Calcif Tissue Int (1987) 40:315–317

Calcified Tissue International

The Effect of Fluoride and Calcium on Spinal Bone Mineral Content: A Controlled, Prospective (3 Years) Study

Tommy Hansson[1] and Bengt Roos[2]

[1]Department of Orthopaedic Surgery I, Sahlgren's Hospital, University of Gothenburg, S-413 45 Gothenburg, Sweden; and
[2]Department of Radiophysics, Sahlgren's Hospital, University of Gothenburg, Sweden

Summary. Daily treatment with 30 mg of sodium fluoride (NaF) and 1 g of calcium over a 3-year period increased the bone mineral content (BMC) in the spines of women (n = 25) with osteoporosis. Determination of the BMC was followed with dual photon absorptiometry (^{137}Cs-^{241}Am) in the third lumbar vertebra. No increase in BMC was found with only 10 mg sodium fluoride in combination with calcium (n = 25), with calcium alone (n = 25), or with placebo (n = 25). No serious side effects were registered. There was, however, minor gastrointestinal distress in one-fifth of the patients taking 30 mg NaF daily.

Key words: Absorptiometry — Calcium — Osteoporosis — Fluoride — Fracture.

Fluoride has been given to humans based on the hypothesis that it stimulates formation of new bone which is normally mineralized if sufficient calcium is provided. Most (60–70%) osteoporotic women respond to fluoride without side effects and studies have shown an increase of bone mass (up to 30–50% in 1 year) and a tenfold decrease of fractures [1–9]. However, these studies have used high doses of NaF (50–80 mg/day), which induce significant side effects, and have not included control groups. Since we, in an earlier trial, found the same effect on the BMC of the spine after medication with 50 mg NaF as with 30 mg NaF daily, this study examined the effect of lower doses of fluoride in women with idiopathic osteoporosis [5].

Send reprint requests to Dr. Tommy Hansson and the above address.

Materials and Methods

Women (n = 100) selected for this study had at least one and a maximum of three vertebral compression fractures within the thoracic or lumbar spines, sustained during minor traumas. Since L3 was the vertebral level used for determination of the spinal bone mineral, a fracture at this level excluded from the study. All the women were postmenopausal, and none had known diseases or was taking a medication that could directly influence the normal skeletal metabolism.

The mean age of the women was 66 (SD 6) years. They were randomly placed into four different treatment groups (A, B, C, and D), each made up of 25 women. The mean age of the women in each group and treatment given is presented in Table 1.

Fluoride was given as sodium fluoride. It was administered in capsules containing 30 (Group A) or 10 mg each (Group B). Calcium was given to both of these groups, and to another that did not receive fluoride (Group C), as a combination of bicarbonate, lactate, and gluconate, 1 g/day. The patients in group D got one daily capsule containing placebo (starch). The patients receiving fluoride took it in the morning and the calcium in the evening.

Roentgenograms of the lumbar and thoracic spines were taken within 1 month after the treatment started and again after three years of treatment. The changes in the BMC of the third lumbar vertebra (L3) were followed with dual photon absorptiometry [12, 13]. BMC was determined at the start of the treatment, at 1 year, 1½ years, 2 years, and 3 years of treatment. Our dual photon absorptiometer uses two radionuclides with different gamma energies (^{241}Americium and ^{137}Cesium) arranged so there is a common collimated radiation beam. The transmitted radiation of both energies is measured with a scintillation detector and nuclear counting instrumentation. The radiation beam is centered over the L3 using an X-ray tube and an image intensifier. Transmission measurements are then performed as a scanning procedure over the vertebra in 4 mm steps. By plotting the attenuated energies at each step, a bone profile curve is obtained from which the BMC is calculated. The stability of the absorptiometer, which is of crucial importance for a high reproducibility especially in a study extended over several years, has been

Table 1. Changes in osteoporotic women of BMC (g/cm) in L3 over 3 years treatment

Group	Age	Treatment NaF	Ca	Year 0	1.0	1.5	2.0	3.0
A	65.2	30	1	2.72	2.94	2.97	3.09[a]	3.18[b]
B	66.4	10	1	2.75	2.77	2.78	2.75	2.83
C	64.6	0	1	2.69	2.68	2.74	2.74	2.68
D	67.2	placebo		2.75	2.81	2.73	2.72	2.67

