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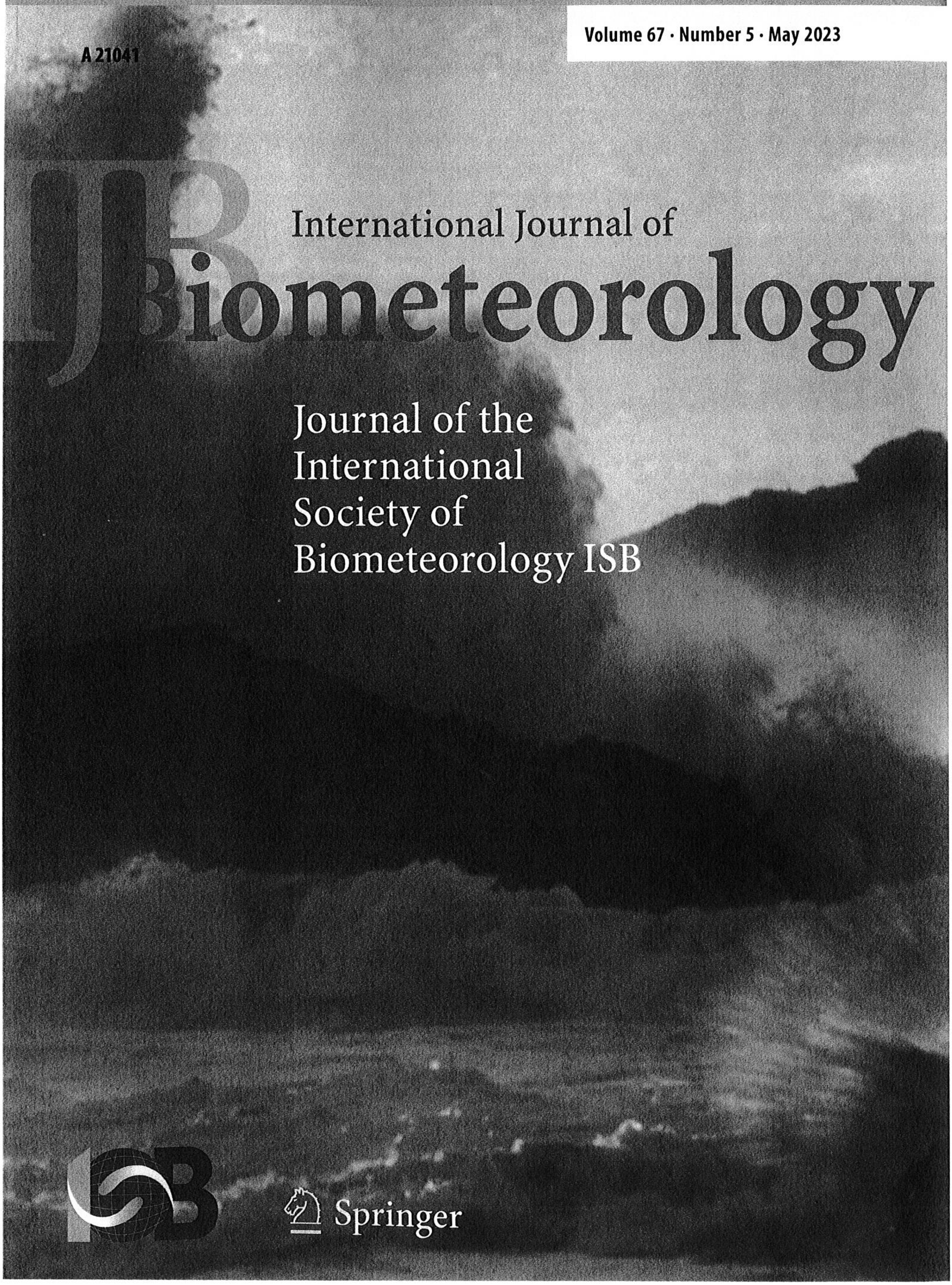

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ORIGINAL PAPER

Assessment of barium diffusion from therapeutic mud wrapped in micro-perforated polyethylene bags towards the human organism

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Abstract

Barium is present within the clay-derived therapeutic mud packs deposed on the patient's skin for treating some rheumatologic conditions. We studied in twenty-four young healthy volunteers the diffusion of Ba from mud wrapped in micro-perforated polyethylene bags and soaked in mineral water. No significant systematic increase in plasma or urine Ba levels was evidenced when comparing pre- and post-treatment samples using inductively-coupled plasma mass spectrometry. These levels were markedly inferior to the recommended thresholds in nearly all the participants. Noticeably variability in blood and especially urine Ba concentrations was large and mainly explained by environmental exposure (alimentation). Interestingly, we evidenced an intense Ba accumulation within the therapeutic mud at the end of the regimen. Because we chose a clay with one of the highest Ba content available in France for medical therapy and participants with an optimal transcutaneous diffusion capacity (young individuals with low-fat mass), we conclude unambiguously that there is no risk of Ba overexposure in patients receiving pelotherapy according to the procedure used in French medical spas.

