

Effect of Sodium Fluoride on Skeletal Mass in Primary OsteoporosisCONF-770731--1  
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Epidemiological observations of a low incidence of osteoporosis in areas of endemic fluorosis suggested sodium fluoride (NaF) as a therapeutic agent for osteoporosis. Reported failures of this treatment may have been due to short periods of administration, inadequate dosage and/or lack of concomitant Ca supplementation, which has been advocated in order to decrease parathyroid hormone secretion. Jowsey and her colleagues (4) reported an increase in new bone formation by quantitative microradiography in eleven patients treated for one year with sodium fluoride and increased objective and subjective effectiveness when NaF, Ca and vitamin D supplements were maintained longer than 3 years (5). The evaluation of therapies for osteoporosis had been limited by a lack of suitable quantitative end points. The technique of in vivo total neutron activation analysis (TBNA) has made possible the precise and accurate measurement of total-body calcium (TBCa) (3). Since almost 99 percent of TBCa is in the skeleton, TBNA gives a direct measurement of skeletal mass and represents an objective criterion of the efficacy of the treatment of osteoporosis.

Patients and Methods. Ten ambulatory Caucasian women and one man, all with primary osteoporosis and vertebral compression fractures, were studied. They received oral NaF (45 mg per day) in 3 divided doses separated 2 hours at least from meals, and oral Ca supplements (one gram per day) in separated doses with meals. In one patient, family problems prevented therapy during a five-month period. The treatment was discontinued after six months in another patient because of severe nausea, and in a third patient after one year because of logistic problems. In the remaining patients, the effects of this therapy were evaluated at an average of 19 months in six patients and 26 months in seven patients. The basal and one year studies were performed under metabolic balance conditions except in one patient. Following the baseline studies all patients were evaluated on an out-patient basis at intervals of 6-9 weeks. TBCa values were compared with the values obtained during treatment in two other groups of osteoporotic patients. One group of thirteen patients was treated with placebo by Chestnut et al., in which TBCa was measured by a similar technique of TBNA with a precision of  $\pm 2$  percent (2). The other group, of seven, was treated by the authors with oral Ca in similar dosage and protocol as in the present study. The patients were allocated without bias to these treatments. The data were analyzed by the Student's "t" test for paired data and with an analysis of covariance to test for differences among regression coefficients using the Student-Neuman-Keuls' multiple range test (6). Calibration with an anthropomorphic phantom indicated a precision of  $\pm 1$  percent for the determination of TBCa by TBNA (3),

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with a radiation dose to the patient of 0.28 rem. Measurements of bone mineral content (BMC) of the distal radius (8 cm site) were also made with a Norland Instrument absorptiometer.

Results and Discussion. All the patients reported partial or marked symptomatic improvement in pain and increased physical activity. Transient nausea was a frequent side effect associated with NaF. The baseline values of TBCa were not significantly different in the three groups of patients. The relative changes in skeletal mass, as evaluated by TBCa are shown in Fig. 1.

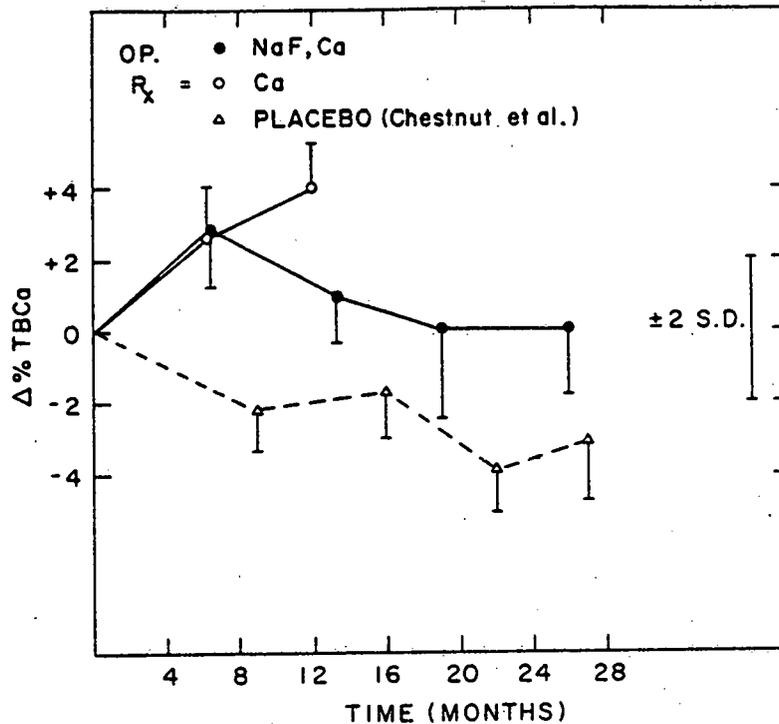


Fig. 1. Percent changes of TBCa, as measured by TBNA, in osteoporotic patients treated with NaF plus Ca, Ca only, and placebo (mean  $\pm$  SEM). The  $\pm$  SD represents the 95% confidence level or reproducibility of our measurements of TBCa.

Statistical analysis indicated no significant difference between the changes in TBCa in the group of osteoporotic patients treated with NaF plus Ca and those patients treated with placebo. However, there was a significant difference between the group treated with Ca alone and with NaF plus Ca ( $P < 0.05$ ), with a mean increase of 4% at one year in the former group. The Ca treatment was maintained for only one year in contrast to the more prolonged treatment of the NaF and Ca group. BMC values did not increase in the NaF plus Ca group with or without correction for bone width. There was no correlation between the changes in TBCa and BMC values during treatment with NaF plus Ca as we have already reported in the other osteoporotic patients (1). X rays of the spine, obtained at baseline, indicated 51 mild and moderate compressions in the eleven patients treated

with NaF plus Ca, indicating the severity of the osteopenia in these patients. Repeated films at one year and at the end of our evaluation period reported 5 and 2 new mild or moderate compressions, respectively; in addition, one mild compression progressed to moderate. In the group of seven patients treated with Ca alone there was one new moderate vertebral fracture at one year, in addition to the basal 15 mild or moderate compressions, with no change in the original eight severe compressions. With the exception of a significant fall of plasma phosphorus at one year, from  $3.5 \pm 0.12$  (mean  $\pm$  SEM) to  $3.3 \pm 0.14$  mg/dl ( $P < 0.02$ ), there was no significant change in the usual blood and urine parameters of calcium and phosphorus metabolism, including alkaline phosphatase, calcium in plasma or in urine. Significant decreases in hemoglobin, hematocrit, MCV and MCHC were observed in the patients treated with NaF plus Ca but not in those treated with Ca alone, although the final values were not in the anemic range.

Summary. The administration of NaF plus Ca to a group of eleven patients with primary osteoporosis did not result in an increase in TBCa as measured by TBNA or in BMC by photon absorptiometry. However, the group of osteoporotic patients receiving Ca alone differed significantly from the group receiving NaF, with initial increase in TBCa, although the treatment of Ca was maintained for only one year. A possible explanation for the lack of effect of NaF here and the previously reported beneficial effect may be the absence of concomitant administration of vitamin D in our protocol. However, no clinical or consistent laboratory manifestation of osteomalacia were observed in our patients.

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