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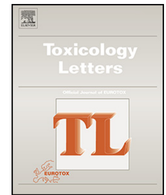

Investigation of saliva as an alternative matrix to blood for the biological monitoring of inorganic lead

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HIGHLIGHTS

- Lead exposure is measured by invasive blood sampling. A non-invasive alternative is desirable.
- We determine lead in blood and saliva in 105 UK workers, presenting a new method for saliva analysis.
- Blood–saliva correlation improves at higher exposures; unchanged by history, smoking or age.
- StatSure device is effective for high levels. Contamination hinders lower-level measurements.
- Saliva lead may be effective as a surrogate for blood lead only in highly-exposed populations.

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ABSTRACT

Introduction: Whole blood is the established matrix for biological monitoring of inorganic lead; however blood sampling is an invasive procedure. Saliva offers a potential non-invasive alternative. This study determines lead in whole blood and saliva. A novel method for saliva sampling and preparation is presented.

Methods: Paired blood and saliva samples were obtained from 105 occupationally exposed UK workers. Saliva was collected using a StatSure sampling device, and a nitric acid digestion step was incorporated. The utility of the device for this application was evaluated. Whole blood was obtained by venepuncture. Analyses were carried out by ICP-MS.

Results: The limit of detection for lead in saliva was 0.011 μg/L. Mean blank-corrected recovery from 10 μg/L spiked saliva was 65.9%. The mean result from blank saliva extracted through the StatSure device was 2.86 μg/L, compared to 0.38 μg/L by direct analysis. For the paired samples, median blood lead was 6.00 μg/dL and median saliva lead was 17.1 μg/L. Pearson's correlation coefficient for saliva lead versus blood lead was 0.457 (95% C.I. 0.291–0.596).

Conclusions: ICP-MS analysis allows sensitive determination of lead in saliva with low limits of detection. The StatSure device is effective for high occupational exposures, but contamination from the device could confound lower-level measurements. Saliva would only be effective as a surrogate for whole blood for highly-exposed populations, although with further work it may have applications as a biomarker of recent exposure.

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1. Introduction

Workers in a wide range of industries are at risk of occupational exposure to lead. Although the adverse effects of acute lead poisoning are well-known, most incidences of lead toxicity occur through the accumulation of lead in the body by repeated exposures to small amounts (Thaweboon et al., 2005). Toxic effects of repeated low-level lead exposures include hypertension,

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alteration of bone cell function and reduction in semen quality (Goyer, 1993). Lead is also classified by the International Agency for Research on Cancer (IARC) as a class 2B carcinogen, indicating that "the agent is possibly carcinogenic to humans" (IARC, 2013). However, the major risk of lead exposure is toxicity to the nervous system, with the most susceptible populations being children, infants and the foetus (Goyer and Clarkson, 2001).

Lead may be absorbed into the body by several different pathways. In the UK, biological monitoring for lead is mandatory under the Control of Lead at Work Regulations (2002) where a worker's risk of lead exposure is considered significant by inhalation, ingestion or dermal absorption (HSC/HSE 2002). Whole blood is currently the matrix most commonly used for the determination of inorganic lead exposure and has been used as such for over fifty years (Agency for Toxic Substances and Disease Registry, 2007). However, blood sampling is an invasive procedure. Sample collection requires a qualified phlebotomist, and therefore incurs expense. The procedure also causes discomfort, which may be a source of stress to workers participating in monitoring. A non-invasive alternative would therefore be desirable.

As well as occupational exposures, lead exposure from environmental sources is increasingly a matter of concern, especially involving populations living in low-income urban communities (Nriagu et al., 2006). A cheap, simple, non-invasive sampling technique would facilitate much more extensive studies of such environmental exposures.

Several studies have explored saliva as an alternative matrix for the biological monitoring of lead (Koh et al., 2003; Nriagu et al., 2006; Barbosa et al., 2006; Costa de Almeida et al., 2009). The use of saliva would have several potential advantages: its collection is non-invasive and therefore there are no concerns over discomfort to participants; collection is straightforward and cheap to carry out; sample storage and transport arrangements are less complex than those for blood; and in addition the ethical approval for sampling is more easily obtained (Nriagu et al., 2006; Morton et al., 2014).