Keywords Barium · Pelotherapy · Thermal muds · Environmental health

Introduction

Barium (Ba), atomic number 56, is an alkaline earth component present in numerous environmental media. Several chemical forms of Ba occur in nature. They include mainly $BaCO_3$ which can be harmful after ingestion, because of its high solubility in acid solutions, as that of the stomach and $BaSO_4$ (used by radiologists for exploring the human digestive tract). These Ba salts seem not to be carcinogenic or teratogenic in animals. Ba is used in various industries (petroleum and its derivatives) and generated by waste sites (Oskarsson 2015; Krishna et al. 2020). It is a non-essential element for the human organism which contains about 22 mg of Ba salts concentrated within the skeleton and teeth and derived mainly from ingestion of water and vegetal products and breathing. Hydrosoluble compounds are associated with health effects. Ba levels in the body are influenced by several factors including the dose, duration, route of exposure, age, sex, genetics, lifestyle, and state of health (Krishna et al. 2020). Circumstances of human overexposure include acute (suicidal ingestion) or chronic poisoning via consumption of contaminated of food and water (often related to waste sites) or mainly professional inhalation exposure (Oskarsson 2015; Krishna et al. 2020; Peana et al. 2021).

The key Ba-associated biological disturbance is significant hypokaliemia leading to myocardial and respiratory disturbances (risk of cardiac arrest and respiratory paralysis) and muscle dysfunction (Oskarsson 2015). Hypertension is the main observable clinical effect in humans following acute exposure (WHO 2015; Peana et al. 2021). In case of long-term intoxication lung deposits (baritosis) and renal failure may appear (Oskarsson 2015). The metabolization of Ba is not well known but its uptake seems similar to that of calcium and strontium (Kravchenko et al. 2014). The feces and urine are the major routes for excretion (about 90% and 10–28%, respectively) (Krishna et al. 2020).

Sébastien Labarthe and Karine Dubourg contributed equally to this work and must be considered as first authors.

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Being present in the soil Ba is found in higher concentrations in some muds (Atun and Bascetin 2003). This material can be used for therapeutic purposes within the context of pelotherapy (Maraver et al.. 2021). The term "pelotherapy" was first coined in the medicoscientific literature in 1934 (Anonymous 1934). During this procedure, patients receive for 9 to 18 consecutive days a cutaneous application of heated thermal mud for a period of 10 to 15 min. Most often, the mud is included in packs (or poultices) deposed on various skin areas (Gomes et al. 2013) (see Material and methods and Fig. 1). Nevertheless, the diffusion of Ba towards the human organism via mud-related cutaneous exposure has not been studied so far. Hence, following the recommendations from the French National Academy of Medicine which expressed the need for excluding potentially harmful consequences (Roques-Latrille et al. 2017), we assess here for the first time plasma and urine Ba concentrations in a sample of individuals treated by a 3-week pelotherapy protocol commonly used in French thermal care facilities.

Material and methods

Participants

Twenty-four young volunteers (eleven males and thirteen females) aged between 18 and 28 years (median: 18) participated in this study. They had been selected on the basis of the following exclusion criteria which included: pregnancy or absence of contraception for women during the study period, body mass index (BMI, weight (kg)/size^2 (m^2)) > 30 kg/m^2 (obesity), known allergy to metals, skin lesions of any type, alteration of skin sensitivity, intolerance to hot, cardiac, renal or pulmonary disorder, acute (inflammatory, infectious or tumoral) disease, drugs non-compatible with a pelotherapy regimen. These subjects were students from our institution and had no professional exposure to Ba. Ba concentrations in tap water from the Dax area where live these individuals were between 0.020 mg/L and 0.026 mg/L (data from the Regional Health Agency 2021).

Inclusion visits were performed by the same physician (FB) and occurred at day 1 (just before the beginning of the pelotherapy procedure) and day 15 (at the end of the procedure). It included, at baseline, a checking for confirming that each individual fulfilled all the criteria for participation and an assessment of the following variables: height and weight allowing the body surface and BMI calculation (formula: weight/(height)^2 expressed in kg/m^2), systolic and diastolic blood pressure (sphyngomanometer, Spengler, Paris), cardiac and respiratory frequencies, and fat mass percentage determined from four skinfold thickness measurement of the biceps, triceps, subscapular, and suprailiac regions on the dominant side using the Harpenden® caliper device (Durnin and Womersley 1974) (Fig. 1). Variations in heart rate and blood pressure between pre- and post-pelotherapy were assessed because they are considered as indicators of Ba acute poisoning (Peana et al. 2021).

Pelotherapy regimen

The native extracted clay originating from Bouillac, Dordogne, France, was conditioned in calibrated mud packs (450 g, 15 × 30 cm, surface on skin: 0.27 m^2) and wrapped in hospital-quality micro-perforated low-density polyethylene obtained by a high-pressure process (Argicur®, Le Buisson, France). This clay was made of 70–80% montmorillonite, 10–15% kaolinite, and 10–15% illite and the pH was at 8–9. Ba concentration was 99.1 mg/kg ± 0.1 dry matter.

The pelotherapy protocol was identical to that used in French thermal centers. Each mud-pack was immerged within 1.5 L mineral water as an initial soaking during 4 h.