Comparisons were made with the initial BMC value
[a] $P < .05$
[b] $P < .01$

tested by 57 measurements of the same Al-phantom over a period of 5 years. The 57 measurements gave a regression line with a slope that differed 0.15% from a straight line [10]. The accuracy of our method has been determined in numerous vertebrae before and after they have been ashed. The accuracy has also been determined by measurements first of vertebrae *in situ* in the body and then after they have been excised from the body. In these experiments the errors in accuracy and reproducibility have been found to be less than 3% [10–12]. A more detailed description of the theory and the measuring technique has been given earlier [11, 12].

Results

The BMC changes in the four different groups are presented in Table 1.

The number of patients who completed the 3-year study were 24 in Group A, 23 in Group B, 22 in Group C, and 19 in Group D. There were no statistically significant changes in the BMC in groups B, C, or D. Group A increased significantly ($P < 0.01$). The absolute increase in BMC in Group A was 0.46 g/cm, which corresponded to a 17% increase over the 3 years of treatment.

The increase of BMC in Group A was statistically significant after 1½ years of treatment, with a majority of the women showing an increase. After 3 years, 19/25 showed an increase, 5/25 showed a decrease. The biggest individual increase over 3 years was 27.1%, while the biggest individual decrease was 4.2%. The mean increase among the responders in Group A was 18.5%. The corresponding decrease among the nonresponders in the same group was 2.2%. The individual changes in Group A are shown graphically in Figure 1. Five of the patients in Group A had adverse reactions probably caused by the treatment. Four had mild gastrointestinal symptoms (nausea and gastritis). One patient developed a peptic ulcer which forced her to abandon the treatment after 10 months. Two of the women with adverse reactions belonged to the nonresponders. Four certainly new vertebral compression fractures were noticed in the entire group

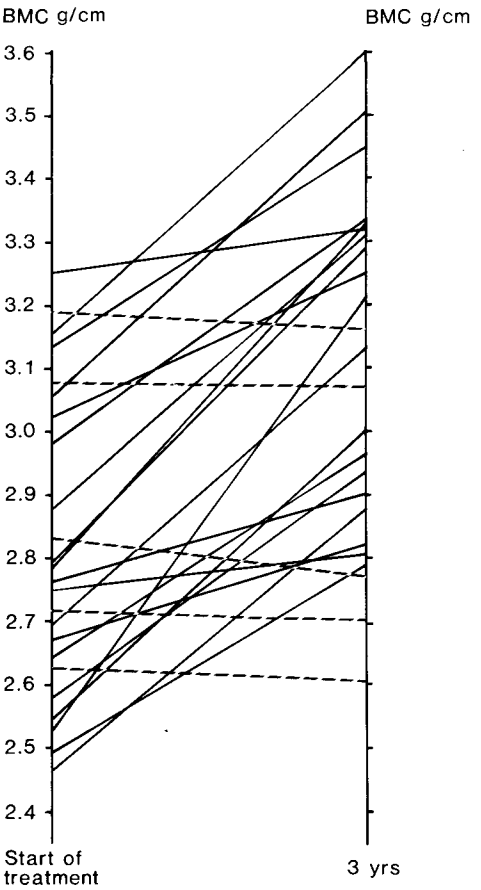

Fig. 1. The individual changes in BMC in group A during 3 years' treatment with 30 mg NaF and calcium. The dotted lines represent the 5 subjects who did not respond to this treatment.

of women; two occurred in Group B and one in Groups C and D respectively.

Discussion

This controlled, prospective study indicated that 30 mg of sodium fluoride and 1 g calcium taken daily significantly increased the BMC in the lumbar spine. The average value after 3 years of treatment among the women in group A was in the lower portion of the normal range for age-matched normals. This increase was not found when only 10 mg sodium fluoride or only calcium was given daily. Pending that the increase of BMC reflected an apposition of bone with normal qualities, the increase of BMC in those 76% who did respond in Group A probably could be of a sufficient magnitude (18.5%) to lower the risk of new fractures due to minor traumas. In another study [14] we found that a BMC deficit of about 15–20% was associated with

an apparent risk of the first vertebral fracture in women of this age; fluoride treatment over only 3 years put a majority of the responding subjects above this threshold.

