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Review

Arsenic exposure in Latin America: Biomarkers, risk assessments and related health effects

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ABSTRACT

In Latin America, several regions have a long history of widespread arsenic (As) contamination from both natural and anthropological sources. Yet, relatively little is known about the extent of As exposure from drinking water and its related health consequences in these countries. It has been estimated that at least 4.5 million people in Latin America are chronically exposed to high levels of As (>50 μg/L), some to as high as 2000 μg/L — 200 times higher than the World Health Organization (WHO) provisional standard for drinking water. We conducted a systematic review of 82 peer reviewed papers and reports to fully explore the current understanding of As exposure and its health effects, as well as the influence of genetic factors that modulate those effects in the populations of Latin America. Despite some methodological limitations, these studies suggested important links between the high levels of chronic As exposure and elevated risks of numerous adverse health outcomes in Latin America — including internal and external cancers, reproductive outcomes, and childhood cognitive function. Several studies demonstrated genetic polymorphisms that influence susceptibility to these and other disease states through their modulation of As metabolism, with As methyltransferase (*AS3MT*), glutathione S-transferase (*GST*), and genes of one-carbon metabolism being specifically implicated. While the full extent and nature of the health burden are yet to be known in Latin America, these studies have significantly enriched knowledge of As toxicity and led to subsequent research. Targeted future studies will not only yield a better understanding of the public health impact of As in Latin America populations, but also allow for effective and timely mitigation efforts.

Contents

1. Introduction . . . 77
2. Methods . . . 78
3. History, occurrence, distribution and exposed population to arsenic from drinking water in Latin American countries . . . 79
    3.1. Andes and Chaco–Pampean Plains: Argentina, Chile and Uruguay, Bolivia, Peru, Colombia, and Ecuador . . . 79
    3.2. Central America: Nicaragua, El Salvador and Costa Rica . . . 80
    3.3. Arsenic exposure in Brazil and Mexico . . . 80
4. Biological markers of arsenic exposure, metabolism, toxicity, and susceptibility . . . 80
    4.1. Biomarkers of arsenic exposure . . . 80
    4.2. Individual variability in urinary arsenic metabolites profile . . . 81
    4.3. Arsenic-induced genotoxicity, oxidative stress and DNA damage . . . 81

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4.4. Genetic susceptibility to arsenic-related adverse health outcomes . . . 82
5. Health effects from arsenic exposure in Latin America . . . 83
5.1. Bladder cancer . . . 84
5.2. Lung cancer . . . 85
5.3. Kidney, liver, and skin cancers . . . 85
5.4. Other chronic health effects . . . 85
5.5. Effects of *in utero* and early childhood exposure . . . 86
6. Discussion . . . 87
Conflict of interest statement . . . 89
Acknowledgement . . . 89
References . . . 89

1. Introduction

Arsenic (As) exposure has likely been a longstanding problem in Latin America, with mummified bodies in Chile showing signs of As exposure from as long as 7000 years ago (Arriaza et al., 2010). In many Latin American countries, soil and groundwater are highly enriched with As due to its high density in the region's abundant volcanic rock and ash. In some countries, mining operations and copper foundries have unearthed As and enhanced its release into groundwater sources for the past few centuries (Ng et al., 2003). Common features of geography and contamination allow Latin America to be classified into three distinct regions: the Chaco–Pampean plain, Andean range, and Central America (Fig. 1). While each of these areas has their own defining characteristics, they share the common burden of having been affected by inorganic As transport into drinking water. High concentrations of As have been found in all sources of drinking water in Latin America, including lake, spring, river and ground water (Castro de Esparza, 2009; Concha et al., 2010). Though this widespread contamination from both natural and anthropological sources has long been a threat to human health in Latin America, relatively little is known about occurrence, distribution, and exposed populations in countries other than Argentina, Brazil, Chile, and Mexico . Only recently has data begun to emerge from such Central American countries as Nicaragua and El Salvador (Cuevas and Bundschuh, 2010). Despite this relative lack of detailed exposure data, it is estimated that at least 4.5 million people in Latin America are currently drinking As contaminated water (>50 μg/L), with some recorded levels as high as 2000 μg/L — roughly 200 times higher than the current World Health Organization (WHO) standard (10 μg/L) for drinking water (Farías et al., 2008; WHO, 2003).