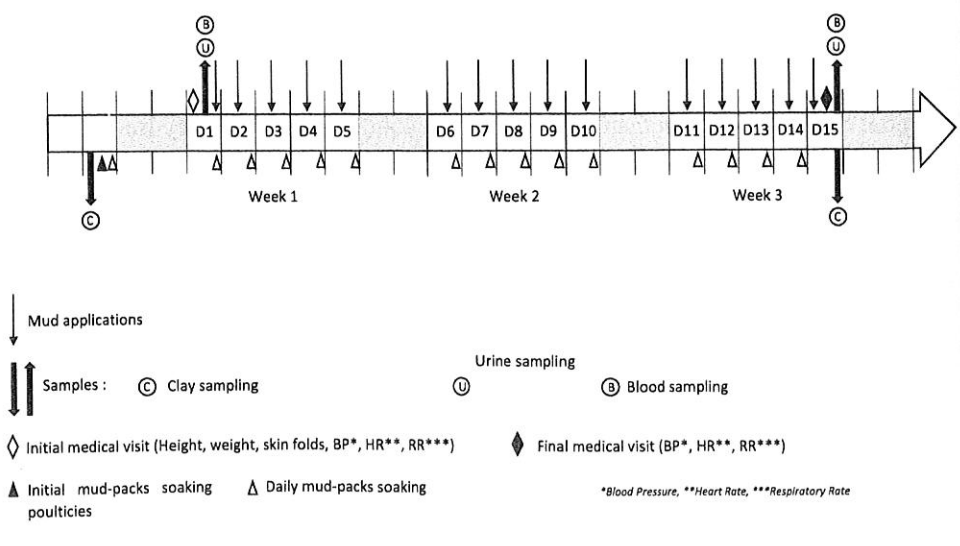


Fig. 1 Summary of our protocol agenda

This mineral water came from Saubusse (Landes, France), a small thermal site located near our institution. Its main physicochemical characteristics were the following: pH: 7.40, conductivity at 20 °C: 1084 µS/cm, Na^{+}: 162 mg/L, K^{+}: 12 mg/L, Ca^{++}: 52 mg/L, Mg^{++}: 19 mg/L, total cations: 246.38 mg/L, HCO_3^{-}: 151.76 mg/L, Cl^{-}: 240 mg/L, SO_4^{-}: 106 mg/L, total anions: 499.54 mg/L, SiO_2: 12,44 mg/L Metal and non-metal concentrations in the clay and mineral water are presented on Table 1. Therefore, these mud packs were put on trays and stored in a heated chamber (Stas Doyer, Muret, France) with recurrent 2-h stages at 70 °C for microbial decontamination and submitted to daily mineral water addition (about 200 mL) in order to maintain a stable level of hydration during the 3-week protocol (Fig. 1). Six-packs (final temperature: 42–47 °C) were applied by the same operator (SL) on shoulders, knees, and dorsal spine of participants in underwear as depicted on Fig. 2, during 15 min for a total of 15 daily sessions (3-week regimen of 5 consecutive days, no sessions on Saturday and Sunday). The same set of six packs was used for each person during all the sessions.

Table 1 Metal and non-metal elements concentration in the tested clay (Argicur®, Le Buisson, France) and mineral water (Saubusse, Landes, France)

Elements	Clay (mg/kg, dry matter)*	Mineral water (mg/L)**
Metals		
Barium (Ba)	***99.1 ± 0.1***	***0.016***
Antimony (Sb)	< 3	< 0.001
Arsenic (As)	4.45 ± 0.1	0.013
Beryllium (Be)	3,6 ± 0.1	< 0.00005
Cadmium (Cd)	< 0.3	< 0.001
Chromium (Cr)	41 ± 0.1	< 0.001
Cobalt (Co)	9.1 ± 0.1	NA
Copper (Cu)	16 ± 0.1	< 0.001
Mercury (Hg)	< 0.050	< 0.0001
Nickel (Ni)	21 ± 0.1	< 0.001
Lead (Pb)	16 ± 0.1	< 0.001
Zinc (Zn)	67 ± 0.1	0.003
Tin (Sn)	< 5	NA
Molybdenum (Mo)	< 1	NA
Vanadium (V)	37 ± 0.1	NA
Iron (Fe)	NA	0.460
Lithium (Li)	NA	0.020
Manganese (Mn)	NA	0.058
Strontium (Sr)	NA	0.740
Aluminum (Al)	NA	0.006
Non-metals		
Fluorine (F)	NA	0.500
Iodine (I)	NA	0.0270
Boron (B)	NA	0.150
Selenium (Se)	< 5	0.001

Data on Barium are marked in bold characters

*Data provided by Argicur®, Le Buisson, France

**Data provided by the Laboratory of Hydrology, University of Bordeaux, France

NA, not assessed

Biological sampling

Blood samples were collected using 4 mL lithium heparine polyethylene sterile tubes (BD Vacutainer®, Becton Dickinson, le Pont de Claix, France). Urine was collected in 100 mL polyethylene sterile flasks (Sarstedt, Nümbrecht, Germany) and transfered in Monovette® sterile tubes (Sarstedt, Nümbrecht, Germany).

Mud packs sampling

Ba levels were also determined in the clay from mud packs. The Ba content of clay was assessed on 5 g aliquots before soaking and at day 15 in two samples: sample 1 from the mixing of mud-pack content from participants 1 to 12 and sample 2 from participants 13 to 24.

