Decreased Bone Formation Explains Osteoporosis in a Genetic Mouse Model of Hemochromatosiss

Titre	Decreased Bone Formation Explains Osteoporosis in a Genetic Mouse Model of Hemochromatosiss
Type de publication	Article de revue
Auteur	Doyard, Mathilde [1], Chappard, Daniel [2], Leroyer, Patricia [3], Roth, Marie-Paule [4], Loréal, Olivier [5], Guggenbuhl, Pascal [6]
Pays	Etats-Unis
Editeur	Public Library of Science
Ville	San Francisco
Type	Article scientifique dans une revue à comité de lecture
Année	2016
Langue	Anglais
Date	2016
Pagination	e0148292
Volume	11
Titre de la revue	PLoS One
ISSN	1932-6203
Mots-clés	Bone development [7], bone fracture [8], Bone Remodeling [9], Hemochromatosis [10], Mouse models [11], Osteoblasts [12], Osteoclasts [13], osteoporosis [14]

Résumé en anglais	Osteoporosis may complicate iron overload diseases such as genetic hemochromatosis. However, molecular mechanisms involved in the iron-related osteoporosis remains poorly understood. Recent in vitro studies support a role of osteoblast impairment in iron-related osteoporosis. Our aim was to analyse the impact of excess iron in Hfe-/- mice on osteoblast activity and on bone microarchitecture. We studied the bone formation rate, a dynamic parameter reflecting osteoblast activity, and the bone phenotype of Hfe-/- male mice, a mouse model of human hemochromatosis, by using histomorphometry. Hfe-/- animals were sacrificed at 6 months and compared to controls. We found that bone contains excess iron associated with increased hepatic iron concentration in Hfe-/- mice. We have shown that animals with iron overload have decreased bone formation rate, suggesting a direct impact of iron excess on active osteoblasts number. For bone mass parameters, we showed that iron deposition was associated with bone loss by producing microarchitectural impairment with a decreased tendency in bone trabecular volume and trabecular number. A disorganization of trabecular network was found with marrow spaces increased, which was confirmed by enhanced trabecular separation and star volume of marrow spaces. These microarchitectural changes led to a loss of connectivity and complexity in the trabecular network, which was confirmed by decreased interconnectivity index and increased Minkowski's fractal dimension. Our results suggest for the first time in a genetic hemochromatosis mouse model, that iron overload decreases bone formation and leads to alterations in bone mass and microarchitecture. These observations support a negative effect of iron on osteoblast recruitment and/or function, which may contribute to iron-related osteoporosis.
URL de la notice	http://okina.univ-angers.fr/publications/ua14597 [15]
DOI	10.1371/journal.pone.0148292 [16]
Lien vers le document	http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0148292 [17]
Autre titre	PLoS ONE
Identifiant (ID) PubMed	26829642 [18]

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