ENDEMIC FLUOROSIS IN SAN LUIS POTOSI, MEXICO. II. IDENTIFICATION OF RISK FACTORS ASSOCIATED WITH OCCUPATIONAL EXPOSURE TO FLUORIDE

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SUMMARY: The city of San Luis Potosi (SLP), Mexico, is located in an area where drinking water contains excessive quantities of natural fluoride. Also in this city is located a small industry that produces hydrofluoric acid. In order to investigate both routes of exposure to fluoride (industrial air and drinking water), we conducted a pilot study in workers of this industry. The study involved 60 male workers, divided into two groups according to their work area: the production and the office groups. Although the exposure to fluoride by the water ingestion pathway was similar for both groups, the occupational exposure to fluoride was 12 times higher in the production area. Workers in this area had higher levels of fluoride in urine than workers in the office area. This difference was observed in the preshift and the postshift samples. A multivariate regression analysis showed that the workplace explained 33% of the fluoride content of the urinary samples, whereas tap water ingestion explained only 8%. The higher air fluoride levels in the production area could explain the high number of workers who present a preclinical phase of skeletal fluorosis. Although our results illustrate the exposure to fluoride of workers in the production area by two pathways, water and workplace air, it would be advisable to explore in more detail the participation of other pathways of exposure, like diet and soft drinks.

Key words: Air fluoride; Drinking water fluoride; Endemic fluorosis; Occupational fluorosis; Skeletal fluorosis.

Introduction

Skeletal fluorosis is the principal health problem associated with occupational exposure to fluoride.[1,2] The most important risk factor in determining whether skeletal fluorosis will occur and how severe it will be, is the total amount of fluoride consumed from all sources.[1,2] At the occupational level, the principal source of fluoride is industrial air, whereas in endemic areas with naturally fluoridated drinking water, the ingestion of contaminated water is the main source of fluoride.[1,2] Therefore, the highest risk would be observed in people that simultaneously are occupational exposed to fluoride and reside in endemic areas with higher than normal levels of fluoride in drinking water.

The city of San Luis Potosi (SLP), Mexico, is located in an area where drinking water contains excessive quantities of natural fluoride.[3] Also, in this city, is located a small industry that produces hydrofluoric acid. In order to investigate both pathways of exposure to fluoride (industrial air and drinking water), we conducted a pilot study in workers of this industry.

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Methods

Study Population

The study, which was conducted in 1994, included 60 male workers selected at random, divided into two groups according to their work area. Two areas were studied, the production area and the office area. The former has been identified as a high risk area because of the exposure to fluoride during the production of hydrofluoric acid, whereas the office was recognized as a low risk area. The workers in the office area were between 24 and 66 years old, had worked at the industry for 1 to 20 years, and had a history of residence in the city of San Luis Potosí of 22.2 ± 18.0 years. The workers in the production area were between 21 and 47 years old, had worked at the industry for 2 to 26 years, and had a history of residence in the city of 22.3 ± 10.6 years. The differences among groups were not statistically significant. An occupational questionnaire was administered to all the workers by the same interviewers.

Skeletal Fluorosis

Prevalence of skeletal fluorosis was determined according to the classification of the DHHS.[1] Preclinical phase was recorded when slight increase in bone mass was detected; whereas clinical phase I was associated with osteosclerosis of the pelvis. Therefore, radiographs of the pelvis (antero-posterior view) were obtained from the workers. The technique of radiographic examinations was standardized as much as possible. An independent observer, without knowledge of the work history of the individual, read all the radiographs. As a quality control for the radiograph interpretation, four workers were also studied by densitometry (vertebral column and region of the hip). The densitometries were read by a second independent observer, also without knowledge of the work history of the individual.

Urinary Fluoride Analysis

NIOSH method, "fluoride in urine", was followed.[4] As an internal quality control program, primary standard reference material was analyzed (QA/QC samples of fluoride in urine from WHO/HEAL/TCC in China). Our fluoride recovery was 104%. Fluoride was measured in preshift and postshift samples.

Drinking Water Samples

Tap water samples were collected from the homes of the 60 workers included in the study. Samples were collected in polyethylene bottles. Fluoride was quantified within 24 h from sampling. Fluoride levels were quantified by adding TISAB buffer to the samples just prior the analysis with a sensitive specific ion electrode. As an internal quality control program primary standard reference material was analyzed (QA/QC samples of fluoride in water from WHO/HEAL/TCC in China). Our fluoride recovery was 106%.

