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BIOPHYSICAL STUDY OF BONE MINERAL IN OSTEOPOROTIC PATIENTS FOLLOWING FLUORIDE THERAPY

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SUMMARY

Crystallographic characteristics and fluoride content of bone mineral are examined in a group of 60 osteoporotic patients before and after fluoride therapy. Bone fluoride content increases in a straight linear relationship with time: No plateau is reached within 80 months of therapy. The apatite crystal of bone is affected by fluoride : the a unit-cell of the lattice decreases, the line-broadening of the 310 X-ray reflection β (310) decreases, and the crystallinity index, measured by infrared spectroscopy, increases. The c unit-cell of the lattice and the line broadening of the 002 X-ray reflection do not vary significantly. Expected significant correlations between a, β (310) and bone fluoride content occur at the end of treatment. The net effect of fluoride therapy is a mineral stronger against dissolution and against compressive strength.

INTRODUCTION

Bone mineral content response to fluoride therapy of osteoporosis has been intensively investigated. Also, the effect of fluoride upon apatite mineral has been thoroughly studied by means of in vitro models and animal experiments. Less known is the effect of fluoride therapy upon the quality of bone mineral in osteoporotic patients. For this reason, crystallographic characteristics of bone mineral are examined in osteoporotic patients before and after fluoride therapy : bone fluoride

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content is determined and its increase with time analysed; crystallinity index, expression of the regularity of the phosphate ion's environment in the apatite crystal, is evaluated by infrared spectrometry. The X-ray line broadening, an expression of the crystal size and/or perfection is determined by X-ray powder diffraction; the a and c crystal lattice parameters, expression of the degree of the ionic substitution in the crystal structure are also determined by X-ray diffraction.

PATIENTS AND METHODS

60 patients from 31 to 75 years old were treated with the association sodium fluoride, calcium phosphate and vitamin D over 36 to 80 months [1]. Bone transiliac puncture biopsies were performed before and after treatment. An intermediary bone biopsy was performed during treatment in 32 patients. Compact bone from the external cortical layer was crushed to powder and used to determine fluoride by means of a specific electrode [2] in all biopsies. In biopsies performed before and after treatment, the external cortical layer was also used to evaluate crystallinity index by infrared spectroscopy [3,4]. When enough bone powder was available, unit-cell parameters were determined and crystal size and/or perfection estimated by X-ray diffraction [5,6].

STATISTICAL EVALUATION OF DATA

The Statistical Package for the Social Sciences (SPSS) [7,8] was used on a CDC CYBER 840 computer. Distribution and variance were analysed. The hypothesis of normality and of homoscedasticity had to be rejected. For this reason, non-parametric analysis was employed : the comparison between the values provided by the same patients before and after treatment was performed by means of the Wilcoxon matched-pairs signed rank test. Groups of patients were compared by means of the Mann-Whitney U test. Spearman rank analysis is used for correlations. Standard deviation is given as a measurement of accuracy.

RESULTS

Bone fluoride content increased significantly ($p < .001$) between the beginning ($.08 \pm .04$ %) and the end ($.49 \pm .26$ %) of the treatment in all patients submitted to the analysis. A good correlation with time was

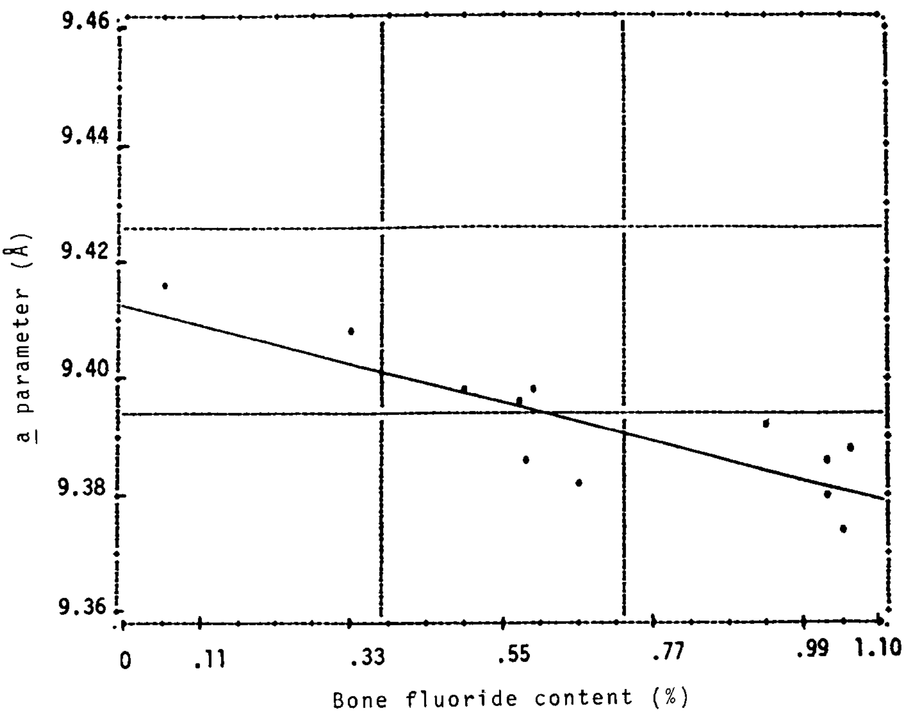

Fig. 1. Variation of the a unit-cell parameter of bone apatite as a function of fluoride content.

observed (rs = .827, p = .001). This increase was linear without any plateau or inflexion point between 0 to 80 months [9].

