MINERAL CRYSTAL COMPOSITION AND STRUCTURE OF NEW BONE AFTER STRONTIUM TREATMENT FOR OSTEOPOROSIS IN GOAT MODEL

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Introduction: Strontium (Sr) and related compounds have become more attractive in the treatment of osteoporosis. As a bone seeking element, 98% of Sr deposits in bone and teeth after orally taken. However, the quality of new bone after Sr incorporation is yet to be extensively investigated.

The aim of this study was to determine the mineral crystal composition and structure of new bone after co-administration of calcium (Ca) with Sr orally in a large animal osteoporosis model.

Materials and Methods: The ovariectomized goat is an acceptable animal model of human postmenopausal bone loss. In this study, 18 aged goats (range of 6–8 years) were ovariectomized to establish an osteoporosis model. One (1) year post-ovariectomy, animals were randomly assigned to four (4) different groups and treated as follows: control group (3 goats); normal Ca diet (Ca), normal Ca plus low Sr diet (Ca+LSr) and normal Ca plus high Sr diet (Ca+HSr) (5 goats per group) respectively for 16 weeks.

All animals were sacrificed 16 weeks after onset of treatment. Sr and Ca contents in femur were determined by inductively coupled plasma-atomic emission spectrometry (ICP-AES). 14 days and 3 days before sacrifice, each animal was injected with 20 mg/kg of tetracycline to obtain a double fluorescent label at sites of new bone. Sr and Ca ions spectra measurement by time-of-flight secondary ion mass spectrometers (TOF-SIMS) was carried out on the labeled new bone area. To determine the mineral crystal properties of new bone, the out layer (periosteum) of tetracycline labeled area was collected. The bone pieces was powdered and defatted to obtain the mineral crystal. Fourier transform infrared spectroscopy (FTIR) was applied to examine the chemical composition of the mineral crystal. Then single crystal was collected by ultracentrifugation for transmission electron microscopy (TEM) examination. Mineral crystal length, width and aspect ratio were determined.

Data were expressed as mean ± SD. The significance of difference was determined using one-way analysis of variance (ANOVA). Difference with p value <0.05 was considered statistically significant.

Results: As shown in Fig.1, Ca alone treatment decreased Sr concentration and Sr ratio in cortical bone slightly. However, Ca combined with Sr treatment increased Sr concentration and Sr ratio significantly.

FTIR spectra of mineral crystal powder isolated from new bone in control and Ca+HSr treated groups showed the characteristic absorption peak of phosphate (PO43-) at 566, 962 and 1044 cm-1. The absorption of HPO42- at 875 cm-1 and CO32- at around 1420-1480 cm-1 was obvious in both the control and Ca+HSr treated groups. There was no significant change in control and Ca+HSr treated groups.

Discussion: In this study, the in vivo effects of Sr co-administration with Ca on mineral crystal properties of new bone in osteoporotic goats were examined. Ca alone treatment slightly decreased Sr level in bone, which due to the similarity and competition between Sr and Ca. Sr was dose-dependently taken by bone in Sr treated groups. In addition, the uneven distribution of Sr as characterized by TOF-SIMS indicated that Sr was mainly deposited in newly formed bone areas. Since the ionic radius size of Sr differs from Ca, it is important to further evaluate the mineral composition and crystal structure of new bone with Sr incorporation.

Although Sr in new bone of Ca+HSr treated groups was much higher than that of control, the incorporation of Sr did not change the main component of bone mineral, which due to the very low ratio of Sr to Ca in the mineral crystal. There was large variation in the size distribution and significant difference in the average dimensions of width and length of crystals. This is because of the ionic radius of Sr, which is larger than that of Ca, implying that Sr incorporation could expand the structural size to induce the increased length and width of bone crystal.

In conclusion, Sr treatment increased Sr concentration in bone significantly while current clinical dosage may not change the chemical composition of bone. The ingested Sr mainly deposited in new bone. The incorporation of Sr increased the mineral crystal size and broadened the size distribution, which may attribute to the deceased fracture risk of bone.

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Figure 1. Strontium concentration and ratio in cortical bone

Table 1: Bone mineral crystal length, width and aspect ratio

<table>
<thead>
<tr>
<th>Group</th>
<th>Length (nm)</th>
<th>Width (nm)</th>
<th>Aspect ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>195±9 5.68</td>
<td>3.96±1.05</td>
<td>4.96±1.47</td>
</tr>
<tr>
<td>Ca+HSr</td>
<td>25.2±1.32 4</td>
<td>6.96±2.07</td>
<td>4.86±1.60</td>
</tr>
</tbody>
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*p<0.05 vs control