Accumulation of trace element content in the lungs of Sao Paulo city residents and its correlation to lifetime exposure to air pollution

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Abstract

Heavy metals are natural and essential elements of the environment and living beings, produced from natural (e.g. volcanic activity and cosmic ray-induced spallation) and anthropogenic processes (e.g. industrial and fossil fuel combustion). Studies showed increase of heavy metal and Polonium-210 concentrations in lung autopsies linked to urban and industrial air pollution. In this preliminary study, we analyzed the levels of heavy metals and Polonium-210 (^{210}Po) in lung tissues in autopsies from residents of the city of Sao Paulo, SP, Brazil. In order to identify the generating sources of the heavy metals in lung a factor analysis was performed. Of the first four factors, which explain 66% of the total variability, three were associated with vehicular sources. The fitting of a regression model with Polonium-210 as the response variable and with the four factors as explanatory variables, controlling for age, sex and tobacco, showed a significant association between the concentration of polonium and the first factor that is generated by catalysts and brakes (coefficient = 0.90, standard error = 0.33, p = 0.016). Our findings suggest an association between the metals trace, from air pollution, and Polonium-210 in lung autopsies.

Introduction

Degradation and contamination of the environment (air, water and soil) by toxic substances is a common problem in urban areas, caused mainly due to human activities (industries, vehicular emissions, irregular disposal of solid waste)[1].

Among these contaminants, some metals deserve to be highlighted because they are toxic even in low concentrations, being their effects direct or a consequence of bioaccumulation. These toxic metals, some commonly known as heavy metals, occur naturally in soil at low concentrations [2], studies have also detected their presence in water for human consumption [3] and also associated with particulate matter suspended in the air [4].

Exposures to heavy metal can occur upon inhalation of contaminated air, by ingestion of contaminated water or food and by contact to contaminated soil/dust, use of cosmetic products. In Brazil there are laws to limit metals in food (Arsenic, Lead, Cadmium, Mercury and Tin) [5], water (for example, arsenic, cadmium, chromium, copper, lead, mercury, nickel, silver, zinc) and as part of air pollution (Lead) [64]. However, there is no specific program of monitoring the presence and levels of these metals in the different environmental compartments [7], except lead presence in the air.

In general, health effects of these toxic metals depends on route, dose and duration of the exposure, as well as the age of the exposed individual [8].

For example, cadmium, lead and mercury have been linked to damage in kidney, bone and lungs, and neurobehavioral and developmental disorders in fetuses, infants and children[1].

Heavy metals are bioaccumulative in ecosystems, and can be biomagnified in animals consumed by human[1]. Moreover, long-range transport of heavy metals in air pollution to remote places far from the sources of emission has been recognized as an important factor when assessing contamination of the environment and health effects in humans[31].

Heavy metals are commonly attached to air particulates (PM), especially those in the submicron category (0.1-1μm) [4]. Fortoul et al. (1996) showed significant increase of heavy metal concentrations in lung autopsies linked to urban and industrial air pollution in residents of the City of Mexico from 1950 to 1980's [9]. Our previous study showed that Polonium-210 (^{210}Po) levels in autopsies were linked to urban pollution and tobacco smoke [10]. ^{210}Po decay onto its immediate heavy metal progenies Bismuth-210 (^{210}Bi) and lead-210 (^{210}Pb) after 138 days in the environment [11], and this metals may deposit and accumulate for years in lungs.

PM is a complex mixture of solid and liquid particles suspended in air, whose physicochemical properties and biological effects vary with location and time [12]. PM play a major role and heavy metal transport in radioactivity [13]. Regional estimation of PM mortality risk is frequently attributed to geographic variability in PM composition, spatial heterogeneity of constituents, topography, emission/removal rate, transport and dispersion, and differences in the population risk [41415]. A recent study showed high concentrations of heavy metal in tree rings in the city of Sao Paulo (Brazil)[11] and its association with air pollution, reinforcing the importance of vehicular emissions on the degradation of air quality and health risks[1617] .

Therefore, in this study we aimed to investigate the association between the concentrations of trace element and ^{210}Po in lung autopsies performed in the Post Mortem Verification Service of the City of São Paulo (SVOC) and lifetime exposure to air pollution in Sao Paulo city, Brazil.

Methods

Tissue Samples

This study is was approved by the Research Ethics Committee of the University of Sao Paulo (number .002.065) and inclusion criteria was: age equal or greater than 18 years, living in the MASP for at least 3 months, have one close relative to provide reliable and complete information during the interview to retrieve information about other sources of exposure, and not presenting macroscopic alterations of the lungs, brain and in the olfactory epithelium. Twenty fresh samples of lungs were obtained from 20 individuals during autopsy procedure at the Death Verification Service of the Capital (**SVOC**).

