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Hip fracture incidence not affected by fluoridation

Osteofluorosis studied in Finland

Iliac crest biopsies were taken from patients with hip fracture from a low-fluoride area (<0.3 ppm), from an area with fluoridated drinking water (1.0–1.2 ppm), and from a high-fluoride area (>1.5 ppm). Fluoride content analysis and histomorphometry of bone were performed. The hip fracture incidence during 1972–1981 was studied in the same areas.
The fluoride content of the bone samples correlated with drinking water fluoride. In patients with hip fracture, both osteomalacia and osteoporosis were common. In the high-fluoride area also osteofluorosis was found in many patients. Osteofluorosis may occur if the fluoride content of trabecular bone exceeds 4,000 ppm and either the volumetric density of osteoid or the osteoid-covered trabecular bone surface is abnormally increased. There was no difference in incidence of hip fracture in the three areas.

Ilkka Arnala
Esko M. Alhava
Reijo Kivivuori[1]
Pentti Kauranen[2]

Department of Surgery, Kuopio University Central Hospital, [1]Kotka Central Hospital, and [2]Department of Chemistry, Kuopio University, Kuopio, Finland

Correspondence: Dr. Ilkka Arnala, Department of Surgery, Kuopio University Central Hospital, SF 70210 Kuopio, Finland

Bernstein et al. (1966) showed that people living in a high-fluoride area (4.0–5.8 ppm) had less osteoporosis and collapsed vertebrae than did subjects from a low-fluoride area (0.15–0.3 ppm). Also, Iskrant (1968) noted that mortality from hip fractures was lower in communities with high levels of natural fluoride in the drinking water. No difference was observed between communities using fluoridated drinking water and communities where the drinking water contained no fluoride. This agrees with Korns (1969). Colbert et al. (1977) found that fluoride concentration in bone was lower in hip fracture patients than in control patients. In Finland, Laitinen et al. (1980) found an increased incidence of hip fracture in areas with low (<0.5 ppm) and high (>2.0 ppm) concentrations of fluoride in drinking water when compared with an area where fluoride concentrations were between these two values. Simonen et al. (1984) found a decreased number of hip fractures among men with a fluoride concentration of 0.9–1.0 ppm in their drinking water. The number of hip fractures in men increased with a fluoride concentration between 1.5 and 2.5 ppm, which was found to be the optimal fluoride concentration in women. Osteomalacia is proposed to be common in patients with femoral neck fractures (Aaron et al. 1974, Hoikka et al. 1982), although osteoporosis is the main reason for fractures of the upper femur (Menczel et al. 1976).

We investigated the mineral metabolism of patients with hip fracture using fluoride content analysis of bone and histomorphometry. Also, we studied the incidence of fracture of the upper femur in three areas of Finland with different fluoride concentrations in the drinking water.

Patients

Low-fluoride area. During surgery, bone biopsies were taken from the anterior iliac crest of 25 patients (18 women) with a hip fracture from a low-fluoride area (fluoride concentration <0.3 ppm) at Kuopio University Central Hospital. The mean age of the patients was 76 (64–86) years. Seven women and one man had been living in an institution for the elderly when the fracture occurred. Three female patients had diabetes, and one of them had rheumatoid arthritis treated with cortisone. One woman had impaired renal function.

Fluoridated-water area. Bone samples from 18 patients (13 women) with a hip fracture in the fluoridated-water area of Kuopio (fluoride concentration 1.0–1.2 ppm) were also taken during operations at Kuopio University Central Hospital. The mean age of the patients was 73 (48–92) years. Four women and 2 men were living in municipal homes when the fracture occurred. Two female patients had diabetes and 1 male patient was an alcoholic. All had normal renal function.

High-fluoride area. At Kotka Central Hospital bone biopsies were taken from 18 patients (14 women) who had undergone surgery for a hip fracture. These patients had lived in a high-fluoride area (fluoride concentration >1.5 ppm). Their mean age was 79 (65–88) years. Four of the patients were living in an institution when they had the fracture. Three of the female patients had diabetes, and one of these diabetics also had hyperthyreosis. One female patient had an elevated serum creatinine level.

The incidence of hip fracture was studied in five communities with a fluoride concentration of 1.5 ppm or more and five with 0.0–0.3 ppm in the drinking water (National Board of Health, Finland, 1974). In Kuopio, patients with a hip fracture who had lived in the fluoridated water area were accepted for the study. Fractures due to severe trauma, such as falls from heights or traffic accidents, were excluded.