It is thought that the lead content of saliva may be related to the unbound fraction in the plasma (Nriagu et al., 2006), and as the plasma composition closely reflects that of the extracellular fluid, measuring salivary lead may therefore indicate the level of exposure to which most bodily cells are subjected (Costa de Almeida et al., 2009). However, using saliva does present some problems, particularly in the collection and preparation of the sample: the flow and ion content of saliva can vary significantly throughout the day; whole saliva may contain other substances such as food debris, bacteria and epithelial cells; and hand-to-mouth behaviour prior to sample collection could cause sample contamination (Barbosa et al., 2006). There is also no widely agreed method to adjust for how dilute/concentrated the saliva collected is (such as creatinine-correction for the analysis of urine).

The literature does not present a standard method for the collection and preparation of saliva samples. The use of stimulants to increase saliva flow, collection of whole saliva versus particular components of saliva, the choice of sampling device and the treatment of the saliva before analysis have been approached very differently by different authors (Koh et al., 2003; Nriagu et al., 2003 Barbosa et al., 2006; Costa de Almeida et al., 2009; Thaweboon et al., 2005; Morton et al., 2014).

Past studies have also produced very different results when comparing lead levels in blood and saliva. The saliva lead: blood lead ratio has varied from <1% (Barbosa et al., 2006) up to 271% P'an AYS, 1981. The correlation reported between saliva lead and blood lead has also varied: P'an AYS, 1981 and Morton et al. (2014) reported good correlations ($r = 0.80$ and $r = 0.69$ respectively) between log(blood lead) and log(saliva lead), Koh et al. (2003) reported a weaker correlation ($r = 0.41$) between log(saliva lead) and blood lead, whereas others have reported poorer correlations (Barbosa et al., 2006; Nriagu et al., 2006; Thaweboon et al., 2005).

In this study, paired samples of whole blood and saliva were collected from UK workers occupationally exposed to inorganic lead, as part of their routine biological monitoring schedule. The authors present a novel method for the collection and preparation of saliva for analysis, using a StatSure (StatSure Diagnostics Systems, Inc., New York, USA) saliva collection device and incorporating a nitric acid digestion preparation step, prior to dilution with an acid diluent. Whole blood was collected by venepuncture and diluted with an alkaline diluent. Analyses of both matrices for lead were carried out by inductively-coupled plasma mass spectrometry (ICP-MS).

The recovery of lead from a 10 μg/L spiked saliva sample using the StatSure device was evaluated, and components of the device tested individually for any lead emanating from them. The correlation between blood lead and saliva lead measurements in an occupationally-exposed cohort was calculated, and multiple regression analyses carried out to explore whether this relationship was affected by age, smoking status or the history of previous lead exposure.

2. Methods

2.1. Study cohort

This study determines lead levels in paired blood and saliva samples from a cohort of 105 UK workers routinely monitored for occupational exposure to inorganic lead. The study was approved by the National Research Ethics Service Committee East Midlands – Nottingham 1 (12/EM/0217). Consenting workers were asked to provide a saliva sample at the same time as their routine blood sample. Descriptive statistics of the sample cohort are provided in Table 1.

Table 1
Descriptive statistics of the sample cohort.

	All samples	History				
		1	2	3	Fluctuating history	No history
Number of paired samples	105	27	42	44	21	40
Number of smokers	53	11	19	19	10	24
Number of non-smokers	52	16	23	25	11	16
Age range (years)	18–65	19–65	19–65	19–65	21–55	18–58
Mean age (years)	37	40	42	42	33	32
Median age (years)	35	44	43	43	33	30
Mean Δ[a] (μg/dl)	0.63	−0.07	−0.53	−0.50	3.01	N/A
Standard deviation Δ[a] (μg/dl)	9.49	0.79	1.19	1.34	16.60	N/A
Median Δ[a] (μg/dl)	−1.00	0.00	−0.80	−0.80	−4.00	N/A
Δ[a] interquartile range (μg/dl)	−2.00–1.00	−1.00–0.89	−1.50–0.00	−1.53–0.19	−7.71–11.00	N/A

[a] Δ = the difference between the result of the study Pb(B) value and the mean of the historical Pb(B) observations.

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