In brief, right after the body is claimed by a relative (next-of-kin "NOK") that signs a term allowing the autopsy procedure, a trained interviewer invited the NOK to participate in our study by explaining its purpose and relevance. Upon acceptance, the relative is taken to a private room where an informed consent form is voluntarily signed authorizing the collection of lung images and tissue samples. Then, a questionnaire about previous health conditions, residential address, sociodemographic details, life habits, smoking status, occupation, time of residence in the MASP and time spent commuting is applied (in supplemental file).

Anthracosis index

The anthracosis index it was measured *in* the pleural surface of the lungs as described previously by Takano et al[3].

Lung samples preparation

The lung tissue samples from upper lobe (20-37g) were placed separately in clean polyethylene bags and kept at - 80 ^{o}C until its transportation to Nuclear and Energy Research Institute (IPEN-CNEN/SP). Special care was taken during handling to avoid external contamination by metals, plastic tools and powder free surgical gloves were used. The tissues were rinsed using purified water in order to remove the blood. The tissues were homogenized using titanium knife. Samples were freeze-dried for the analyses until their constant weight was obtained. In this process of freeze-drying mean weight, losses (in percentage) were obtained: 82.0±6.0 for lung. The dried samples were grounded manually to obtain a fine powder that were placed in polyethylene vials. Prepared samples were stored in a refrigerator at -20°C until neutron activation analysis (NAA).

Determination of ^{210}Po in human samples

Determination of ^{210}Po in the lung tissue samples was conducted according to the methods described by Villa et al[4].

Neutron Activation Analysis Procedure

Aliquots of about 150 mg of dried tissue samples were irradiated in the IEA-R1 nuclear reactor along with the synthetic standards of the elements [18]. Short and long period irradiations with a thermal neutron flux of about 4 x 10 12 n.cm –2 .s –1 were performed for the element determinations such as Br, Ca, Ce, Cl, Cr, Co, Cs, Fe, Hf, K, La, Mn, Na, Rb, Sb, Sc, Se. Th and Zn. After adequate decay times, the irradiated samples and standards were measured using a Model GC3019 hyperpure Ge detector coupled to Digital Spectrum Analyzer DSA 1000, both from Canberra. Spectra were collected and processed using Canberra Genie 2000 Version.

Samples and standards were measured at least twice for different decay times. Counting times from 200 to 50,000 seconds were used, depending on the half- lives or activities of the radioisotopes considered. The radioisotopes measured were identified according to their half-lives and gamma ray energies. The element concentrations were calculated by comparative method.

Statistical analysis

In order to identify the generating sources of the element traces in lung a factor analysis was performed [19]. The applied method was the Principal Components based on a robust correlation matrix composed by Spearman's correlation coefficients between elements concentrations, with Varimax rotation.

The association between ^{210}Po and the factors representing the metals, adjusted for age, sex and tobacco was initially assessed using multiple linear regression fitted by least squares. A residual analysis suggested the existence of outliers and robust regression models based on MM-estimators were considered. Non-significant variables and interactions were dropped from the initial model step by step of the fitting process. The models were fitted via the *rlm* function from the MASS library in the R software package [20].

Results

Twenty individuals with average age of 69.0 (standard deviation = 18.3) years were studied. Thirty eight percent (n = 8) were smokers and 57% (n = 12) were male. The mean concentration of ^{210}Po in the lungs was 2.65 (Bq/kg) (standard deviation = 3.07). The descriptive analysis of individual characteristics and ^{210}Po are presented in Table 1. In Table 2 are depicted the anthracosis index and Po210-Lung results.

Table 1
Descriptive statistics of the individual characteristics

Variable	Mean	Std Dev(*)	Minimum	Median	Maximum	N	%
Age (years)	68.95	18.33	28	71	93		
Male						12	57.1
Years living in Sao Paulo	50.7	13.02	21	50	69		
Smoker or former smoker						8	38.1
Environmental tobacco smoke						11	36.6
Daily commuting (hours)	1.70	2.21	0	0.66	8		
(*) standard deviation							

Table 2

Descriptive statistics of anthracosis and ^{210}Po(Bq/kg)

Variable	Mean	Std Dev(*)	Minimum	Median	Maximum	N
Anthracosis	0.22	0.15	0.0019	0,19	0.54	16
Po210-Lung	2.66	3.08	0.37	1.48	12.61	20
(*) standard deviation						

The observed concentrations of Br, Ca, Ce, Cl, Cr, Co, Cs, Fe, Hf, K, La, Mn, Na, Rb, Sb, Sc, Se, Th and Zn are summarized in Table 3, and their distributions are represented in the box-plots in Figure S1. These results indicate high variability of the elements concentrations. The Spearman correlation coefficients between the concentrations of the elements are shown in Table S1.