Industrial Air Samples

The method of Bonney and Farrah[5] was followed. Gaseous fluoride was measured with personal sampling pumps. Samples were obtained for an 8.0 hour period at least monthly during the last seven years. Fluoride levels were quantified in the aqueous solution where the fluoride from the alkaline impregnated cellulose pad was transferred. Measurements were done with a sensitive specific ion electrode. Standards for gaseous fluoride were used.[5]

Statistical Analysis

The distribution of urinary fluoride levels was skewed. Therefore values were log-transformed. Fluoride levels in urine between groups of workers were compared by t test. Within groups, the differences between preshift and postshift samples were analyzed with paired t test; one-tailed test was used with a significance level of α=0·05.[6] Simple linear regression models were used to defined significant predictors of fluoride in urine. These predictors were then included in a multivariate regression model.[6] The analyses were carried out with the SPSS-PC statistical package.

Results and Discussion

Exposure to Fluoride

We obtained samples of drinking water from the workers' residences and no differences were observed in the fluoride content between the groups. For the office group, fluoride levels in samples of tap water collected at the workers' residences (n = 24) had a mean of 2.29 mg/L (range 0.67 - 3.75 mg/L), whereas for the production group, the samples collected at the workers' residences (n = 36) had a fluoride mean level of 2.22 mg/L (range 0.54 - 4.36). At the plant, the only source of potable water had a fluoride level of 0.69 mg/L. With these results, and considering that the differences in water consumption between office and production workers were not significant; it can be established that the exposure to fluoride by water ingestion was similar for both groups. In contrast, the occupational exposure to fluoride was 12 times higher in the production area than in the office area (Table 1). The fluoride mean concentration in air at the production area for the period 1987-1988, was close to the recommended NIOSH's exposure limit of 2.5 mg/m^3.[2] When compared, air fluoride levels in the production area were lower during the period 1990-1994 than during the period 1987-1988 (Table 1). However, some samples (Table 1) continued to be above average (air levels in the upper limit of the range).

TABLE 1. Fluoride concentration in workplace air (mg/m^3)

AREA	n	YEAR	MEAN	S.E.	RANGE
Office	3	94	0.017	0.005	0.01 - 0.02
Production	25	87-88	1.78	0.30	0.07 - 4.54
Production	57	90-94	0.21	0.07	0.02 - 2.02

Eight hours samples. Results are given as geometric mean. n = number of samples. S.E. = standard error. The office area was monitored only during the study period.

Table 2. Preshift and postshift urinary concentrations of fluoride (mg/L)

	AREA	n	G. MEAN	S.E.	RANGE
PRESHIFT	office	24	1.79	1.09	0.7 - 4.6
	production	36	3.98	1.13	0.7 -15.9
POSTSHIFT	office	24	2.25	1.10	0.8 - 4.9
	production	36	5.12	1.09	1.4 -18.9

The mean differences were statistically significant. Between areas $p < 0.001$. Between shifts: in office area $p < 0.03$; in production area $p < 0.01$.

TABLE 3. Pearson correlations of fluoride in urine and different continuous variables

VARIABLE	r	p
fluoride content in water (mg/L)	0.31	0.007
age (years) *	- 0.24	0.03
time working in industry (years) *	0.10	0.22
time of residence (years) *	- 0.21	0.08

* These variables were log transformed for the analyses

TABLE 4. Predictors of fluoride in urine

VARIABLE	ß	S.E.	p
Tap water ingestion	0.08	0.02	0.002
Workplace	0.33	0.05	0.001

R^2 = 0.45. ß is the estimated coefficient of the variable in the regression, S.E. is the standard error and p is the significance. Water ingestion in mg/L. Workplace refers to office or production areas.

TABLE 5. Skeletal fluorosis prevalence among workers

AREA	n	Normal	Preclinical phase	Skeletal fluorosis I	Others
Office	20 (100%)	12 (60%)	3 (15%)	1 (5%)	4 (20%)
Production	35 (100%)	16 (46%)	13 (37%)	2 (6%)	4 (11%)

Others refer to lesions not related to skeletal fluorosis . Diagnoses were done by radiograph analysis. Four workers in the office area and one worker in the production area were lost for this part of the study. The differences were not statistically significant.

TABLE 6. Densitometry of the vertebral column and of the hip

AREA	Normal	Preclinical phase	Skeletal fluorosis I	Skeletal fluorosis I
Vertebral Column L1-L4	105	103	129 *	114 *
Neck of the Femur	112 *	111 *	115 *	121 *
Ward Region of the Femur	103	102	106	137 *
Greater Trochanter of the Femur	99	110 *	118 *	123 *

Each column represent a worker with the diagnosis obtained by radiographs. Percentage of bone density was adjusted by age, weight and race. * Bone densities 10% above the normal reference value.