On average, crystallinity, measured by infrared spectroscopy and by X-ray diffraction, increased significantly: the crystallinity index rose from 64.2 to 66.5 ($p < .001$) and the (310) reflection peak, β (310), decreased from .53 ± .03 to .45 ± .05 $°2\theta \cos\theta/\lambda$ ($p = .035$). The (002) reflection peak broadening β (002) did not change significantly : the improvement of crystallinity only affects the size in width of the crystal.

In the 7 patients investigated, the $\underline{a}_o$ reticular parameter decreased significantly ($p = .018$) from 9.42 ± .01 Å before treatment to 9.39 ± .01 Å after treatment. It was not possible to detect any significant difference for the c parameter between the beginning and the end of treatment .

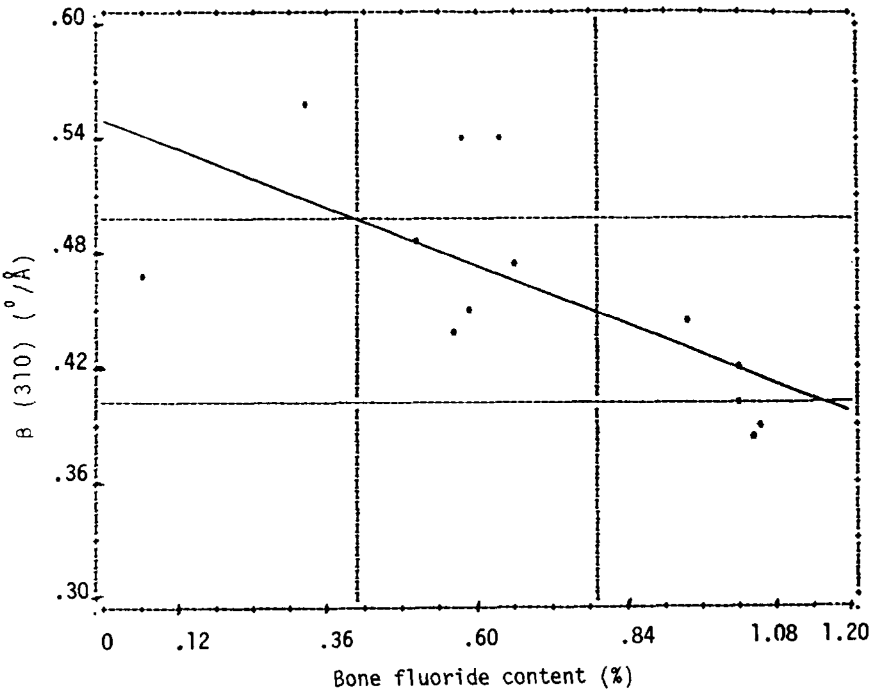

Fig. 2. Variation of the X-ray line broadening, β(310), of bone apatite as a function of fluoride content.

At the beginning of the treatment, very few correlations were observed. Concerning the crystallographical properties, only β (310) and β (002) were significantly correlated (rs = .6879, P = .007) indicating that crystallinity variations occured in the same way along length and width of crystal. After treatment, this correlation was no longer found , but bone fluoride content correlated significantly with the a parameter (rs = -.7912, p = .002) indicating an OH substitution by F (Fig. 1) and β (310) (rs = -.7510, p = .002) indicating an increase of size and/or crystalline perfection along the width of crystals (Fig. 2). Crystallinity index was not significantly correlated to bone fluoride content.

DISCUSSION

Changes in bone crystallinity measured by means of X-ray diffraction are in agreement with previous work dealing with fluoride therapy in osteoporotic patients [9, 10, 11]. This therapy promotes the growth of crystals and/or crystalline perfection along the width of those crystals but not along their length. This was already observed in experimental F^--treated mice and in cows fed in fluoride contaminated grazing-grounds [12]. The crystallinity index also increases during fluoride therapy, as it increases in fluorotic patients [13] and experimental animals [14]. However, in these two conditions a significant correlation was observed between bone fluoride content and crystallinity index. Such a correlation is not observed presently . This could be explained by the generally high crystallinity index of osteoporotic patients [3, 15], the low difference of values between the onset and the end of treatment, and the low interval of bone fluoride content. Nevertheless, the increase in crystal size and/or perfection along the width of crystals is sufficient to explain a decreased dissolution rate, an increased compressive strength [9, 16], and OH^- substitution by F^- to explain a decreased solubility [17] of mineral in fluoride treated patients. The correlation between bone fluoride content and a parameter only, is in accordance with observations in fluorotic patients [13], fluorotic and experimental F^--treated animals [12]. As the a value of fluorapatite, 9.3684 Å, is not attained, it is expected that a longer time of treatment would increase the mechanical and chemical properties of bone mineral. However a distinction should be made between the improvement of bone mineral quality and bone tissue quality: relation between mineral component and organic component of bone should be investigated; and relation between clusters of mineral should be taken into account [18].

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