Ba dosing technology

After collection, samples were conserved at + 4 °C and transported at this temperature using ice packs (TSE Medical, Lyon, France) during less than 24 h. Ba dosages in plasma, urine, and therapeutic materials (clay, water) were performed using inductively-coupled plasma mass spectrometry (ICP-MS) (Elan DRCe®, Perkin Elmer, Villebon sur Yvette, France) at the laboratory of Toxicology, Hôpital Lariboisière, Paris. Biological samples were prepared for dosing according to the classical nitric acid dilution method (Cesbron et al. 2013; Hoët et al. 2013). Clay samples were immerged within 50 mL ultrapure water under agitation overnight and therefore centrifuged. The supernatant was used for dosing.

ICP-MS detection limits for Ba are respectively 0.01 µg/L with plasma (Cesbron et al. 2013), 0.135 µg/L with urine (Hoët et al. 2013), and 0.001 µg/L with water (Rosborg et al. 2003). Urinary Ba concentration was divided by creatinine concentration to obtain a creatinine-adjusted urinary concentration, expressed as µg/g of creatinine.

Interpretation of results

Our results were compared with the most restrictive European thresholds (Cesbron et al. 2013): plasma < 1.22 µg/L and urine < 6.97 µg/L and < 6.00 µg/g creatinine (Hoët et al. 2013). Continuous data were described by their means ± standard deviations and compared by t-test (or

Fig. 2 Topography of mud packs application (6 × 0.27 m.[2])

Mann–Whitney test when appropriate); categorical data were described by percentages and compared by chi-square test (or Fisher exact test when appropriate). We used the Wilcoxon test (significance level set at p: 0.05) to compare Ba concentrations before and after pelotherapy. Statistical analyses were performed using the IBM SPSS Statistics 25 software.

Ethics

All the participants have given their written consent. This protocol, registered on clinicaltrials.gov (identifier: NCT04111653), was in accordance with the ethical standards of the institutional and national research committee (approved by an independent ethic committee: *Comité de Protection des Personnes, Région Centre Ouest 1*, Tours, France under the n°2019T2-2019) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Results

The characteristics of the 24 participants are reported in Table 2. Mean and range were respectively for body surface: 1.76 m^2/1.49–2.13, BMI: 21.63 kg/m^2/16.65–26.18), and fat mass percentage: 19.0%/7.3–29.2. Ba concentrations in plasma and urine before and after pelotherapy are shown in Figs. 3 and 4. Overall, no significant variation in plasma (p: 0.48) or urine (absolute values, p: 0.96, urinary Ba levels/urinary creatinine, p: 0.70) Ba concentrations were evidenced. Ba was above the recommended threshold in two individuals who experimented significant variations in Ba plasma levels when comparing day 1 and day 15 results: n°13 with a + 85% increase and n°14 with a − 57% decrease. The largest variations were observed in individuals n° 8: + 143% and n° 10: − 74%. In both cases, Ba levels remained low and markedly inferior to the threshold. Urinary Ba levels were all markedly inferior to the safety limit except for the pre-pelotherapy sample from case n°20 when considering the Ba/creat ratio. One individual (n° 17) demonstrated a marked increase at day 15 (+ 830% and even + 1292% regarding Ba/creat) (Fig. 4) constrasting with very low and decreasing plasma levels (Fig. 3). Thus, variability in blood and especially urine Ba concentrations was large, unrelated to pelotheray and probably explained by environmental exposure (alimentation) as reported in the literature (WHO 2001; US EPA 2005; Kravchenko et al. 2014; Oskarsson 2015; Peana et al. 2021). Interestingly participants n°13 and 14 who have demonstrated marked variations in plasma Ba between pre- and post-pelotherapy had changed of residency during this period which could argue in favor of the modification of environmental exposure regarding food and drinking water. The small size of the sample did not allow us to investigate the effect of BMI, fat mass percentage or sex on Ba diffusion. No increase in BP and HR was observed when comparing pre- and post-pelotherapy values (Fig. 5).

There was a marked increase in Ba concentration in the clay from mud packs when comparing day 1: 99.1 µg/L and day 15: 178.7 (sample 1) and 153.5 µg/L (sample 2). Our final plasma and urine Ba levels and these results on therapeutic clay support the hypothesis of a Ba retention within the therapeutic material and therefore a negligible tendency to diffusion towards the human organism.

Table 2 General characteristics of tested individuals ($n = 24$)

N°	Age (years)	Sex	Size (m)	Weight (kg)	Body surface area (m^2)	BMI (kg/m^2)	Fat mass (%)	SBP (mm Hg)	DBP (mm Hg)
1	18	F	172	57	1.67	19.27	18.4	110	70
2	18	F	155	52	1.49	21.64	26.3	130	75
3	18	M	189	86	2.13	24.08	13.8	110	80
4	18	M	176	68	1.83	21.95	11.8	130	80
5	18	M	176.5	68	1.84	21.83	14.5	120	70
6	18	F	170	64	1.74	22.15	19.3	135	85
7	18	F	169	66	1.76	23.11	28.3	110	80
8	18	F	171	55	1.64	18.81	16.9	125	90
9	18	F	168.5	58	1.66	20.43	16.3	145	80
10	18	F	175	51	1.62	16.65	17.9	125	75
11	21	M	181	74	1.94	22.59	17.0	135	90
12	18	M	172.5	50	1.59	16.80	11.8	110	80
13	21	M	180	72	1.91	22.22	16.1	140	85
14	19	F	167	73	1.82	26.18	27.1	120	70
15	19	F	163	65	1.70	24.46	28.7	120	80
16	19	F	157	52	1.51	21.10	23.4	105	70
17	18	F	163	58	1.62	21.83	22.4	120	80
18	18	M	180	75	1.94	23.15	20.3	119	85
19	28	F	158	53	1.52	21.23	29.2	130	80
20	25	M	177	56	1.69	17.87	7.3	110	70
21	22	M	180	76	1.95	23.46	15.2	110	70
22	22	M	186	78	2.02	22.55	16.1	130	80
23	22	F	160	60	1.62	23.44	25.6	105	70
24	23	M	181	73	1.93	22.28	12.7	120	80