Arsenic in drinking water causes a number of adverse health effects, including skin lesions that often appear relatively soon after exposure (within 5–15 years of exposure). Long term As exposure damages several internal organs and has been linked to bladder, lung, and skin cancers. Though evidence of As-related disease in Latin America was first described in the 1920s (Goyenechea, 1917), more systematically gathered data on adverse health effects did not emerge until the mid 1970s. In the mid 1970s, elevated mortality and incidence of respiratory disease from As exposure were observed in the endemic areas of Chile (Borgoño et al., 1977; Rosenberg, 1974; Zaldivar, 1980; Zaldivar and Ghai, 1980). Since the 1990s, research from Chile, Argentina and Mexico has demonstrated malignant and non-malignant effects of As exposure. Though much of the findings were based on retrospective case–control or ecological studies that lacked individual exposure data, consistent association was found between high As concentration and the risk of lung and bladder cancer (Hopenhayn-Rich et al., 1996a; Smith et al., 2006). Recent epidemiologic investigations have found a long latency period for lung cancer and other As-related chronic diseases, even when exposure was limited to a discrete period either during early childhood or *in utero* (Smith et al., 2006). Exposure during these times has also been implicated in adverse reproductive outcomes in mothers and impaired cognitive development in children (Hopenhayn-Rich et al., 2000; Hopenhayn et al., 2003a). Recent studies have examined the possible mechanisms of toxicity that bring about these adverse health outcomes, including genotoxicity, oxidative stress, and impaired DNA repair (Dulout et al., 1996; Engstrom et al., 2007, 2009, 2010).

A number of studies in Latin America have not only helped to establish the link between As exposure and these health outcomes, but also explored the underlying exposure-disease mechanisms and individual susceptibility. Research in Argentina has focused mainly on bladder cancer, describing increased risks and, more recently, exploring how it could be related to susceptibility markers such as Transforming Growth Factor-α (TGF-α) (Valenzuela et al., 2007), polymorphic influences on metabolism (Moore et al., 2004), and exposure-induced chromosomal aberrations (Moore et al., 2002). South American studies related to lung cancer have taken place largely in Chile, reporting an increase in disease risk from discrete childhood exposure (Smith et al., 2006) and exploring the effect of genetic polymorphisms (Steinmaus et al., 2006). Mexico has been a focus for research on As-related skin disease (Valenzuela et al., 2007), including studies on influence of metabolism (Loffredo et al., 2003), DNA damage (Engstrom et al., 2010), and genetic polymorphisms (Sampayo-Reyes et al., 2010).

In addition to drinking water, food is another source of As in Latin American countries. A few studies from As endemic areas in Latin America have indicated that food contributes up to 50% of total As intake (Del Razo et al., 2002; Diaz et al., 2004; Navoni et al., 2007; Queirolo et al., 2000). High amount of As has been detected in fish, cow milk, grains and vegetables including potato, onion, beet, pumpkin, radish, cabbage and beans in Bolivia, Brazil, Chile, Ecuador, El Salvador, Honduras, Mexico, Nicaragua and Peru. Cow milk from Argentina and Mexico are shown to have As (Sigrist et al., 2010). At least two studies from Chile and Brazil have found high amount of As in different species of fish that exceeds FAO/WHO recommended value and current guideline set by Brazil (Lavanchy Dougnac, 1999) (Macedo, 2010). Food preparation with As contaminated water has also found to increase As content in cooked food (Ackerman et al., 2005; Munoz et al., 2002; Navoni et al., 2007; Vélez et al., 1997). In order to reduce risk of As exposure and accurately assess As exposure, As contamination from food needs to be given more attention. Please see the paper on As contamination from food in Latin American counties in this issue of the journal (Bundschuh et al., 2011a). This paper will first describe the historical and current occurrence of As exposure throughout Latin America. That will lead to a review of studies on how As is metabolized in the human body and the various biological markers that exist to measure exposure and metabolism. Based on our review of 82 peer reviewed papers and reports, we then describe specific health outcomes in Latin America, noting the work that has been done to establish general causality, as well as efforts that have been made to understand how these specific diseases are induced. There will be a separate description of studies that investigates general biochemical changes in disease induction, including any modifying effects of genetic variations and biomarkers. This paper closes by