Extended treatment of primary osteoporosis by sodium fluoride combined with 25 hydroxycholecalciferol

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SUMMARY Nineteen patients suffering from primary osteoporosis, all having at least one vertebral collapse, initially received 50 mg of sodium fluoride alone per day for 6-18 months. Subsequently fluoride was associated with 25-50 μg of 25 OH cholecalciferol (calcifediol) per day for 6-18 months in 12 of these patients and 9 were treated for 31-58 months. As control group, 9 patients were given placebo for 6-18 months. The effect of the treatment was assessed by three methods: 1) the metacarpal index (MI) determined by radiogrammetry, 2) the calcium content of the hand bone (Ca) measured by local neutron activation, 3) the iliac bone histomorphometry. MI and (Ca) did not change significantly at any time in any group. In each group there was a significant increase in trabecular bone volume, osteoid volume, osteoid surfaces and a significant decrease in mineralization fronts. On the other hand, the changes in osteoblastic surfaces, osteoclastic surfaces, number of osteoclasts/mm² were not significant in any group. No change was observed in the placebo group. These data suggest that the increase in the trabecular volume of fluorided bone is mainly due to the increase in osteoid which itself is due to a bone mineralization defect despite the association of calcifediol. This is probably one of the reasons why (Ca) does not change significantly.

Key words: Osteoporosis, Bone mineral Content, Histomorphometry, Fluoride, Vitamin D.

INTRODUCTION

Primary osteoporosis is one of the chief causes of infirmity particularly of the elderly woman. The cost of health due to bone fractures, and more especially the fractures of the femoral neck complicating osteoporosis, is responsible nowadays for considerable expense. In Great Britain 10% of orthopedic beds were occupied in 1977 by women with fractures of the femoral neck. In the United States 125,000 fractures of the femoral neck cost a billion dollars in 1979 (1). The discov-
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ery of an efficient treatment for osteoporosis, which would allow for a reduction of the risk of bone fractures, remains a very important medical problem. The idea of treating osteoporosis by sodium fluoride was attractive because chronic fluoride intoxication, hydrotelluric (2), industrial (3) or even drug induced (4) can produce osteoclerosis. However, to state positively that fluoride is effective in primary osteoporosis is not an easy task (1). In order to evaluate the efficiency of a treatment associating sodium fluoride (FNa) and 25 Hydroxycholecalciferol (calcifediol) extended over a period of two years, we attempted to estimate the improvement of osteopenia by using three methods: 1) a metacarpal index, 2) the hand bones calcium content, 3) bone histomorphometry.

PATIENTS

Twenty-eight patients, 18 women between the ages of 54 to 77 and 10 men between 45 to 70 years of age were initially included. They were all suffering from primary osteoporosis. The diagnosis of osteoporosis has been radiologically established by the presence of at least one vertebral compression.

Firstly, 19 patients received 50 mg per day FNa alone, administered orally in a dose of 25 mg sprinkled over their food at each lunch and dinner meal for 6-18 months. Afterwards, 12 of these patients, while continuing to receive the same daily dose of FNa were given 25 to 50 ~g of calcifediol per day for a period of 6-18 months. The daily dose of calcifediol was adjusted in function of the calciuria which at each control should remain below 300 mg per day. Nine of these osteoporotics, 7 women and 2 men, accepted to continue the treatment combining FNa and calcifediol for 31 to 58 months.

Nine osteoporotics, 6 women and 3 men aged between 54 to 58 were given a placebo (N. acetyl hydroxyproline, 400 mg per day) for 6-18 months and composed the control group.

METHODS

All measurements were carried out by blinded reviewers.

The metacarpal index MI was measured on the four last right metacarpals according to a method based on Dequeker (5). The intra-observer coefficient of variation of 10 consecutive measurements equalled 2%. For each patient the measurements were carried out before treatment and after each treatment period.

The calcium concentration of the bones (Ca) was achieved by neutron activation according to a technique published elsewhere (6), the principle of which we can only recall. Submitted to a bombardment by thermal neutrons, calcium 48- a stable isotope of natural calcium of very weak isotopic abundance (0.185 %)- is transformed into radioactive calcium 49. The latter disintegrates with a half life of 8.8 minutes by emitting high energy gamma photons (3.10 MeV). The intensity of the gamma rays measured with a sodium iodide scintillator is proportional to the mass of stable calcium exposed to the flux of neutrons. By comparing the induced activities of 49-Ca to those of a standard irradiated and measured in identical conditions, the mass of stable calcium contained in the bone segment studied can easily be calculated. The irradiation is carried out with neutrons emitted by isotopic sources of californium 252 (252-Cf), particularly well adapted to the measurements of calcium by localised activation. The radioactivity thus induced into the hand is registered between 1.10 and 3.5 MeV with the aid of a gamma spectrometric multi-channel device. The radioactivity of 49-Ca is obtained by integration of the 3.10 MeV peak cleared from contributions due to 24-Na and 38-C1 (about 10% in a normal subject). The bone volume of the hand is measured indirectly. Preliminary measurements carried out in vitro allowed us to determine a relationship between the bone volume and its projected surface determined by planimetry on an