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Urinary Fluoride: Dependence on pH, Creatinine Excretion, and Occupational Exposure

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Human urinary fluoride as measured in single void samples is widely indicated as a way to assess environmental /occupational exposure to fluorine and its compounds. Some discrepancy, however, still persists as to which is the adequate way to express this parameter. Cook (1986) presents results of single void urine samples expressed in ppm of fluoride, a unit which has had wide acceptance since the extensive revision of Hodge & Smith (1977) on the subject. NIOSH (USA) has partially based its recommendations for TLV of air fluoride on the basis of their data. NIOSH criteria found further support in a very long series of data (Dinman & James (1983) where the geometric mean of single void samples of 12803 workers in the aluminum industry not exceeding 4 mg/l in pre-shift and 8 mg/l in post-shift conditions, corresponded to epidemiological evidence indicating the absence of other signs of fluoride exposure. The World Health Organisation (WHO 1984) recommendations on Fluorine and Fluorides, which summarize over 400 references, indicate that 4 mg/l urine in pre-shift conditions and 8 mg/l in post-shift are adequate toxicological levels to control fluoride occupational exposures, although the provision is made that the correlations between ambient air and urine fluoride levels need further documentation. Although the meaning of average urinary levels appears fairly clear on the basis of studies of large groups of workers, the question of interpreting individual (temporary or permanent) deviations from the group average deserves further consideration.

Pharmacokinetic studies (Ekstrand et al. 1982; Ekstrand & Ehrnebo 1983) show that urinary fluoride is affected by urinary flow and pH apart from the influence of occupational exposure. Accordingly, the interpretation of urinary fluoride data would improve in meaning if data on 24h samples and fluoride clearance were simultaneously available. In the toxicological practice, however, this is seldom possible, and the best interpretation of the results obtained with single void samples should be seeked

(Hojo 1982). A correction for creatinine content is normally included in results obtained with this type of samples (Petry 1985; Lauwerys 1986). According to Kono et al. (1985), the clearance of fluoride (CF), defined as:

$$CF(mg/ml) = UF(mg/ml) \cdot V(ml/min) / SF(mg/ml) \cdot Sf \quad (1)$$

Where UF is the concentration of urinary fluoride at a point in time, V is the urinary flow, SF is the serum fluoride concentration and Sf a corporal size factor, was found to be proportional to the creatinine clearance (CCr) in a population of healthy individuals (n= 1088, ages 35 to 88), the proportionality factor R:

$$CF = R \cdot CCr \quad (2)$$

being 0.46 for individuals in the age group below 59 yr. Dividing CF by the homologous CCr, which amounts to expressing CF per unit of Glomerular Filtration Rate (GFR), it follows:

$$UF/UCCr = 0.46 \cdot SF/SCCr \quad (3)$$

which shows that the ratio of instantaneous fluoride and creatinine concentrations is proportional to the ratio of their seral concentrations.

Results are here presented on urine and creatinine concentration in single void urine samples of healthy workers with mild occupational exposure to fluorides, evaluated through continuous air monitoring at the work place, and the contributions of pH ,creatinine concentration and exposure to the observed values. A recommendation to evaluate individual fluoride exposures is formulated.

MATERIALS AND METHODS

Urine single void samples corresponding to routine semester screening were obtained from 90 healthy workers with mild fluoride occupational exposure. Pre-shift samples (45) were obtained at the begining of job exposure, after a 48h period of shift rest (PSR); post shift samples (45) were obtained immediately after the end of the 5th working day (PSS). After overnight storage at 5 degC. ,fluoride concentration was determined in 8 ml aliquots through automated ion-specific potentiometry (ISP),(Ares 1986), after addition of a metal complexant and TISAB pH buffer (Orion 1977), and the values were corrected for normal specific gravity (1024). Creatinine was determined in separate aliquots using a modified Folin-Wu method.

Samples of air at the work place during the previous 2

Table 1. Codes and meaning of the variables included in the analysis of variance to investigate the contribution of urine pH , creatinine and exposition, to urine fluoride levels.