Table 3
Descriptive statistics of the concentrations of chemical elements in the lung (µg / kg)

Heavy metal	N	Mean	StDev	Minimum	Median	Maximum
Br	20	40.4	55.5	15.3	26.4	273.6
Ca	20	2756.0	6310.0	564.0	1080.0	29319.0
Ce	19	294.5	235.0	39.6	245.6	1019.4
Cl	20	16229.0	4995.0	10690.0	15901.0	27401.0
Co	20	93.7	34.8	25.7	94.0	149.0
Cr	20	1047.0	906.0	121.0	695.0	3743.0
Cs	20	141.8	51.1	20.4	144.1	211.9
Fe	20	1090.9	428.1	398.4	980.3	1784.5
Hf	18	22.8	21.4	4.6	16.8	77.1
K	20	7558.0	1324.0	5289.0	7158.0	9663.0
La	20	222.4	124.5	61.4	213.1	465.2
Mn	20	702.4	313.9	182.9	657.0	1669.0
Na	20	10339.0	3466.0	6345.0	10308.0	20858.0
Rb	20	16.7	3.8	11.1	16.3	23.9
Sb	20	193.4	139.9	16.6	164.8	591.4
Sc	20	29.1	30.9	3.6	22.5	124.0
Se	20	499.8	137.8	228.0	472.5	871.0
Th	20	37.5	32.0	2.7	30.8	113.3
Zn	20	55.8	11.5	42.5	52.2	87.4

Table 4 contains the rotated factor loadings of the heavy metals in the 6 first factors. The number of factors was selected based in the scree plot in Figure S1. Together, these six factors account for 84% of the total data variability. Based on these results the factors can be interpreted as follows: Factor 1 is associated with the catalyst material and the vehicle brakes, Factor 2 is related to metals in the lung tissue itself. Factors 3 and 4 represent metals related to vehicular emissions. Factor 5 don’t have interpretation and factor 6 is related to soil resuspension [21,22]

Table 4
Rotated factor loadings. Values greater than 0.5 are highlighted in bold. The percentage of total variance explained by each factor is also presented in the table

Heavy metal	Factor1	Factor2	Factor3	Factor4	Factor5	Factor6
Br	0.44	0.11	**0.50**	**-0.58**	-0.01	-0.14
Ca	-0.20	-0.35	-0.42	**-0.54**	-0.12	0.27
Ce	0.45	0.58	-0.01	-0.30	-0.28	0.40
Cl	-0.43	-0.33	**0.68**	-0.25	0.12	0.21
Co	**0.81**	-0.23	-0.13	0.20	-0.42	0.02
Cr	**0.67**	-0.18	0.07	0.51	0.05	0.36
Cs	**0.54**	0.21	-0.40	-0.04	0.53	0.12
Fe	0.33	0.20	0.26	0.11	-0.39	-0.66
Hf	**0.88**	-0.06	-0.05	0.07	0.13	-0.11
K	-0.32	**0.59**	-0.12	0.04	-0.55	0.14
La	**0.61**	0.49	0.30	-0.25	0.16	0.27
Mn	**0.63**	-0.07	0.19	-0.22	0.34	-0.43
Na	-0.69	-0.36	0.42	-0.04	-0.03	0.10
Rb	-0.40	**0.65**	-0.21	0.25	0.46	-0.12
Sb	**0.71**	-0.54	0.11	0.01	0.18	0.19
Sc	**0.95**	0.02	-0.06	0.02	0.01	0.02
Se	-0.22	-0.68	-0.42	0.05	-0.06	-0.13
Th	**0.92**	-0.19	0.06	0.07	-0.30	0.04
Zn	0.15	-0.08	**-0.57**	**-0.68**	-0.06	-0.20
% Variance explained	0.35	0.14	0.11	0.09	0.08	0.07

The first four interpretable factors, in addition to age, sex and tobacco, were considered as explanatory variables in an initial regression model, with ^{210}Po concentration as the response variable. In a backward robust model fitting process, predictor variables that had no additional significant contribution to explain the concentration ^{210}Po, in the presence of the other predictors, were excluded from the model, one by one. A summary of the results in the final step of the model fitting is presented in Table 5. The results indicate that, for individuals of the same age and sex, ^{210}Po concentration tends to increase with the increase in vehicle emissions.