Methods

From each patient two bone samples were taken from the iliac crest for histomorphometric analysis and fluoride determination. The fluoride content was evaluated potentiometrically using a fluoride selective electrode (Alhava et al. 1980), and undecalcified bone specimens were examined histomorphometrically using light microscope (Merz 1967). The parameters measured are expressed as the volumetric density of trabecular bone (Vv), the volumetric density of osteoid (Vvo), osteoid-covered trabecular bone surface (OS), and trabecular resorption surface (RS).

Data from the patients with a hip fracture were collected from case reports at Kuopio University Central Hospital, Kotka Central Hospital, and Hamina Hospital. The results (women + men; age 50 years or more) were expressed as a 10-year incidence of fractures. A direct method for standardization (Armitage 1971) was used. Population data were derived from local communal statistics for 1980 using the sum for the examined population as standard.

All variables were examined by linear regression analysis to determine correlations between fluoride content in bone and volumetric density of bone and osteoid, as well as osteoid-covered surface and resorption surface.

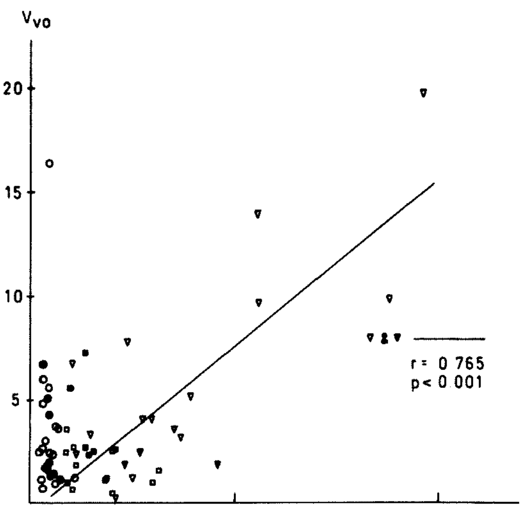

Figure 1

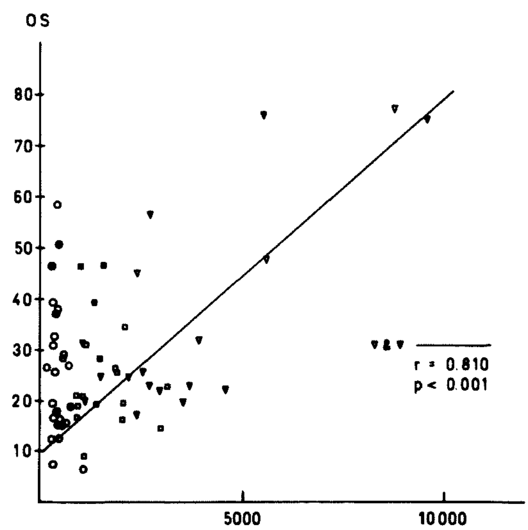

Figure 2

Figure 1. Linear regression analysis for fluoride content of cancellous bone and volume density of osteoid in the hip fracture patients from the examined areas. F = fluoride content of bone, Vvo = volumetric density of osteoid. Open signs represent women and solid signs men. Circles are cases from the low-fluoride area, squares from the fluoridated-water area, and triangles from the high fluoride area.

Figure 2. Linear regression analysis for fluoride content of cancellous bone and osteoid-covered surface of bone in the hip fracture patients. F = fluoride content of bone, OS = osteoid-covered surface of trabecular bone.

Table 1. Fluoride content and histomorphometric values (mean ± SD) for 25 hip fracture patients from the low-fluoride area, 18 patients from the high-fluoride area, and 18 hip fracture patients from the fluoridated-water area. ns = not significant

Tissue component	Low-fluoride area	P	High-fluoride area	P	Fluoridated area
F mg/g	0.45±0.19	<0.001	3.72±2.39	<0.025	1.59±0.69
Vv	12.3±3.0	ns	11.8±3.9	ns	13.4±3.8
Vvo	3.3±3.3	<0.05	5.5±5.1	<0.025	2.4±1.7
OS	25.4±13.6	ns	35.7±40.4	ns	25.4±10.8
RS	5.0±1.9	<0.05	3.8±1.0	<0.05	5.0±1.9

Mann-Whitney's *U* test was used for comparing variables between the groups of hip fracture patients.

A binomial *t* test was used to compare the incidences of fractures of the upper end of the femur in the various parts of Finland.

Results

Fluoride content of trabecular bone was higher in the fluoridated water area than in the low-fluoride area (Table 1). The histomorphometric variables in patients from the low-fluoride area were not different from those from the area with fluoridated drinking water. The volumetric density of osteoid and osteoid-covered trabecular bone surface were increased above normal limits (3.4 and 37 per cent, respectively) in some patients (Figures 1 and 2) in both areas. In linear regression analysis there was no correlation between fluoride content in bone and histomorphometric parameters in these areas.