Abbreviations used: *M*, male; *F*, female; *BMI*, body mass index; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure

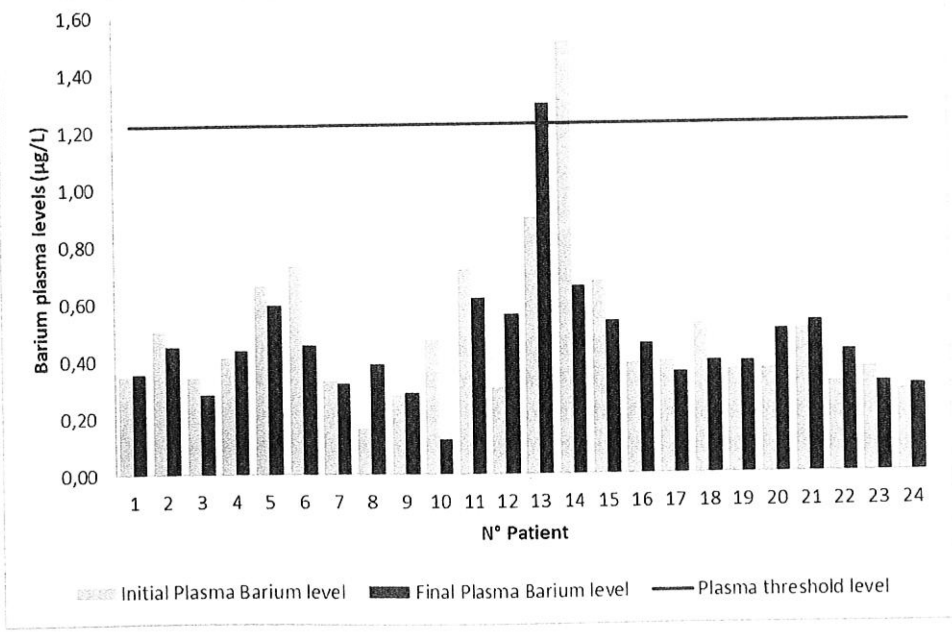


Fig. 3 Evolution of barium levels between pre- (day 1) and post- (day 15) pelotherapy in plasma ($n = 24$). The horizontal bar at 1.22 µg/L represents the upper normal limit (95th percentile) according to Cesbron et al.. 2013

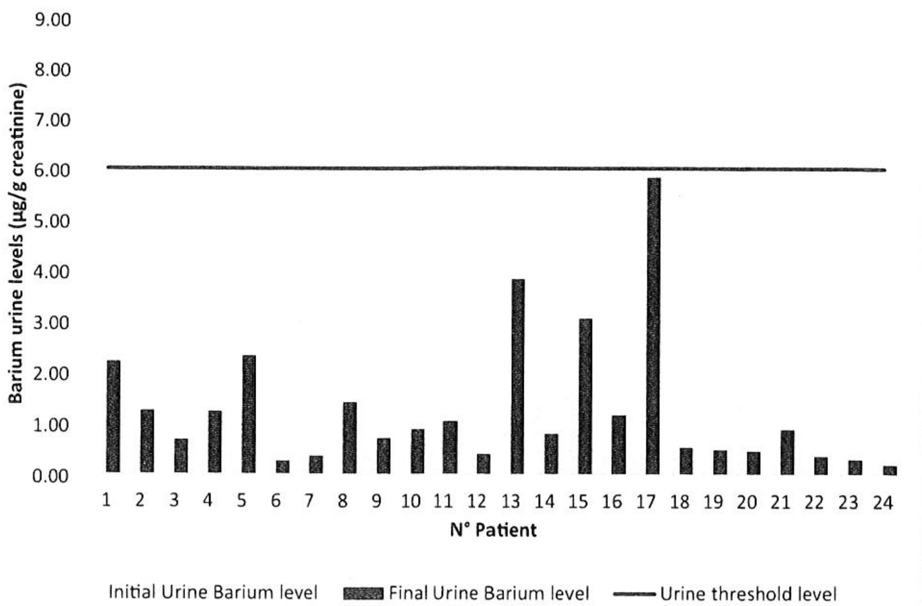
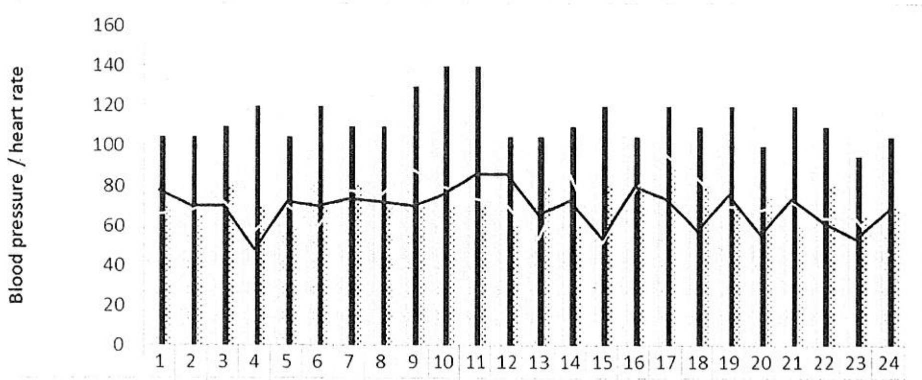


