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Body burden of toxic metals and rare earth elements in non-smokers, cigarette smokers and electronic cigarette users

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ABSTRACT

Smoking is considered an important source for inorganic elements, most of them toxic for human health. During the last years, there has been a significant increase in the use of e-cigarettes, although the role of them as source of inorganic elements has not been well established. A cross-sectional study including a total of 150 subjects from Brasov (Romania), divided into three groups (non-smokers, cigarette smokers and electronic cigarettes smokers) were recruited to disclose the role of smoking on the human exposure to inorganic elements. Concentration of 42 elements, including trace elements, elements in the ATSDR's priority pollutant list and rare earth elements (REE) were measured by ICP-MS in the blood serum of participants. Cigarette smokers showed the highest levels of copper, molybdenum, zinc, antimony, and strontium. Electronic cigarette (e-cigarette) users presented the highest concentrations of selenium, silver, and vanadium. Beryllium, europium and lanthanides were detected more frequently among e-cigarette users (20.6%, 23.5%, and 14.7%) than in cigarette smokers (1.7%, 19.0%, and 12.1%, respectively); and the number of detected REE was also higher among e-cigarette users (11.8% of them showed more than 10 different elements). Serum levels of cerium and erbium increased as the duration of the use of e-cigarettes was longer. We have found that smoking is mainly a source of heavy metals while the use of e-cigarettes is a potential source of REE. However, these elements were detected at low concentrations.

1. Introduction

Contamination by heavy metals and, more recently, by rare earth elements (REE) and other minor elements (ME), has increased during the last decades due in part to their high use in technological and electronic devices (Hussain and Mumtaz, 2014). Although some heavy metals are necessary for life, most are considered non-essential and some have adverse health effects to humans—and other vertebrates—even at very low concentrations (Tchounwou et al., 2012). Moreover, some essential elements are included in the ATSDR's (Agency for Toxic Substances and Disease Registry) priority pollutant list for being toxic to living organisms at high concentrations (ATSDR, 2018; Tchounwou et al., 2012). Thus, a total of 23 elements are included in the ATSDR's priority pollutants list: silver (Ag), aluminum (Al), arsenic (As), barium (Ba), beryllium (Be), cadmium (Cd), cobalt (Co), chromium (Cr), copper (Cu), lead (Pb), manganese (Mn), mercury (Hg), nickel (Ni), palladium (Pd), plutonium (Pu), antimony (Sb), selenium (Se), strontium (Sr), thallium (Tl), thorium (Th), uranium (U), vanadium (V), and zinc (Zn) (ATSDR, 2018).

REE and ME have been classified as evidently or potential occupational and environmental health risk factors by several international organizations (Pagano et al., 2015b). These elements have been increasingly and widely used in industry, agriculture, as well as in our daily life since they are very useful—or almost indispensable—for the manufacturing of all kinds of today's technological devices (Tansel, 2017). Thus, REE and ME are being mobilized from the few sites where they are abundant to be employed at an industrial scale, and therefore distributed all over the planet (Bozlaker et al., 2013). Thus, a number of

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"emerging pollutants" have appeared and are currently detected in living beings, including humans (Henriquez-Hernandez et al., 2017a, 2017b; Pagano et al., 2015a, 2015b).

Smoking is considered an important source for inorganic elements intake, mainly for some trace elements and other biochemically important elements (Chiba and Masironi, 1992). Thus, while cadmium or cupper are highly concentrated in cigarettes, for other elements—i.e. selenium—this association is inverted or even irrelevant (that is the case of mercury) (Bernhard et al., 2005). Anyhow, cigarette smoking interferes with the carefully controlled metal homeostasis of the human body and has to be considered as harmful to health. On the other hand, electronic cigarettes (e-cigarettes) are products that deliver a nicotine-containing aerosol—commonly called vapour—to users by heating a solution made up of propylene glycol or glycerol, nicotine and flavouring agents invented in their current form by Chinese pharmacist Hon Lik in the early 2000s (Grana et al., 2013). According to a report published by the Center for Tobacco Control Research and Education University of California, although young people are rapidly adopting e-cigarettes, there is a high level of dual use of e-cigarettes and conventional cigarettes among adults, mainly due to the belief that electronic cigarettes help to stop smoking. In that sense, all population-based studies of adult use show the highest rate of e-cigarette use among current smokers, followed by former smokers, with little use among non-smokers (Dockrell et al., 2013; King et al., 2013). However, e-cigarettes have not been proven to help people quit smoking (Grana et al., 2013). E-cigarettes pollute the air less than conventional cigarettes, but they do not emit "harmless water vapour" (Grana et al., 2013). Vapours' toxicant intake varies depending of which different e-liquids are used, the type of vaporizers, battery power settings and vaping regimes (Gillman et al., 2016; Sleiman et al., 2016). In that sense, formaldehyde, acetaldehyde, acrolein, diacetyl, acetol, glycidol, nicotine, nicotyrine, acenaphthene, isovaleraldehyde, formaldehyde, benzaldehyde and benzene have been detected in the vapour of e-cigarettes (Auer et al., 2017; Sleiman et al., 2016). However, other chemicals are not directly present in the e-liquids, but are either released from hardware components of the e-cigarette such as metal and silicate particles (Williams et al., 2013). It has been demonstrated that increasing battery outputs generates also increasing levels of some residues such as carbonyls (Kosmider et al., 2014). Moreover, the surface of the heating coil can reach temperatures as high as 110 °C using batteries > 10 watts, which conditions the level of volatile substances emitted by the e-cigarettes (Geiss et al., 2016). The effect that e-cigarettes may have in the uptake of inorganic elements—contained in e-liquids or as part of the electronic device—to the organism is unknown.

