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Original Article

Hylonome

Patterns of bone loss in bed-ridden healthy young male subjects: Results from the Long Term Bed Rest Study in Toulouse

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Introduction

Loss of bone mineral is one of the main concerns of the Space Agencies in the planning of long-term space missions. Therefore, the Agencies are at present supporting bed rest studies. Because the effects on muscles and bones in the lower extremity during space flight are very similar[1,2], bed rest is accepted as a ground-based model for it. The latter suggests also that the main cause of the bone loss observed during space flight is immobilization and not weightlessness *per se.*

Obviously, such bed rest studies provide a chance to study the specific effects of immobilization, without interference of other diseases. In that sense, and also because the countermeasures that the Space Agencies have started to develop may be efficient in the near future, bed rest studies may also be of interest for clinical medicine. So far, two types of countermeasures have been considered. Resistance exercise is thought to preserve the leg musculature, and hopefully it thus will conserve the bones. Secondly, bisphosphonates as a potent inhibitor to bone resorption should be considered as a possible countermeasure.

Material and methods

The Long Term Bed Rest Study in Toulouse was designed to test the influence of fly-wheel resistance exercise and of pamidronate on the loss of bone mineral and muscle mass and function during 90 days of bed rest with -6° head down tilt (HDT). Fifteen days prior to the HDT, 60 mg Pamidronate was injected intravenously into 7 subjects. During the HDT, the fly-wheel group (9 subjects) exercised twice every first and 3 times every other week. Together with the 9 subjects of the control group, there were thus 25 healthy subjects between 23 and 41 years of age that participated in the study.

Bone mineral content (BMC) was measured with peripheral computed tomography (pQCT, XCT 2000, Stratec, Pforzheim, Germany) at 4% (epiphysis), 14% (metaphysis), 33% and 66% (both diaphysis) of the tibia length from its distal end. At the forearm, it was measured at 4% and 60% of the radius length. Muscle cross-section was measured by pQCT at 66% of the tibia length and at 60% of the radius length. Two measurement sessions were run during baseline data collection, and thereafter on days HDT28 and HDT89, and for one year during recovery, starting 14 days after reambulation. In the 14 subjects of the first campaign, only the left limbs were measured. In the 11 subjects of the second campaign, the right limbs were also measured during base line data collection and during recovery. Additional measurements of the left limbs were performed every two weeks during HDT in the second campaign.

Results

After 89 days of HDT, muscle cross-section was significantly decreased both at the forearms as well as at the calf. Flywheel exercise reduced, but did not completely prevent, the loss of calf muscle cross-section in the exercise group as compared to the pamidronate and control groups. It was also partly effective in reducing the loss in BMC at the tibia epiphysis by about 50%, as compared to the control group. In the pamidronate group, loss in BMC was comparable to the flywheel exercise group. No change was observed in forearm BMC in any of the groups.

Generally, the changes in BMC depicted a much greater inter-individual variability than the changes in calf muscle cross-section. On average, the loss of BMC was greatest at the tibia epiphysis (mainly made up of trabecular bone).

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This, however, was not true for all individuals. Subject E2, for example, had greater losses in BMC in the tibia diaphysis than in the epiphysis. As an analytical consequence of this observation, there was no significant correlation found between the bone losses at the different sites of the tibia.

Given the considerable inter-individual variability of bone changes and the poor coherence of the bone loss within the left tibia of the same individuals, one might put into question the reliability of our pQCT measurements. Four arguments, however, support the notion that the observed variability represents true and meaningful biological variation rather than 'measurement noise'.

Firstly, the short-term error, which has been assessed during the study, was substantially smaller than the inter-individual variability. Secondly, measurements performed every two weeks on the 11 subjects of the second group yield very 'smooth' curves, suggesting good measurement precision. Thirdly, the intra-bone coherence of bone loss was re-established after 14 days of re-ambulation. And fourthly, comparison of the changes in BMC at identical sites of the left and right tibia in the 11 subjects of the second group yielded high correlation co-efficients. The latter suggests that a systematic rather than systemic factors may help to explain the observations made: symmetry is obviously maintained, despite a large variety in patterns of bone loss.

Interesting observations have also been made with respect to the time course of bone loss. Different from our expectations, the rate of bone loss was insignificant or small during the first 4 weeks at all tibia sites measured. The different tibia sites were comparable in showing a significant and substantially increased rate of bone loss between days 29 and 89 of HDT. After re-ambulation, however, differences were found with the loss in bone mineral content continuing at the distal epiphysis and metaphysis, but with increases in BMC at the tibial diaphysis.

Discussion

As expected, bone mineral was lost in the tibia during 90 days of bed rest. This loss was mitigated by fly-wheel exercise and medication with pamidronate. The loss of bone mineral in subjects of the treatment groups suggests that the countermeasures were not completely effective. The observation, however, that the loss of bone mineral in some subjects of the untreated group was very slow suggests that factors other than mechanical usage interfere. Such other factors could be locally guided (e.g., recruitment of osteoclasts from the marrow space) or systemic (e.g., renal Ca^{++} excretion capacity). There is, however, a strong systematic guidance to the patterns of bone loss, as shown by the strong symmetry of changes in BMC at the left and right tibia.

Another set of observations could be summarized as 'hysteresis' effects. Loss in bone mineral really starts only after four weeks of immobilization, and it continues for at least 2 weeks after re-ambulation. The latter could possibly be due to an increase in micro damage driven remodelling activity (evidenced by the loss in BMC at the metaphysis which was negligible during bed rest but substantial during re-ambulation), or due to the mineralization lag. The delayed onset of bone loss, however, is hard to explain by the osteoclast activation time (in the range of days). Even more puzzling is the rapid gain in BMC at the tibial diaphysis during re-ambulation.

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References

1. Grigoriev AI, Morukov BV, Oganov VS, Rakhmanov AS, Buravkova LB. Effect of exercise and bisphosphonate on mineral balance and bone density during 360 day antiorthostatic hypokinesia. J Bone Miner Res 1992; 7(Suppl.2):S449-S455.
2. Oganov VS, Rakhmanov AS, Ternovoi SK, Novikov VE, Dubonos SL. Mineral density of human skeletal bones in modeling of decreased gravity load. Kosm Biol Aviakosm Med 1989; 23:43-46.