Table 5

Results in the final regression model with ^{210}Po as response variable

Predictor	Coefficient	Standard error	t-value
Intercept	6.7	1.4	4.64
Male	-1.9	0.50	-3.88
Age (years)	-0.05	0.02	-2.86
Factor 1	0.90	0.33	2.73

Discussion

The concentrations of metal and ^{210}Po traces in human lung tissue from São Paulo city residents indicated that there is a close association between exposures to air pollution. Urbanization process has promoted a better quality of life, however, it has also caused a series of environmental impacts that directly or indirectly affect human health, such as air pollution. In Sao Paulo city, weak national and local environmental legislation, unplanned urbanization, industrial structure, unsustainable pattern of energy consumption and generation and road based transportation are major drivers of our deteriorated air quality.

The effects of air pollution on human health vary from moderate to severe effects and depend on the concentration to which individuals are exposed, its composition, age and presence of preexisting diseases.

The presence of heavy metals associated with fine particulate matter is one of the determinants of health risks posed by air pollution. Different studies that evaluated the elemental composition of particulate air pollution from Sao Paulo city have shown positive results for the following metals: SO4(2-), NO3-, NH4+, Zn, Fe, Al, Ba, Cu, Pb, Mn and Ni [23]

Particulate matter is generated essentially by the incomplete burning of fossil fuels and biomass. Other particles can be generated from sources unrelated to the combustion process, such as brake, tire, clutch and road surface release [24]. In general, it consists of a central elementary carbon core and on its surface other compounds are bounded, such as metals [25,26]. In addition, PM are capable of carrying radioactive particles [27].

In this study we demonstrated that the presence of Po210 in lungs of Sao Paulo city residents is associated with vehicular emission/air pollution. Other metals detected in lung tissues are also related to exposure air pollution and time of residence in the city and time spent commuting are also determinant.

After inhalation, Radon and its progenies can deposit somewhere along the respiratory tract, increasing the risk of cancer2 and non-cancer diseases [28] Radon is the second leading cause of lung cancer resulting in approximately 21,000 lung cancer deaths each year in the US (EPA). In Europe, it is estimated that approximately 3,000 deaths are caused by exposure to radon annually. The World Health Organization (WHO) estimates that radon is the leading cause of lung cancer, accounting for up to 14% of cases worldwide [13]

Some metals are required for different cellular functions and homeostasis, however, depending on the dose and exposure duration they can be toxic affecting different physiological processes. Most of the evidence on the negative effects of inhaling heavy metals inhalation come from occupational exposures[29]. For example, occupational exposure to cobalt metal or cobalt-containing hard metal is associated with respiratory effects such as asthma, interstitial lung disease, wheezing, and dyspnea (https://www.atsdr.cdc.gov/toxprofiles/tp33.pdf). Studies on the effects of environmental exposure to low levels of heavy metals in humans, as chromium are scarce, however prolonged occupational exposure are related to negative effects on the respiratory system, kidney and liver and cancer [30]

Zinc is found as ZnO in particulate air pollution [31] and depending on the inhaled concentration it can induce respiratory distress in response to metal deposition [32]

A meta-analysis conducted by Catalini et al. [33] evaluate the concentrations of metals in lung tissue as factors involved into the development of lung cancer. Results have shown that Zn and Cu were the metals more represented, and there is no clear relationship between concentrations and age. Just one study included in the meta-analysis found a positive correlation between Ni and Cr concentrations and age [34]. Among smoker, concentrations of Al, Cd, Cr, Ni, Pb and Mn were higher, but results could be biased by past occupational exposure to metals Tsuchiyama et al [35]Cr and Pb showed the highest concentrations.

Although it is descriptive study using a small sample, it has many strengths. The detailed interview with a family member about the individual's daily activities, potential occupational exposure, tobacco use, time spent in traffic, and the assessment of lifetime exposure using the pulmonary anthracosis index made it possible to control factors that could bias the results of the analysis.

The analysis and characterization of the presence of these metals in the lungs of residents of the city of Sao Paulo allows us to more plausibly infer and suggest the contribution of the exposure to air pollution to different diseases associated with exposure to heavy metals and radioactive elements, such as lung cancer, hematological and neurodegenerative diseases. Besides, knowing which metals are Hence, knowing

In addition, knowledge about the presence of metals in human tissues may allow us to identify new sources of exposure and create measures to reduce or protect human health

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Declarations

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Data availability statement: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Human experiment statement: All legal guardians signed the informed consent before the pathological procedures (supplementary material). This study was approved by the Research Ethics Committee of the University of Sao Paulo (number 2013/21728) in accordance with relevant regulations.

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