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SHORT COMMUNICATIONS

Changes in Skeletal Metabolism after the Administration of Demineralized Bone Proteins and Fluoride

Bone is a tissue with an extraordinary capacity for remodeling and growth, which, in part depends upon the participation of nutrients as well as local and systemic hormones and growth factors (6, 16). Many of these growth factors, known as bone derived growth factors (BDGF's), have been characterized (5, 8). Biological activities of BDGF's have been evaluated by the use of implant models (11), in culture of bone cells (14) and exceptionally by systemic administration (8, 13). On the other hand, fluoride has been considered as a nutrient with capacity to stimulate bone growth and trabecular bone mass (4). In this context, the aim of this experimental study involved the oral administration of bone derived extracellular proteins and fluoride to evaluate the effects on bone composition, growth and metabolism with appropriate methods. This new and relevant information about the role of putative bone growth factors and their potential interactions with fluoride completes a previous assay with bone proteins previously carried out (13).

The bone-inductive preparation was obtained as previously described (11). Two different groups of male wistar rats (n = 8) with initial weights about 110 g were randomly assigned to receive control protein (casein 0.5 g/kg), and bone derived proteins plus fluoride as sodium fluoride at doses of 0.5 g/kg and 2.5 mg/kg, respectively. All the treatments were administered by gavage in aqueous vehicle. The animals were fed with a semipurified diet and a previously described dosage pattern for agents with osteogenic action was used (12).

After an experimental period of 31 days, tibial and femoral bones of both legs were excised, weighed and frozen until the analysis of different indicators of protein turnover (11). The data were statistically analyzed through the Student's *t* test.

The increase in relative weights of tibial and femur bones suggests specific effect on skeletal growth. Furthermore, the incorporation of fluoride ions into hydroxyapative crystals may affect bone composition (3, 5), which could explain the lower bone mineral and collagen content in the animals after fluoride administration, since fluoride has been involved in the induction of resorptive processes depending on the cumulative dose reaching bone (15). The experimental results show an increase on processes involved in bone formation on those animals orally treated with bone proteins, plus fluoride which is in agreement with our previous studies where the bone inductive preparation was used (13). Furthermore, in the fluoride administered animals, an important potentiation has been noted in different indices related to osteoformation such as osteocalcin and other indicators of bone protein synthesis (Ks and K_{RNA}). On the

Table I. *Bones weight, skeletal composition and other indices of bone turnover from rats orally treated during 31 days with control protein and bone proteins plus fluoride (Means ± SD).* *p < 0.05 between control and bone proteins + F groups.

Variables	Control	Proteins+F
Tibia (%BW)	0.15±0.01	0.17±0.1*
Femur (%BW)	0.19±0.01	0.21±0.1*
Moisture (%)	34.8±1.5	36.3±1.0*
Mineral salts (%)	57.2±1.1	56.2±0.9*
Collagen (%)	9.6±0.9	7.8±1.7*
Malate-DH (U/g)	494±64.6	540±149
Lactate-DH (U/g)	997±84.6	1079±69.3*
Alkaline phosph. (U/g)	45.6±8.6	55.4±7.2*
Acid phosph. (U/g)	7.6±0.9	7.8±1.7
Ks (%/day)	23.0±8.1	39.3±12.9*
K_{RNA} (mg prot./mg RNA)	5.2±1.8	8.8±3.1*
Serum osteocalcin (U)	0.9±0.2	5.6±3.0*

other hand, recently some systemic effects have been reported after the oral administration of certain types of collagen (18) and other substances of protein nature such as insulin, thyrothropin releasing factor, luteinizing hormone releasing factor or vasopressin (7). Additionally, some very low molecular-weight peptides of osteoblastic origin have been shown with capacity to stimulate osteoblast mitogenesis (1). It could be suggested that proteins contained in bone extract act on the activation of enzymes such as malate and lactate dehydrogenase, participating on protein and nucleic acid synthesis (11). The supplementation with fluoride results in important increases on bone weights, but also on measurements related to osteoformation affecting bone moisture, mineral content and collagen proportions, which could be associated to a potentiating effect of fluoride, while the protein resorptive processes are increased to a higher extent.

Key words: Skeletal metabolism, Bone derived proteins, Fluoride, Oral administration.

Palabras clave: Metabolismo óseo, Proteínas óseas, Fluoro, Administración oral.

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