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Blood levels of toxic metals and rare earth elements commonly found in e-waste may exert subtle effects on hemoglobin concentration in sub-Saharan immigrants

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ABSTRACT

Pollution by heavy metals and more recently by rare earth elements (REE) and other minor elements (ME) has increased due in part to their high use in technological and electronic devices. This contamination can become very relevant in those sites where e-waste is improperly processed, as it is the case in many countries of the African continent. Exposure to some toxic elements has been associated to certain hematological disorders, specifically anemia. In this study, the concentrations of 48 elements (including REE and other ME) were determined by ICP-MS in whole blood samples of sub-Saharan immigrants with anemia (n = 63) and without anemia (n = 78). We found that the levels of Fe, Cr, Cu, Mn, Mo, and Se were significantly higher in the control group than in the anemia group, suggesting that anemia was mainly due to nutritional deficiencies. However, since other authors have suggested that in addition to nutritional deficiency, exposure to some elements may influence hemoglobin levels, we wanted to explore the role of a broad panel of toxic and "emerging" elements in hemoglobin deficiency. We found that the levels of Ag, As, Ba, Bi, Ce, Eu, Er, Ga, La, Nb, Nd, Pb, Pr, Sm, Sn, Ta, Th, Tl, U and V were higher in anemic participants than in controls. For most of these elements an inverse correlation with hemoglobin concentration was found. Some of them also correlated inversely with blood iron levels, pointing to the possibility that a higher rate of intestinal uptake of these could exist in relation to a nutritional deficiency of iron. However, the higher levels of Pb, and the group of REE and other ME in anemic participants were independent of iron levels, pointing to the possibility that these elements could play a role in the development of anemia.

1. Introduction

Environmental pollution has increased greatly in recent years, and in some areas it has reached levels that may even be toxic to living beings (Luzardo et al., 2014; Shakir et al., 2017). Among environmental pollutants, toxic heavy metals and metalloids are among the most dangerous since they are also not biodegradable and tend to accumulate in environmental compartments (Hussain and Mumtaz, 2014; Kakuschke et al., 2010; Shakir et al., 2017). While small concentrations of some elements are needed for life, most are considered non-essential and some are very toxic to most vertebrates including humans, even at very low concentrations (Tchounwou et al., 2012). In addition, elements considered essential follow an hormetic dose-response curve, and may also be toxic to living organisms if some concentrations are exceeded (Tchounwou et al., 2012).

According to their high degree of toxicity, four elements are usually highlighted among others: arsenic (As), cadmium (Cd), lead (Pb), and mercury (Hg) (Camacho et al., 2014; Hussain and Mumtaz, 2014;

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Wittsiepe et al., 2016). However, every two years the Agency for Toxic Substances and Disease Registry (ATSDR) publishes a list of priority chemicals that are determined to represent the most significant potential threat to human health because of their known or suspected toxicity, together with the potential human exposure. In this list there are currently 19 other elements that add up to the four already indicated [silver (Ag), aluminum (Al), barium (Ba); beryllium (Be), cobalt (Co), chromium (Cr), copper (Cu), manganese (Mn), nickel (Ni), palladium (Pd), plutonium (Pu), antimony (Sb), selenium (Se), strontium (Sr), thallium (Tl), thorium (Th), uranium (U), vanadium (V), and zinc (Zn)] (CDC, 2017). It is well documented that Co, Cr, Cu, Mn, Ni, Se, and Zn are life essential elements when at low levels of exposure. However, for all these elements, including the essential elements, there is relevant scientific literature documenting their toxic effects, having been reported as damaging organelles and cellular components, as well as enzymes, proteins and macromolecules, some of them even at low levels of exposure. Many of these metals are also involved in the generation of reactive oxygen species and free radicals. Moreover, some of them are also classified as either "known" or "probable" human carcinogens based on epidemiological and experimental studies showing an association between exposure and cancer incidence in humans and animals (Tchounwou et al., 2012).

Additionally, there are a number of elements, the rare earth elements (REE) and other minor elements (ME), which are increasingly coveted due to the large number of technological applications for which they are already indispensable (Tansel, 2017). In geochemical terms these elements would be those whose concentrations in the earth's crust are higher than 100 ppm but lower than 0.1%. However, this rule is loosely applied, and despite their name, some of these elements are relatively abundant in the earth's crust (i.e. cerium is as abundant as copper). However, it is true that their location in the crust is very irregular and tends to concentrate on certain points of the planet, and also tends to occur together in nature, and is difficult to separate from each other. This set of elements, dubbed "the new petroleum", is of growing concern because its enormous range of applications makes them mobilized from the few sites where they are abundant - 90% of known mines are currently located in China (Zhuang et al., 2017) - to be distributed all over the planet (Bozlaker et al., 2013), especially once the useful life of the devices containing them ends (Hussain and Mumtaz, 2014). For this reason, REE have been included among the new and emerging occupational and environmental health risks by several international organizations (Pagano et al., 2015a). However, to date, very little is known about the toxic effects of long-term exposure to such substances. Some toxic effects have been documented at high exposures in vivo, in vitro, or in clinical studies, including cytotoxicity, cytogenetic effects and organ damage (Pagano et al., 2015a; Pagano et al., 2015b), but to the best of our knowledge, no toxicity study has been done at levels similar to those of environmental exposure.