A lower incidence of compression fractures after fluoride/calcium treatment has been reported from studies in osteoporotic patients [2, 4, 10]. As in these earlier studies, however, not all individuals respond to fluoride treatment and there are some mildly adverse side effects even at low doses. The lack of response may reflect lack of bone cell activity, an absence of precursor bone cells, or a simple failure to elevate blood fluoride levels (possibly associated with noncompliance in those with side effects). Some studies [2, 3] have failed to show positive responses to fluoride on the predominantly compact bone (75%–95%) of the distal radius (even in patients who responded vigorously in iliac crest biopsy [2]), but this discrepancy from our results could be explained, for example, by a difference in effectiveness of this agent on trabecular bone of the axial skeleton. As with previous studies on compact bone, however, no effect of calcium supplementation was evident in the spine. Given the normal calcium intake of Swedish patients (about 800 mg/day), it is not clear if the calcium provided with the fluoride therapy is necessary in this population, thought it may be of value in the populations where a lower dietary intake provides insufficient mineralization resources for the fluoride-induced bone.

Acknowledgments. The study was supported by the Swedish Medical Research Council (17X-6576) and Asker's Foundation.

References

1. Baylink DJ, Bernstein DS (1967) The effects of fluoride therapy on metabolic bone disease: a histologic study. Clin Orthop 55:51–85
2. Briancon D, Meunier PJ (1980) Le fluor en pathologie et en thérapeutic osseuses: son application au traitement des ostéoporoses. Lyon Med 243:183–94
3. Christiansen C, Christiansen MS, McNair P, Hagen C, Stocklund KE, Transboel I (1980) Prevention of early postmenopausal bone loss. Eur J Clin Invest 10:273–279
4. Franke J 1978 Our experience in the treatment of osteoporosis with relatively low sodium fluoride doses. In: Courvoisier B, Donath A, Baud CA (eds) Fluoride and bone. Hans Huber Publishers, Bern, Switzerland, pp 238–241
5. Hansson T, Roos B. (1978) Osteoporoses. Effect of combined therapy with sodium fluoride, calcium and vitamin D on the lumbar spine in osteoporosis. AJR 126:1294–1297
6. Jowsey J, Riggs BL, Kelly PJ, Hoffman DL (1972) Effect of combined therapy with sodium fluoride, vitamin D and calcium in osteoporosis. Am J Med 53:43–49
7. Reutter FW, Olah AJ (1978) Bone biopsy findings and clinical observations in long-term treatment of osteoporosis with sodium fluoride and vitamin D. In: Courvoisier B, Donath A, Baud CA (eds) Fluoride and bone. Hans Huber Publishers, Bern, Switzerland, pp 249–255
8. Riggs BL, Hodgson SF, Hoffman DL, Kelly PJ, Johnson KA, Taves D (1980) Treatment of primary osteoporosis with fluoride and calcium. JAMA 243:446–449
9. Riggs BL, Seeman E, Hodgson SF, Taves DR, O'Fallon WM (1982) Effect of the fluoride/calcium regimen on vertebral fracture occurrence in postmenopausal osteoporosis. N Engl J Med 306:446–450
10. Ringe JD, Kruse HP, Kuhlencordt F (1978) Ergebnisse einer Langzeittherapie der primären Osteoporose mit Natriumfluorid. Dtsch Med Wochenschr 103:248–252
11. Roos BO, Sköldborn H (1974) Dual photon absorptiometry in lumbar vertebrae. I. Theory and method. Acta Radiol 3:266–280
12. Roos BO (1975) Dual photon absorptiometry in lumbar vertebrae. II. Precision and reproducibility. Acta Radiol 3:291–303
13. Roos B, Hansson T (1980) Dual photon absorptiometry in lumbar vertebrae. An experimental study of the baseline error. Acta Radiol 19:111–114
14. Hansson T, Roos B (in press) The bone mineral content of the lumbar spine at the occurrence of the first vertebral crush fracture. Clin Orthop

Received March 27, 1986, and in revised form October 31, 1986.