Fig. 4 Evolution of creatinine-adjusted urinary barium levels expressed as mg/g of creatinine between pre- (day 1) and post- (day 15) pelotherapy ($n = 24$). The horizontal bar at 6 µg/g creatinine represents the upper normal limit (95th percentile) according to Hoët et al.. 2013



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
D1 SBP	110	130	110	130	120	135	110	125	145	125	135	110	140	120	120	105	120	119	130	110	110	130	105	120
D1 DBP	70	75	80	80	70	85	80	90	80	75	90	80	85	70	80	70	80	85	80	70	70	80	70	80
D15 SBP	105	105	110	120	105	120	110	110	130	140	140	105	105	110	120	105	120	110	120	100	120	110	95	105
D15 DBP	70	65	80	70	60	70	80	70	70	70	70	60	80	60	80	80	90	80	70	75	60	80	65	70
D1 HR	66	68	72	58	70	60	78	76	88	80	74	70	54	86	52	78	96	84	70	68	72	64	64	46
D15 HR	78	70	70	48	72	70	74	72	70	76	86	86	66	73	54	80	74	58	76	56	74	62	54	68

N° Patient

Fig. 5 Systolic (SBP)/diastolic (DBP) blood pressure (mm Hg) and heart rate (HR) (beats/min) variations between pre- (day 1) and post- (day 15) pelotherapy regimen in our 24 participants

Discussion

In France, about 6,000,000 mud-based treatments are delivered to 400,000 patients per year (Ainouche et al. 2014). A series of clinical and biological studies support the efficacy of this approach especially for treating osteoarthritis (Xiang et al. 2016; Ortega et al. 2017; Maraver et al. 2021). In 2017, the French National Academy of Medicine drew the following conclusion based upon a literature review: *Transdermal absorption can be discussed for ionized Barium and/or soluble salts. The data are few, the issue remains unclear. So investigations have to explore transfers of barium from muds to the blood. The data obtained from biological investigations and vigilance would draw conclusions on the (un) suitability of the presence of barium in thermal muds* (Roques-Latrille et al. 2017). For the first time, we assessed the diffusion of Ba from mud packs wrapped in micro-perforated polyethylene bags towards the body fluids (plasma and urine). Our study demonstrates unambiguously that this pelotherapy administered as in our experiment is not associated with a harmful exposure to Ba. We acknowledge the fact that mud was included in polyethylene containers and deposed on small areas of skin. In order to strengthen the validity of our conclusions, we chose experimental conditions which could favor Ba diffusion towards the human body. First, our participants were young non-obese individuals acknowledging the fact that both aging (Roskos et al. 1989; Roskos and Maibach 1992) and subcutaneous fat excess (Cheymol 1993) reduce the skin diffusion of drugs. Second, we selected a clay with a higher Ba content than that observed in the French real-life practice (99 mg/kg *versus* 84 mg/kg) (Roques-Latrille et al. 2017). However, this content is far below the levels that could be found in some particular geological contexts as, for instance, up to 636 mg/kg in the North American shale composite (Gromet et al. 1984). Our procedure (duration of exposure, clay quantity and temperature, application sites) was that proposed in everyday French pelotherapy. We used the ICP-MS technique which represents the most preferred method for metals dosage (Goullé et al. 2005; Łukasik-Głębocka et al. 2014; Oskarsson 2015). In the human body, Ba can be dosed in whole blood, plasma, erythrocytes, urine, or hair (Goullé et al. 2005). We chose to assess plasma and urinary levels which have been both commonly included in biomonitoring studies especially in our country (Goullé et al. 2005; Cesbron et al. 2013; Poddalgoda et al. 2017). In addition, nearly all Ba in the blood is present in the plasma (Oskarsson 2015). Of note, urinary Ba levels reflect recent exposure (i.e., the past 3 days since exposure) and do not significantly differ between males and females (CDC 2009). They represent sensitive indicators of Ba exposure because it has been shown that in occupationally exposed welders they were elevated up to 60 times above the average population (Zschiesche et al. 1992). The 95th percentile of urinary Ba levels was 6.8 μg/L in the USA (CDC 2009).

Throughout the protocol period, the majority of Ba remained within the clay, and therefore, only small amounts of this metal were disponible for transcutaneous diffusion. Following pelotherapy, we did not detect significant BP elevation (but conversely decrease in both systolic and diatolic values) nor changes in HR which represent the most frequent acute poisoning effects associated with Ba (WHO 2015; Peana et al. 2021).

