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Investigation of Saliva as an Alternative to Blood Samples for the Biological Monitoring of Inorganic Lead

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Background

Workers in a wide range of industries are at risk of occupational exposure to lead. The toxic effects of inorganic lead have been known for centuries and in 2006 inorganic lead was reclassified as a probable human carcinogen (group 2A) by the International Agency for Research on Cancer. In the UK, routine biological monitoring for blood lead is compulsory for workers exposed to inorganic lead and lead compounds. This study investigates the feasibility of saliva as a less invasive matrix for the determination of lead exposures in workers.

Previous work by the Health and Safety Laboratory (HSL, in partnership with the Health Protection Agency) demonstrated a relationship between blood and salivary lead levels based on log-transformed data (correlation coefficient 0.65, $p<0.001$). Coventry Diagnostics have also developed a salivary lead method using commercially-available saliva sampling devices and nitric acid digestion. Their work on samples from environmental lead exposures (blood lead <10µg/dl) showed good agreement between blood and salivary measurements (mean results agreed with a 97.5% confidence interval) and demonstrated a 1:1 relationship.

Methodology

Paired samples of whole blood and saliva were collected from workers occupationally exposed to inorganic lead, as part of their routine biological monitoring schedule. One hundred and five workers provided samples. Saliva samples were collected using the Statsure sampling device (Figure 1), and blood samples by the standard routine sampling procedure. The saliva samples were frozen (in the device) upon receipt, and analysed as a single batch.

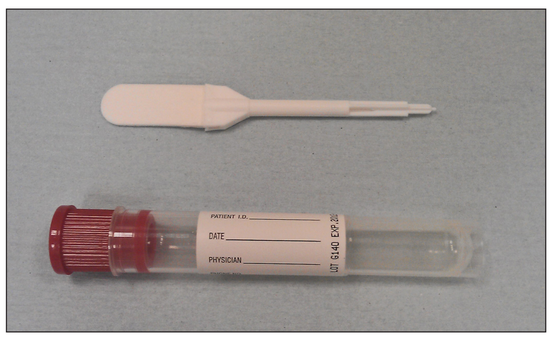

Figure 1: Statsure saliva sampling device – consisting of sampling paddle with volume indicator (above) and collection bottle with buffer (below).

Prior to analysis, each sampling device was thawed, mixed on rollers for 1 hour and then vortex-mixed for 10 seconds. The paddle was removed and discarded, and a 0.5ml aliquot of the saliva/buffer mixture was added to 0.5ml concentrated nitric acid in a sealed polypropylene tube. The tube was vortex-mixed for 10 seconds and heated for 1 hour at 100°C. After cooling, the mixture was diluted ten-fold (diluent: 1% nitric acid, 10µg/l Pt internal standard), resulting in an overall dilution of saliva of 1 in 40. Spiked saliva quality control material (2µg/l) was prepared and an aliquot extracted through a sampling device prior to analysis.

Analysis was carried out by inductively-coupled plasma mass spectrometry (ICP-MS, Thermo Fisher X7 Series 2) in normal mode with direct nebulisation, measuring ^{208}Pb and using ^{195}Pt as an internal standard.

Statistical analysis was carried out on the entire sample group, and also on a subset consisting of workers with a "steady" exposure history (i.e. blood lead levels stable for the previous two or more measurements).

Results

Summary statistics for the two datasets are shown in Table 1.

Table 1: Summary statistics for all workers and for workers with a "steady" history.

	All workers		Workers with "steady" history	
	Salivary Pb (µg/l)	Blood Pb (µg/dl)	Salivary Pb (µg/l)	Blood Pb (µg/dl)
Mean	40.2	8.34	31.3	7.68
Median	17.1	6	16.3	6
Range	3.4 - 349.4	1 - 53	3.4 - 167.7	1 - 22
Std. Dev.	56.1	7.99	32.8	5.36

Log-transformed salivary lead values for all workers were plotted against log-transformed blood lead (as in previous work). A relationship between the data was demonstrated (Pearson correlation coefficient $r = 0.457$, $p<0.001$) (Figure 2).

However, when only the data from subjects with a "steady" exposure history were considered, a stronger relationship ($r = 0.528$, $p<0.001$) was observed (Figure 3). In both datasets the ratio of blood lead: salivary lead was approximately 5:2.

Mean recovery of lead from 10µg/l spiked saliva using the device was 70.6% (n=8, SD = 1.70µg/l). Quality control material showed intra-assay variation of 1.9% (n=5).

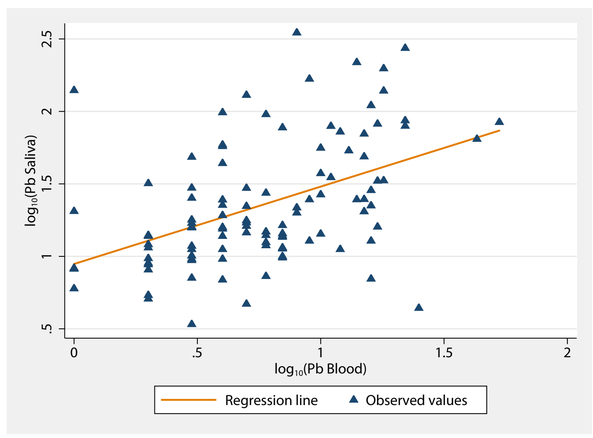

Figure 2: Correlation ($r = 0.457$, $p<0.001$) between log-transformed salivary and blood lead levels in workers.

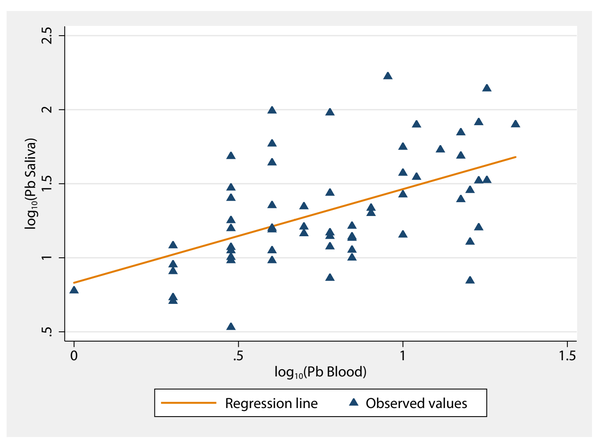

Figure 3: Correlation ($r = 0.528$, $p<0.001$) between log-transformed salivary and blood lead levels in workers with "steady" lead exposure history.

Discussion

The results demonstrate a statistically significant correlation between blood and salivary lead levels in workers. This correlation is stronger in workers with a "steady" exposure history. However, both correlations are quite weak, with a high degree of variability. There are several possible reasons for this variability, including differing kinetics between the two sample matrices, variable sample collection volume and possible routes of sample contamination – oral contamination before saliva collection (e.g. from hand to mouth behaviour) or contamination emanating from the sampling device itself.

Analysis of blank saliva passed through the device showed variable levels of contamination, with concentrations ranging from 1.9 – 7.8µg/l above that of directly analysed blank saliva. Further investigation found that this contamination came from the sampling paddle. An older version of the device used in a previous study did not show such contamination – however, the design of the sampling paddle was altered in the new device. Although this contamination may be relatively minor for measurement of lead exposure at occupational levels; it could prove problematic for measurement of environmental exposures.

The ratio of blood lead:salivary lead of approximately 5:2 differs from the 1:1 ratio previously found by Coventry Diagnostics. This may be due to differences between the environmental exposures measured in that study and the occupational exposures measured in this. Further comparative work could be carried out to investigate whether this is the case.

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