Urinary Fluoride Levels

Preshift samples were provided during the morning of the first day following the 48 hours rest period of each worker. Postshift samples were provided during the morning of the fifth day of the working period. Results are shown in Table 2. Workers of both areas had statistically significant higher urinary fluoride levels in the postshift sample. Furthermore, workers in the production area had higher levels of fluoride in urine than workers in the office area. This difference was observed in the preshift and the postshift samples. The higher fluoride levels in the urine of

workers belonging to the production area can be explained by a higher exposure to fluoride due to the levels of fluoride in air registered at this area (Table 1).

Interestingly, 72% of the workers in the production area had fluoride urinary levels above the preshift biological exposure index of 3.0 mg/L,[2] whereas only 8.3% of the workers in the office area had levels above this index. Whether this difference can be explained by a higher fluoride excretion, due to an increased body burden of fluoride in workers of the production area, is a matter that certainly needs further research. However, in agreement with this interpretation, it has been described that large amounts of fluoride were excreted for prolonged periods by persons who lived for many years in areas with high fluoride water levels and who subsequently moved to areas with low fluoride levels.[7] The postshift biological exposure index of 10.0 mg/L[2] was surpassed by 5.6% of the workers in the production area, but by none of the office's workers.

The correlation coefficient between different continuous variables and urinary fluoride levels showed significant results only with age and fluoride content in water (Table 3). Urinary fluoride and workplace areas also showed significant differences ($p < 0.001$). With the significant variables of the univariate analysis, a fitted multivariate regression model was obtained. In this model workplace explained 33% of the fluoride content of the urinary samples, whereas tap water ingestion explained only the 8% (Table 4). Together, the workplace and the tap water ingestion explained 45% of the total fluoride in urinary samples. In consequence, we have to take other sources into account in order to totally explain fluoride exposure. Among them, we had previously identified the following: boiled water; "soft drinks"; and food preparation with boiled water.[3]

Skeletal Fluorosis

In our study, skeletal fluorosis was defined according to the classification of the Department of Health and Human Services, USA.[1] Table 5 shows the distribution of skeletal fluorosis among the two workers' groups. The production workers had a higher although not significant prevalence of the preclinical phase of skeletal fluorosis than office workers. It is noteworthy that among the office workers, 20% ($n = 4$) had signs of skeletal fluorosis. This suggests that environmental exposure (excluding occupational exposure) would lead to severe impairment.

As a quality control for the radiograph-based diagnosis of skeletal fluorosis, four workers were also studied by densitometry (Table 6). The results obtained by densitometry were concordant with data obtained by radiographs (Table 5). Workers with a diagnosis of skeletal fluorosis (clinical phase I) had a higher bone density than workers without signs of skeletal fluorosis (normal).

Three of the four skeletal fluorosis cases in the office group were found among workers older than 45 years, whereas 73% of the cases in the production group were found in workers aged 35 years or more. The reason for the appearance of skeletal fluorosis in younger workers in the production area, could be the additional exposure to fluoride due to the presence of this mineral in workplace air (Table 1). A clear association between changes of early skeletal fluorosis and time of occupational exposure has been reported.[8] However, in our study, no correlation was found between the frequency of skeletal fluorosis and the time working in the industry. This could be explained by the fact that in our study workers were exposed to fluoride by two different pathways (water and workplace air), there-

fore, the changes associated to skeletal fluorosis are not due just to the occupational exposure.

In agreement with previously reported data,[8] there was no correlation between the presence of abnormal pelvic radiograph findings and the presence of musculoskeletal complaints. This could be easily explained, assuming that the prevalence of musculoskeletal complaints depend more on occupational activities than on the exposure to fluoride.

Conclusions

As expected, these results proved that workers in the production area are at risk of fluorosis because of their exposure to fluoride by two pathways: water and workplace air. However, considering that the workplace and the tap water ingestion explained only 45% of the total fluoride in urinary samples; it would be advisable to study other sources for fluoride exposure in this population, such as: boiled water; "soft drinks"; and food preparation with boiled water.[3] Furthermore, it is clear that the alteration in bone density, or modification of the trabecular structure, are nonspecific indicators of fluoride toxicity. Therefore, there is a need to find more specific biomarkers for skeletal fluorosis, especially for the preclinical phase. The biomarkers could be a major advance in detecting early skeletal fluorosis, and for developing health programs to prevent crippling fluorosis.

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