PSR: Pre-shift (Post-rest) samples
PSS: Post-shift samples.
X(1): Urine pH
X(2): Urine fluoride concentration (mg/l, corr. spec. grav.)
X(3): Urine creatinine concentration (mg/l)
X(4): Urine fluoride concentration (mg F/g Creat.)
X(5): PSR-PSS Code (0,1)

Linear regression analysis of variance:

MODEL I : X(4)= f(X(1),X(3)); X(5)=0
MODEL II : X(4)= f(X(1),X(3)); X(5)=1.
MODEL III : X(4)= f(X(1),X(3),X(5))
MODEL IV : X(2)= f(X(1),X(3),X(5)).

months were obtained continuously by means of static samplers at a mean target flow of 50 l/min; the air was pumped through a filter paper (40 u nominal pore size) into adequate impingers containing NaOH 0.025 M. Total soluble fluorides (gaseous + fine particulate) were measured with ISP as above.

A linear regression analysis of variance of the results was performed according to the criteria in Draper & Smith (1969). Table 1 describes the meaning and codes of the variables contained in the analysis and the different Models which were inspected for the partition of the variance of urine analysis into its various contributors.

RESULTS AND DISCUSSION

Table 2 shows the frequency distribution analysis of total soluble fluoride concentration in work place air samples, during the 60 days previous to the time at which the urine samples were obtained. The data characterize a mild fluoride exposure, with the usual lognormal pattern, the average of which corresponds to about 30% of the recommended TLV (NIOSH, loc cit.).

Table 3 shows the results of the linear regression analysis of variance showing the contribution of various urine sample parameters to urinary fluoride. The individual pairwise correlations as well as their regression coefficients and significances are shown. The F value corresponds to the ratio of the variance

Table 2. Frequency vector of the lognormal distribution of gaseous+particulate fluoride air concentrations (mg/m3) at the workplace during 60 days previous to worker urine analysis.

INTERVAL	RANGE	FREQUENCY
1	0.00 - 0.67	101
2	0.68 - 1.35	51
3	1.36 - 2.03	16
4	2.04 - 2.71	2
5	2.72 - 3.38	1
AVERAGE: 0.77		S.D.: 0.67

attributable to the regression model as compared to that attributable to error and/or unknown sources of urinary fluoride variations.

The analysis of MODELS I and II shows that urinary fluoride (mg F/g creat.) is significantly explained by urine pH and creatinine content, in PSR samples. MODEL I (significance at $p<0.001$) allows estimating the urinary fluoride on the basis of urine pH and creatinine, as:

$$UF = 1.77 - 0.142\ UpH - 0.11\ UCr \qquad (3)$$

where UF is in mf F/g creat. and UCr is in g/l.

After occupational exposure (MODEL II), although the correlation between urinary fluoride and creatinine is still significant, it only explains a small amount of the variance of UF.

The contributions of occupational exposure (variable X(5)) to UF, expressed both in terms of mg F/g creat. and in mg F/l are shown in MODEL III and IV. Exposure is the most important contributor to UF and accounts for about 70% of its variance. Urine creatinine is a significant contributor of about 2% of the residual variance. The correlation and amount of variance attributable to exposure diminishes when UF is expressed on a volumetric basis, as in MODEL IV. The significance of the overall model is lower than that of MODEL III and the values of UF expressed in mg/l are shown to be less correlated with creatinine content and more affected by urine pH (see the computed 't' value).

It can be concluded that urinary fluoride in single void samples expressed in relation to creatinine content is a better indicator of occupational exposure than the same expressed on a volumetric basis, and is less affected by

Table 3. Regression models and analysis of variance of urinary fluoride levels showing the contribution of urine pH, urine creatinine and occupational exposure.

