteristics of the biomarker is reviewed. Specifically, the followings are addressed: sample collection and preparation methods, establishment of the exposure–biomarker relationship, intraindividual variability and reproducibility of measurements, and biomarker–disease investigations. Drawing from a rapidly growing body of literature, current knowledge of these biomarker validation steps is assessed. Therefore, this review brings attention to the important issue of biomarker validation, laying the framework for future studies measuring elemental composition of nails.

Keywords: Arsenic; Selenium; Exposure; Toenail; Biomarker validation

Contents

1. Introduction

Assessment of chronic exposure to essential and nonessential elements is an area of emerging interest in environmental and nutritional epidemiology, as the roles of elements in disease development unfold. When estimating

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chronic disease risk in epidemiological studies, minimizing error in exposure assessments is essential. Given the presence of multiple exposure pathways, the use of biomarkers lends promise to reducing measurement error in traditional exposure assessments, which often rely on recall or aggregate exposure measurements (Rothman, 1993; Decaprio, 1997). To make progress in this area it is critical to understand how the exposure biomarker relates to intake of the contaminant or nutrient of interest and what factors may modify this association (National Research Council (NRC), 1987), thus moving toward biomarker validation.

Validity of an exposure biomarker is described as the relationship between the biomarker and the actual exposure (Maruvada and Srivastava, 2004). Factors affecting biomarker validity are categorized as intrinsic biomarker characteristics or as pertaining to the analytical procedures (Dor et al., 1999). In general, intrinsic characteristics of the biomarker include specificity to the pollutant of interest, significance in terms of exposure and knowledge of the exposure–biomarker relationship, understanding of background levels in the general population, knowledge of inter- and intraindividual variability (reproducibility), and modification of the biomarker or exposure–biomarker relationship by other variables (Dor et al., 1999). Analytical factors affecting validity include effects of timing of collection, possibility of contamination, and standardization of protocol (Dor et al., 1999). These factors are interrelated, and a more complete understanding of each can assist in moving toward sound application of the biomarker. Fig. 1 demonstrates this interrelatedness while highlighting biomarker characteristics and analytical processes specific to validation of human nails as an exposure biomarker.

Biomarker validation is a critical step that should be considered prior to application of the biomarker to epidemiological studies, since exposure misclassification and biomarker measurement error can result in inaccurate estimations of disease risk (White, 1997; Gordis, 2000). The validation process is an iterative procedure resulting in a degree of validation, however, and is not usually satisfactory before biomarkers are implemented (Schulte, 2001; World Health Organization, 2001). Human nails, which have been used to measure concentrations of and exposures to essential and toxic elements, are no exception to this observation. Arsenic and selenium have been measured most extensively in human nails, and therefore concentrations of these elements in nails have most frequently been proposed as an exposure biomarker in epidemiological studies (Michaud et al., 2004; Beane-Freeman et al., 2004; van den Brandt et al., 1994; Garland et al., 1995). Data that can be used in biomarker validation and application exist primarily for these two elements; therefore, this review focuses on the utility of nail clippings in measuring arsenic and selenium exposure.

Nail, blood, urine, and hair have all been considered for exposure monitoring. Nail clippings have advantages over the other biological materials frequently analyzed for arsenic and selenium content. Nail clippings are thought to reflect exposures that have occurred over the past 6–12 months and, as opposed to blood and urine, are a marker of longer exposure periods (Hunter et al., 1990; Goyer and Clarkson, 2001). Urine and blood selenium concentrations reflect recent intake, on the order of several days for urine (van Dael et al., 2001) and several weeks for blood-based measures (Longnecker et al., 1993). Arsenic is cleared from the blood and excreted in the urine in a matter of hours following exposure; therefore, these markers are ideal for monitoring acute exposures (Walker and Griffin, 1998; NRC, 1999). Hair and nails retain the highest concentration of arsenic due to the content of keratin, a group of proteins containing disulfide bonds (Hopps, 1977; NRC, 1999). Elements in hair and nails are removed from metabolic processes after formation and thus may be stable markers of past exposure (Hopps, 1977), compared with blood or urine.

Collection of both hair and nails is noninvasive and allows for easy long-term storage. Hair presents

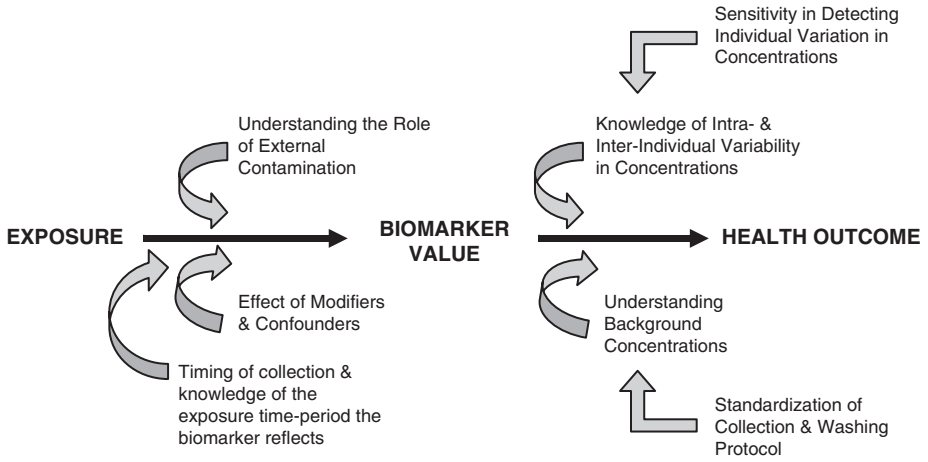

Fig. 1. Understanding the exposure–biomarker–disease relationship: interrelatedness of recommended biomarker validation steps.