We have designed this study with the objective of measuring the blood concentrations of a total of 42 elements, including trace elements, elements in the ATSDR's priority pollutant list and REE—lanthanides and other ME—in a group of 150 subjects from Brasov (Romania). The series was divided into three groups (non-smokers, cigarette smokers and e-cigarettes users) and the results among groups were compared with the aim of disclosing the role of cigarette smoking and e-cigarette use as a source of inorganic pollutants.

2. Material and methods

2.1. Study design and participants

We conducted a cross-sectional study that included 150 Romanian subjects. All the subjects responded to a call made to participate in the present investigation. It was done in the context of the Faculty of Medicine of the Transilvania University of Brasov (Romania). Recruitment was done between December 2017 and February 2018. The series was formed by 58 non-smokers, 58 conventional cigarette smokers, and 34 e-cigarette users. All users of e-cigarette were ex-smokers. However, dual users—defined as persons who smoke cigarettes and use e-cigarette at the same time—were excluded from the study. The classification was based in self-reports of the participants. Demographical data were obtained and a face-to-face interview aimed to know details about the smoking status was also done. The questionnaire was designed exclusively for this purpose and data were recorded on paper and subsequently digitalized. Participation in the study was totally free and no one received any compensation.

All participants signed an informed consent before taking the sample. The study design was approved by the Ethical Committee of the Faculty of Medicine, Transilvania University of Brasov, Romania. Blood samples were obtained from all of the participants. All samples were obtained in the morning and the participants were informed not to smoke or use e-cigarette prior to the blood collection. Samples of blood were collected in 4 mL heparinized tubes (BD Vacutainer, LH 68 I.U. Lithium Heparin, BD-Plymouth, PL6 7BP, UK), maintained at 4 °C, and centrifuged at 1000 g for 15 min to separate the serum. The obtained serum was kept at − 20 °C until chemical analysis. Samples were sent to the University of Las Palmas de Gran Canaria for subsequent analysis.

2.2. Standards, samples and elements

We determined the serum concentration levels of 43 elements, including the trace elements and other REE and ME considered "emerging pollutants" (ATSDR, 2018; Tansel, 2017). Since, chromium was not considered for reasons of analytical confidence, the total number of elements finally included in this study was 42 (Additional file 1).

Samples consisted of 130 μL of serum, 1120 μL of ammonia solution (0.05% of EDTA, 0.05% of Triton X-100, and 1% of NH_4OH), and 50 μL of internal standards (ISTD) until a total final volume of 1.3 mL. ISTD solution was composed by Sc (scandium), Ge (germanium), Rh (rhodium), and Ir (iridium) at a stock concentration of 20 mg/mL each. Pure standards of elements in acid solution (5% HNO_3, 100 mg/L) were purchased from CPA Chem (Stara Zagora, Bulgary). Two standard curves (ten points, 0.005–20 ng/mL) were made to avoid interferences between elements: a) one using a commercial multi-element mixture (CPA Chem Catalog number E5B8·K1.5N.L1, 21 elements, 100 mg/L, 5% HNO_3) containing all the essential elements and main heavy metals; and b) other multi-element mixture tailor-made in our laboratory from individual elements (CPA Chem), which contained the REE and ME, as previously reported (Henriquez-Hernandez et al., 2017a).

2.3. Analytical methods

An Agilent 7900 ICP-MS (Agilent Technologies, Tokyo, Japan) with standard nickel cones, MicroMist glass concentric nebulizer, and Ultra High Matrix Introduction (UHMI) system was used for all measurements. The Integrated Sample Introduction System (ISIS) was configured for discrete sampling. The UHMI system was operated in robust mode. The 4th generation Octopole Reaction System (ORS4) was operated in helium (He) mode to reduce polyatomic interferences. A tuning solution consisting in a mix of Cs (cesium), Co (cobalt), Li (lithium), Mg (magnesium), Tl (thallium), and Y (yttrium) was used before the analysis for optimization of instrumentation. Quantification of the elements was made in the MassHunter v.4.2. ICP-MS Data Analysis software (Agilent Technologies).

The analytical method was optimized and validated, as previously reported (González-Antuña et al., 2017; Henriquez-Hernandez et al., 2017a). Recoveries obtained ranged from 89% to 128% for REE and ME, and from 87% to 118% for ATSDR's toxic heavy elements and essential elements. Linear calibration curves were found for all elements (regression coefficients > 0.998). The method limit of quantification (LOQ) was calculated by quantifying fifteen replicates of blanks, using 0.130 μL of alkaline solution. The LOQs were calculated as the concentration of the element that produced a signal that is three times higher than that of the averaged blanks. The accuracy and precision of this method was assessed using fortified alkaline solution (0.05, 0.5, and 5 ng/mL) in substitution of sample. In general, the calculated