	Variable	Mean	SD	Correlation x vs. y	Regr. Coeff.	Comp. 't'
MODEL I;	1	5.62	0.45	-0.168	-0.14	-1.65
(n = 45)	3	3017.47	1610.25	-0.562	-0.0001	-4.64
	4	0.62	0.31			
	Intercept = 1.77					
	F value = 11.67					
MODEL II	1	5.68	0.58	0.068	-0.08	-0.33
(n = 45)	3	2205.66	918.25	-0.353	-0.0009	-2.40
	4	3.59	2.34			
	Intercept = 5.13					
	F value = 3.00					
MODEL III	1	5.64	0.52	0.175	-0.09	-0.33
(n = 90)	3	2635.57	1371.85	-0.368	-0.0002	-2.32
	5	0.48	0.50	0.709	2.47	8.45
	4	1.92	1.88			
	Intercept = 1.88					
	F value = 32.00					
MODEL IV	1	5.64	0.52	-0.049	-0.48	-0.78
(n = 90)	3	2635.57	1371.85	-0.046	0.0004	1.74
	5	0.48	0.50	0.653	5.526	8.27
	2	4.13	3.98			
	Intercept = 3.98					
	F value = 23.10					

eventual changes in urine pH (arising, from instance, from dietary differences).

It is further recommendable to use the deviation of individual samples from the equation:

$$UF\ (mg\ F/g\ Creat.) = 1.884 - 0.089\ UpH - -0.2\ UCr + (2.47) \quad (5)$$

where UF is the estimate obtained with MODEL III, as a parameter to localize individuals whose occupational exposition to fluoride departs from the target population average. The actual numeric value of the last right hand side term depends on the average intensity of occupational exposure occurring in each case. Elimination of this term gives an estimate of expected normal pre-shift urinary fluoride.

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REFERENCES

Ares J (1986) nDimensional calibration of Al/F kinetic paths. Analyt. Chim. Acta 187: 181-194

Cook PP (1986) Health protection of workers. In: UNEP - IPAI Reg. Tr. Workshop Envin. Managmnt. Alum. Smelt. Coop. Dubai Al. Co. p. 129, London

Dinman B, James RM (1983) Semiannual urinary fluoride analyses among aluminium smelter workers:1970-1981 In: Fluorides. Effects on vegetation, animals and humans. J.L. Shupe (ed) Paragon Press S.L. City

Draper NR, Smith H (1966) Applied regression analysis. Wiley, N. York

Ekstrand J, Spak J, Ehrnebo M (1982) Renal clearance of fluoride in steady state condition in man. Acta Pharmacol. Toxicol. 50: 321-325

Ekstrand J, Ehrnebo MJ (1983) The relation between plasma fluoride,urinary excretion rate and urine concentration of fluoride in man. J. Occup. Med. 25:745-748

Hodge CH, Smith FJ (1977) Occupational fluoride exposure. J. Occup. Med. 19:12-39

Hojo Y (1982) Single-void Selenium levels expressed in terms of creatinine content as an effective and convenient indicator of human selenium status. Bull. Envir. Cont. Toxicol. 29:37-42

Kono K, Yoshida Y, Yamagata H, Takeda Y, Harada A, Doi KB (1985) Fluoride clearance in the aging kidney. In: Fluoride research, Tsunodda H, Yu MH (ed). Elsevier, Amsterdam, p. 407

Lauwerys RR (1986) Occupational Toxicology In: Cassarett Doull's Toxicology. Klaasen CD, Andur MO, Doull J (ed) MacMillan, New York p. 902

NIOSH (1977) Occupational Diseases a Guide to their recognition. Washington D.C. US Dept. of Health, Educ. and Welf. p. 31 Publ. no. 77-181

Petry H (1985) Erkrankungen durch Fluor und seine Verbindungen. In: Arbeitsmedizin, Valentin H, Lehnert S,Petry H, Weber G, Wittgens H, Woitowitz HJ. Thieme Verlag, p. 106 (1985)

WHO World Health Organization (1984) Fluorine and fluorides, Environmental Health criteria 36, Geneva, p. 77

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