Results from the high-fluoride area revealed a difference in fluoride content, the volumetric density of osteoid, and trabecular resorption surface compared with the low-fluoride and the fluoridated-water area. In the high-fluoride area, the fluoride content of bone and volumetric density of osteoid were increased, and the resorption surface was decreased. For the other variables, there were no differences between the areas (Table 1). In the high fluoride area, 10 of the 18 patients had Vv values less than 10 per cent. In linear regression analysis, fluoride content of bone was correlated with Vvo and OS (Figures 1 and 2). As an exception when compared with the other two areas, fluoride content in bone correlated also with the osteoid seam width ($r = 0.582, p < 0.01$). In the high-fluoride area, osteofluorosis could be diagnosed in 22 per cent of the patients.

The incidence of hip fractures did not differ between the three areas (Table 2), nor did the types of upper femoral fractures differ from each other in the area with different fluoride content in the drinking water.

Table 2. Ten-year incidence of hip fractures in the areas with different fluoride concentrations in drinking water

Age group	10-year incidence/10,000 (No. of fractures)		
	Low-fluoride area	Flouridated water area	High-fluoride area
50–59	1.2 (5)	1.9 (13)	0.7 (3)
60–69	7.8 (27)	7.7 (38)	8.0 (28)
70–79	16.4 (39)	16.3 (50)	20.5 (52)
80–	93.2 (64)	93.6 (85)	74.0 (57)
Total	12.4 (135)	11.9 (186)	12.4 (140)

Discussion

The increasing amount of osteoid in the high-fluoride area suggests the presence of osteofluorosis because the volumetric density of osteoid is higher there than in the other two areas. Compared with the other hip fracture groups, the volumetric density of trabecular bone was not changed in the high-fluoride area. Therefore, the total bone mass was unchanged, even though the amount of unmineralized bone was increased.

In the epidemiologic study the hip fracture incidence did not differ significantly in three areas with different concentrations of fluoride in the drinking water. Results of this survey are reliable, even though the sample was small, because there is no difference between these results and the results for the Finnish population of the same age group in 1968 (Alhava & Puittinen 1973). Our results show that high- or low-fluoride intake neither protects against nor increases the risk of hip fractures. Previous results from epidemiologic studies are controversial (Iskrant 1968, Colbert et al. 1977, Bernstein et al. 1980, Laitinen et al. 1980, Simonen et al. 1984). According to the histomorphometric and epidemiologic results, there seems to be no use for fluoride in the prophylaxis of osteoporosis. Investigation of other types of fractures would give more information about the role of fluoride intake for the risk of fractures in these different areas.

The histologic findings for both osteomalacia and fluoride-induced osteoid increase are rather similar; therefore, osteofluorosis cannot be diagnosed only by histomorphometric evaluation of trabecular bone. Biochemical tests are also of minor importance because they may be normal in osteomalacia (Daw et al. 1979, Jenkins et al. 1973). Determination of the serum concentrations of different vitamin D metabolites, especially 1.25(OH)2D, may be helpful. Hoikka et al. (1982) found significantly lower concentrations of 25(OH)D and 24.25(OH)2D in patients with hip fracture than in healthy controls matched for age and sex. In our study, there was no difference between the same low-fluoride area and the fluoridated water area in concentrations of these vitamin D metabolites. The vitamin D status in patients with hip fracture is probably also equal in the high-fluoride area. For final diagnosis of osteofluorosis, the fluoride content of the bone specimens should be analyzed. Baud et al. (1978) came to the same conclusion when they studied the value of bone biopsy in diagnosing industrial fluorosis.

The threshold value for toxic fluoride concentration in bone has not yet been clearly established. Jackson and Weidmann (1958) assumed that in dry, fat-free cancellous bone the critical level would be 4,000–6,000 ppm. Baud et al. (1978) concluded that a fluoride concentration higher than 4,000 ppm in trabecular bone would confirm the diagnosis of bone fluorosis. Findings in our study lead to the conclusion that fluorosis is evident if the fluoride content of ashed trabecular bone exceeds 4,000 ppm and one of the osteoid parameters (Vvo or OS) is above normal. This has also been shown in our previous cadaver material (Arnala et al. 1985). Therefore, the diagnosis of osteofluorosis demands both determination of fluoride content of the bone specimen and histomorphometric analysis. If concomitant osteomalacia is suspected, a trial with vitamin D may be useful. If one of the osteoid parameters remains above normal, a high-fluoride content in bone confirms the diagnosis of osteofluorosis.

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