MICROGRAVITY SCIENCES AND PROCESSES SYMPOSIUM (A2)
Microgravity Sciences Onboard the International Space Station and Beyond - Part 2 (7)

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OSTEOPROTECTIVE EFFECTS OF OSTHOLE IN HINDLIMB SUSPENSION RAT MODEL

Abstract

Purpose: Bone loss is a substantial barrier to human in long-term spaceflight. It is well known that microgravity is the major factor to induce bone loss in space. Although measures have been developed to protect against osteopenia in spaceflight, the outcomes are of limited effectiveness. Recent studies have revealed that osthole (OST), a coumarin-like derivative extracted from Chinese herbs, significantly prevents bone loss in ovariectomized rat model. The purpose of this study was to investigate the effect of OST on simulated microgravity-induced bone loss of rats after 4 weeks of hindlimb suspension (HLS). Methods: Three-month-old female Wistar rats were hindlimb suspended and treated with vehicle or OST (10mg/kg/day) for 4 weeks (n = 6). Total bone mineral density (BMD) and biomechanics index of femur were measured and the trabecular bone parameters were analyzed by microCT. The morphology of tibia was observed with Van Gieson (VG) staining. The mRNA expression levels of OPG and RANKL in tibia were detected by qRT-PCR. The concentrations of BALP, OCN and TRACP-5b in serum were determined by Elisa. Results: The total BMD and the index of biomechanics of femurs were significantly decreased in HLS group compared with the control group, which were recovered in OST group to a large extend. MicroCT analyses showed that OST treatment could restore the cancellous BMD, trabecular bone volume (TV/BV), thickness (Tb.Th) and number (Tb.N), and decrease trabecular separation (Tb.Sp) and structure model index (SMI). VG staining results also showed good recovery of trabecular bone number, separation and thickness in OST group compared with HLS group. These data reveal that OST treatment prevents the loss of bone mass and strength induced by simulated microgravity. On the other hand, the ratio of OPG/RANKL in tibia was dramatically enhanced in OST treatment group compared with HLS group. In addition, OST treatment attenuated HLS-induced up-regulation of TRACP-5b concentration and down-regulation of BALP and OCN concentration in serum, suggesting OST suppresses simulated microgravity-induced bone resorption and improves bone formation. Conclusions: These results suggest that OST could protect against bone loss induced by simulated microgravity through repressing bone resorption and improving bone formation in vivo.