Variability in plasma and especially urine Ba concentrations was markedly high. Several participants demonstrated important decreased plasma or urine Ba levels after pelotherapy. No association between pelotherapy and the evolution of Ba contents in participants could be established. There is a large amount of data supporting that Ba concentration variations in human organisms are mainly related to differences in Ba concentration in food and, at a lesser extent, in drinking water (WHO 2001; US EPA 2005; Kravchenko et al. 2014; Oskarsson 2015; Peana et al. 2021). In France, the Ba daily dietary intake has been estimated at 6.4 μg/kg per day in adults (range: 5.86–6.99, 95th percentile: 10.5), with bread representing the main source, and including a concentration of 44 μg/L in drinking water (ANSES 2011). The collection of precise data regarding dietary intake during the study period was beyond the scope of this study. However, it is noteworthy that there was a geographic modification of residency occurring during the study period in the two participants who demonstrated the most important variations in Ba levels: n° 13 from Andernos (150 km northward) before moving to our city and n° 14 from Northern France to Pontonx (Landes). One can speculate about the influence of a probable difference in Ba intake. Our protocol design did not include a systematic assessment of residency changes in our participants during the study period; therefore, this point cannot be discussed further. However, we have no precise data on the correlation between Ba levels in the human organism and in drinking water and diet (WHO 2001; Moffett et al. 2007) except the study of Kato et al. (2013) regarding Ba levels in urine and in well drinking water.

The chemical and physical properties of clays represent a very complex issue (Carretero 2020). Clays demonstrate particular heat capacities which are influenced (among many other factors) by the intensity of water soaking (Knorst-Fouran et al. 2012). They are able to absorb and exchange cations according to their mineral content and pH (for example kaolinite cation exchange capacity is around 3–18 milliEq/100 g at pH 7) and interact with water (Huggett 2005). Interestingly, our clay is made of 70–80% montmorillonite which demonstrates a high capacity of cations and propensity for Ba (Ba^{2+}) adsorption and swelling (Atun and Bascetin 2003). Hence, montmorillonite may be used as a powerful nano-adsorbent agent for all metals from the environment (Altigh et al. 2021). Furthermore, in an experimental model using several Spanish spa peloids and artificial human sweat, no significant leaching of Ba in the sweat was observed (Carretero et al. 2010). Here, from the beginning to the end of the pelotherapy protocol, we found increased Ba concentration in mud packs (an about doubling) after repeated water soaking. This clearly shows that Ba is able to easily permeate the pore openings of our polyethylene containers. In conclusion, the study demonstrated that there is no significant penetration of Ba in the human body after the application of mud wrapped in microperforated polyethylene bags with the geological material and procedure used in French medical spas. The capacity of Ba transcutaneous diffusion has not been documented hitherto but large quantities deposed on the skin may generate lesions (WHO 2001). Of course, BP and HR monitoring did not notice significant increases suggesting acute Ba poisoning (Fig. 5). Our results support the "organic hypothesis" in balneotherapy (Varga 2010) suggesting that inorganic ions are marginally taken up by the human body. Other metals present in clays may be of concern for pelotherapy, and we are currently targeting this point within the context of an additional specific study.

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Author contribution Sébastien Labarthe: conceptualization, investigation, formal analysis, writing review & editing; Karine Dubourg: conceptualization, funding acquisition, project administration, writing review & editing; Jérôme Dimet: formal analysis; Frédéric Bauduer: conceptualization, methodology, investigation, supervision, writing original draft.

Declarations

Conflict of interest The authors declare no competing interests.

References

Ainouche R, Tabone W, Bouvier CE, Renaud V (2014) Usage thérapeutique des boues thermales, panorama du thermalisme français en 2013. Bull Assoc Fr Therm 25:7–11

Altigh ZBQ, Sardari P, Moghiseh E, Lajayer BA, Hursthouse AS (2021) Purified montmorillonite as a nano-adsorbent of potentially toxic elements from environment : an overview. Nanotechnol Environ Eng 6:12

Anonymous (1934) Pelotherapy. Nature 133:288

ANSES (2011) Second French total diet study (TDS 2) report 1. Inorganic contaminants, minerals, persistent organic pollutants, mycotoxins, and phytoestrogens. Maisons-Alfort: French Agency for Food, Environmental and Occupational Health & Safety. http://www.tds-exposure.eu/sites/default/files/WP1/RapportEAT2EN1.pdf. Accessed 3 Jun 2015

Atun G, Bascetin E (2003) Adsorption of barium on kaolinite, illite and montmorillonite at various ionic strengths. Radiochim Acta 91:223–228

Carretero MI, Pozo M, Martin-Rubi JA, Pozo E, Maraver F (2010) Mobility of elements in interaction between artificial sweat and peloids used in Spanish spas. Appl Clay Sci 48:506–515

Carretero MI (2020) Clays in pelotherapy. A review. Part I: mineralogy, chemistry, physical and physicochemical properties. Appl Clay Sci 189:105526

CDC (2009) Fourth national report on human exposure to environmental chemicals. Department of health and human services centers for disease control and prevention, Atlanta, USA

Cesbron A, Saussereau E, Mahieu L, Couland I et al. (2013) Metallic profile of whole blood and plasma in a series of 106 healthy volunteers. J Anal Toxicol 37:401–405

Cheymol G (1993) Clinical pharmacokinetics of drugs in obesity. Clin Pharmacokinet 2:103–114

Durnin JV, Womersley J (1974) Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. Br J Nutr 32:77–97

