EFFECT OF WHOLE-BODY VIBRATION AND IGF-I ON BOTULINUM TOXIN A-INDUCED BONE DEGRADATION

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INTRODUCTION

Muscle strength is essential for bone development and homeostasis as stated in the "functional muscle-bone-unit" concept [1]. The relationship between these tissues was impressively demonstrated in a murine model in which Botulinium neurotoxin (Botox) induced muscle paralysis results in bone degradation [2]. It is also establised that high-frequency mechanical loading has an anabolic effect on bone and muscle [3,4], but the underlying mechanism has not yet been identified. Insulin-like growth factor-I (IGF-I) plays an important role in bone formation [5]. This growth factor regulates osteoblast proliferation and differentation [6] and is involved in the response of bone to mechanical loading [7].

The objective of the study was to analyse the effect of whole-body vibration and IGF-I on bone degradation caused by Botulinum toxin A (BTA) induced muscle paralysis.

METHODS

Thirty female C57BL/6 mice (16 wk) were randomly assigned into six groups (n = 5 each): basic control (BC), saline (CON), BTA (IM), BTA+whole-body vibration (IM+WBV), BTA+IGF-I (IM+IGF-1) and BTA+whole-body vibration+IGF-I (IM+WBV+IGF-I).

BTA (1.0 unit/0.1 ml) or an equal volume saline was applied by IM injection in both the quadriceps and calf of the right leg at the start of the study. The IM+IGF-I and IM+WBV+IGF-I groups received daily SC injections of human IGF-I (1 µg/day). The IM+WBV and IM+WBV+IGF-I groups underwent whole-body vibration (NOVOTEC Medical, 25 Hz, 2.1 *g*, 0.83 mm) for 30 min/day, 5 day/wk. The mice were sacrificed after four weeks of intervention. Femora were assessed by pQCT (Stratec). Transverse sections were scanned at the distal femoral metaphysis (15%, 17.5% and 20% bone length measured from the distal joint line) and at the midshaft (50% bone length). The voxel size was 500 µm × 70 µm × 70 µm. Trabecular parameters (cross sectional area, bone mineral density and bone mineral content) were determined as the means of the three slices at the distal femoral metaphysis. Cortical parameters (cross sectional area, bone mineral density, bone mineral content, cortical thickness, periosteal and endosteal circumference) were evaluated at the midshaft. Thereafter, the bones were loaded until failure with a three point bending test. Ultimate load, deformation and energy to failure were determined from the load-deformation curve. Ultimate stress, strain and elastic modulus were calculated [8].

RESULTS AND DISCUSSION

The IM group showed a decrease in both trabecular (-20%, $p < 0.05$) and cortical (-3%, $p < 0.05$) bone mineral density compared to CON group. Furthermore, the IM+IGF-I group displayed a decrease in trabecular (-18%, $p < 0.08$) and cortical (-3%, $p < 0.05$) bone mineral density. The IM+WBV+IGF-I had only a lower cortical bone mineral density (-3%, $p < 0.05$). The mechanical properties were lower in all intervention groups but significant differences were detect only in the ultimate force (-9%, $p < 0.05$) between the IM+WBV+IGF-I and the CON group. In addition, ultimate stress was decreased in the IM+IGF-I group compared to the CON group (-19%, $p < 0.05$).

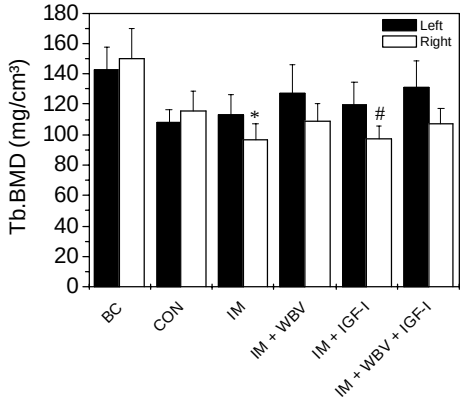

Figure 1: Trabecular bone mineral density (Tb.BMD). Values presented as means ± SD, *different to CON ($p < 0.05$), #different to CON ($p < 0.1$)

CONCLUSIONS

BTA induced muscle paralysis leads to bone degradation as described earlier [2]. Our data suggest that whole-body vibration may compensate the BTA-induced bone loss. The results also provide further evidence that skeletal unloading induces resistance to IGF-I. It has been shown that IGF-I administration in vivo did not stimulate bone growth and formation in the unloaded bone [9].

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