The hematological system is a frequent target of the toxic effects of many heavy metals (Dai et al., 2017; Jomova and Valko, 2011; López-Rodríguez et al., 2017), and it has been demonstrated that environmental exposure to some of them has a strong influence on the hematological parameters in some vertebrates, such as common carp (Vinodhini and Narayanan, 2009). In particular, some elements, such as titanium, arsenic, cadmium, lead or copper, have been associated with the development of anemia (mainly by hemolysis) in people exposed to high concentrations of these heavy metals (López-Rodríguez et al., 2017; Parvez et al., 2017). However, some hematological effects have also been related to environmental low-level exposure to certain elements. Thus, it has been reported that the environmental exposure to low concentrations of arsenic seems to produce a subtle decrease in hemoglobin concentration (López-Rodríguez et al., 2017). This toxic effect of arsenic could be considered a contributor, as an environmental cause, to the development of anemia in children (López-Rodríguez et al., 2017).

Recent studies in sub-Saharan African immigrants have revealed they pose a high prevalence of red cell abnormalities, with an incidence of anemia of up to 10%, microcytosis of up to 25%, and hemoglobinopathies of up to 12% (de-la-Iglesia-Inigo et al., 2013). In the particular case of anemia, especially in the inhabitants of developing countries, it is generally assumed that iron deficiency is the main cause (Camaschella, 2017; van den Broek et al., 1998), and at least 50% of the anemia cases have been blamed on iron deficiency (van den Broek et al., 1998). However, it has been described that there are complex interactions between the different essential elements with iron, so that they potentially may have a role on the development of IDA. Thus, synergistic deficiencies of iron and other essential elements involved in hematopoiesis, such as copper, chromium or nickel, or macroelements such as sodium and potassium, could hypothetically contribute to the development of IDA. On the other hand, it has been described that the increase in the exposure to iron-antagonistic elements such as cobalt, zinc, or high copper or chromium, as well as macroelements such as calcium, may limit the intestinal absorption of iron, also leading to the development of IDA (Bjorklund et al., 2017). However, the role of other contributing factors, whether of nutritional, infectious, genetic or environmental type, is seldom studied simultaneously (Foote et al., 2013). At the same time it has been described that in Africa environmental levels of contamination by heavy metals (and more recently by REE and MM) are increasing, especially in relation with the informal e-waste processing (Nnorom and Osibanjo, 2008; Wittsiepe et al., 2016).

So, we have designed this study, in which we determined the blood concentrations of a panel of 48 elements, including essential elements as well as elements related to electronic waste in a group of 63 sub-Saharan immigrants with anemia. These results were compared with those obtained from a group of 78 sub-Saharan immigrants without anemia, who were matched by age, sex and geographical origin with the participants in the anemia group. Using these two groups, the main goal of this investigation was to explore the possibility that a potential relationship exists between anemia and toxic and emerging minor elements, in addition to essential elements. Another relevant goal of this work was to investigate if immigrants from e-waste recycling sub-Saharan countries show higher exposure to e-waste related elements than those from other countries.

2. Material and methods

2.1. Study population

In this study we used a part of a series of whole blood samples that were prospectively and sequentially obtained from sub-Saharan immigrants irregularly arrived to the island of Gran Canaria (Canary Islands, Spain) during the last years of 2010 decade. The samples were obtained in the context of their general health examination and screening of imported diseases (Luzardo et al., 2014), within the first two months of their temporal lodging in shelters. In a retrospective search on the biobank we selected whole blood samples from patients with anemia (n = 63), and we searched for blood samples that would make up the control group among immigrants without anemia (n = 78). Blood samples from the control group were selected according to gender, age and country of origin to seek parity with the group of immigrants with anemia. All participants from the original series (and subsequently those in this study) underwent a physical examination to rule out the presence of signs or symptoms of disease and provided their written consent for the use of their biological samples for research. A supplementary face-to-face interview in English or French following a pre-established questionnaire was performed (Sanz-Peláez et al., 2008). All patients whose samples were included in the biobank (and therefore in this study) had a complete biochemical and hematological analysis, as well as a complete serological study, both for viral and parasitic diseases. Additionally, all subjects were evaluated for the presence of parasites by performing fecal exams (Ritchie and Kato techniques), urinalysis and a Knott test. For this study only patients who