Gomes C, Carretero MI, Pozo M, Maraver F, Cantista P, Armijo F, Legido JL, Teixeira F, Rautureau M, Delgado R (2013) Peloids and pelotherapy: historical evolution, classification and glossary. Appl Clay Sci 75–76:28–38

Goullé JP, Mahieu L, Castermant J, Neveu N, Bonneau L, Lainé G, Bouige D, Lacroix C (2005) Metal and metalloid multi-elementary ICP-MS validation in whole blood, plasma, urine and hair. References values. Forensic Sci 153:39–44

Gromet LP, Haskin LA, Korotev RL, Dymek RF (1984) The "North American shale composite": its compilation, major and trace element characteristics. Geochim Cosmochim Acta 48:2469–2482

Hoët P, Jacquerye C, Deumer G, Lison D, Haufroid H (2013) Reference values and upper reference limits for 26 trace elements in the urine of adults living in Belgium. Clin Chem Lab Med 51:839–849

Huggett JM (2005) Clay minerals. In: Selley RC, Robin L, Cocks M, Plimer IR (eds) Encyclopedia of geology. Elsevier, Amsterdam, pp 358–365

Kato M, Kumasaka MY, Ohnuma S, Furuta A, Kato Y, Shekhar HU et al. (2013) Comparison of barium and arsenic well drinking water and in human body samples and novel remediation system for these elements in well drinking water. PLoS ONE 8:1–6

Knorst-Fouran A, Casas LM, Legido JL, Coussine C, Bessieres D, Plantier F, Lagiere J, Dubourg K (2012) Influence of dilution on the thermophysical properties of Dax peloid (TERDAX®). Thermochim Acta 539:34–38

Kravchenko J, Darrah TH, Miller RK, Lyerly HK, Vengosh A (2014) A review of the health impacts of barium from natural and anthropogenic exposure. Environ Geochem Health 36:797–814

Krishna S, Jaiswal A, Sujata GM, Sharma DK, Ali Z (2020) Barium poisoning with analytical aspects and its management. Int J Adv Res Med Chem 2:20–27

Łukasik-Głębocka M, Sommerfeld K, Hanć A, Grzegorowski A, Barałkiewicz D, Gaca M, Zielińska-Psuja B (2014) Barium determination in gastric contents, blood and urine by inductively coupled plasma mass spectrometry in the case of oral barium chloride poisoning. J Anal Toxicol 38:380–382

Maraver F, Armijo F, Fernandez-Toran MA, Armijo O, Ejeda JM, Vazquez I, Corvillo I, Torres-Piles S (2021) Peloids as thermotherapeutic agents. Int J Environ Res Public Health 18:1965

Moffett D, Smith C, Stevens Y, Ingerman L, Swarts S, Chappell L (2007) Toxicological profile for barium and barium compounds. Agency for toxic substances and disease registry. US Department of Health and Human Services, Atlanta, Georgia

Ortega E, Gálvez I, Hinchado MD, Guerrero J, Martin-Cordero L, Torres-Piles S (2017) Anti-inflammatory effect as a mechanism of effectiveness underlying the clinical benefits of pelotherapy in osteoarthritis patients: regulation of the altered inflammatory and stress feedback response. Int J Biometeorol 61:1777–1785

Oskarsson A (2015) Barium. In: Nordberg GF, Fowler BA, Nordberg M (eds) Handbook of the toxicology of metals, vol II. Specific Metals. Elsevier, London, pp 625–634

Peana M, Medici S, Dadar M, Zoroddu MA, Pelucelli A, Chasapis CT, Bjorklund G (2021) Environmental barium: potential exposure and health-hazards. Arch Toxicol 95:2605–2612

Poddalgoda D, Macey K, Assad H, Krishnan K (2017) Development of biomonitoring equivalents for barium in urine and plasma for interpreting human biomonitoring data. Regul Toxicol Pharmacol 86:303–311

Regional Health Agency (2021) https://orobnat.sante.gouv.fr

Roques-Latrille CF, Trèves R, Queneau P, Bontoux D (2017) Opinion of the French National Academy of Medicine on the evaluation of the health risks related to the presence of barium in clays constituting the thermal muds and the absence of sanitary control of the thermal mud. Bull Acad Natl Med 201:13–38
Rosborg I, Nihlgard B, Gerhardsson I (2003) Hair element concentrations in females in one acid and one alkaline area in South Sweden. Ambio 32:440–446
Roskos KV, Maibach HI, Guy RH (1989) The effect of aging on percutaneous absorption in man. J Pharmacokinet Biopharm 17:617–630
Roskos KV, Maibach HI (1992) Percutaneous absorption and age: implications for therapy. Drugs Aging 2:432–449
US EPA (2005) Toxicological review of barium and compounds. US Environmental Protection Agency, Washington DC
Varga C (2010) Balneoprevention: new approaches. Int J Biometeorol 56:195–197
WHO (2001) Barium and barium compounds. Concise International Chemical Assessment Document 33. WHO, Geneva
WHO (2015) WHO guidelines for drinking water quality. WHO, Geneva
Xiang J, Wu D, Li J (2016) Clinical efficacy of mudpack therapy in treating knee osteoarthritis. Am J Phys Med Rehabil 95:121–131
Zschiesche W, Schaller KH, Weltle D (1992) Exposure to soluble barium compounds: an interventional study in arc welders. Int Arch Occup Environ Health 64:13–23

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