Hepcidin improves postmenopausal bone loss by inhibiting PGC-1β reverse regulation of osteoclasts though reducing iron

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Abstract

Iron, as a necessary trace element of the body, is involved in many physiological processes. Recent studies have found that disorder of iron metabolism, especially iron overload, can lead to bone mass reduction and even related to postmenopausal osteoporosis. Hepcidin is a key regulator of iron homeostasis in vivo, and its metabolic disorder can also lead to abnormal bone metabolism, but the mechanism is still unknown. In this study, we first found that the concentration of hepcidin in serum was significantly decreased in postmenopausal patients with osteoporosis and was positively correlated with bone mineral density. Osteoporosis model was established in ovariectomy mice. And then overexpression of hepcidin showed that it could significantly improve bone mass and rescue the phenotype of bone mass loss. Overexpression of hepcidin partially reduced the number and function of osteoblasts, but greatly reduced the number of osteoclasts and the differentiation of osteoclasts in vivo. It has been found that iron can activate mitochondrial synthesis and osteoclast differentiation by cooperating with the expression of PGC-1 β. In this study, the differentiation of osteoclasts in vitro was detected. We found that overexpression of hepcidin could significantly inhibit ROS production, mitochondrial biosynthesis and PGC-1 β expression, and also decrease the expression of PGC-1 β in bone of mice. These data suggest that hepcidin can protect osteoporosis by reducing the level of iron in bone tissue, cooperating with PGC-1 β to reduce the production of ROS and the number and function of mitochondria, and then inhibiting the differentiation and reabsorption of osteoclasts.

Image

Figure 1

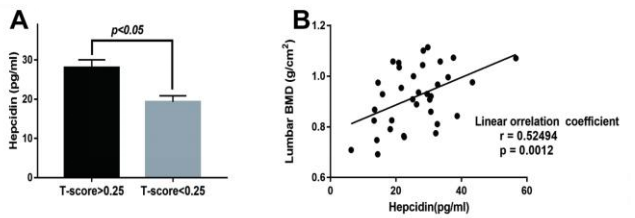


Fig. 1 Bone metabolism is regulared by hepcdin. (A) Postmenopausal women (n = 35; age = 62.11 ± 5.9) serum hepcdin are down-regulated in osteoporosis women (T score ≤ 2.5). (B) Lumbar BMD and serum hepcind showed positive linear correlationship; the coefficient r = 0.52494 and statistically significant P = 0.0012.

Figure 2

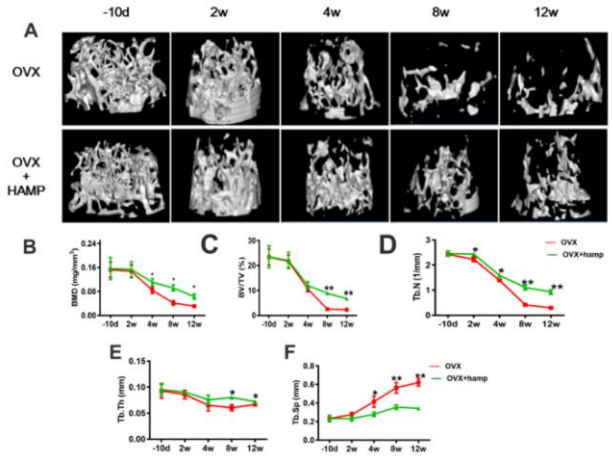


Fig. 2 Hepcidin overexpression delays bone loss induced by ovariectomy. (A) The loss of bone was delayed with high level hepcidin. (B - F) Micro-CT showed that the distal femur bone mineral density and relevant parameters percent bone volume(BV/TV), trabecular thickness(Tb.Th), trabecular number (Tb.N) and trabecular separation(Tb.Sp) in OVX and OVX + hepcidin overexpression group. The asterisks (*, **) indicate significant differences at P < 0.05, 0.01.



Hui Zhang, a medical graduate student, whose boss is Professor Youjia Xu, is now studying for a doctorate from Soochow University and has been engaged in iron and bone metabolis research.

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