Vitamin A and Bone
Studies *in vivo* and *in vitro*

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet, kommer att offentligen försvaras i Hjärtats aula, Vita stråket 12, Sahlgrenska Universitetssjukhuset, Göteborg, den 18 december 2018, klockan 9.00

av Viktė Lionikaite

Fakultetsopponent:
Riku Kiviranta

*Associate Professor and Medical Consultant in Endocrinology*

University of Turku, Finland

Avhandlingen baseras på följande delarbeten


Vitamin A and Bone
Studies in vivo and in vitro

Viktė Lionikaitė
Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Abstract

Background: Excess vitamin A is associated with decreased cortical bone and increased risk of fractures in humans. The aim of the present thesis was to assess the importance of vitamin A on the skeleton and bone cells in in vivo animal studies and mechanistic in vitro experiments. In vivo, we used clinically relevant doses of vitamin A to investigate its effects on bone after prolonged administration and on the anabolic bone response to mechanical loading. In vitro, we aimed to determine how retinoids affect inflammatory- and physiologically-induced osteoclast formation and how retinoids affect periosteal osteoclast progenitors.

Methods: In vivo, mice were fed diets containing clinically relevant doses of vitamin A for durations of 4 and 10 weeks and prior to and during 2-week mechanical loading of the tibia. In vitro, we investigated the effects of retinol on human monocytes and mouse bone marrow macrophages induced to form osteoclasts by physiological and inflammatory cytokines, and on periosteal cell cultures.

Results: In vivo, we found that clinically relevant doses of vitamin A are able to reduce cortical bone mass by means of increased resorption and to decrease the anabolic bone response to mechanical loading due to reduced bone formation. In vitro, our results indicate that all-trans retinoic acid (ATRA), the active metabolite of retinol, inhibits physiologically- and inflammatory-induced osteoclastogenesis, however, in mouse periosteal bone cell cultures, the addition of ATRA enhances osteoclastogenesis.

Conclusion: Our results demonstrate the importance of vitamin A status to bone health. Fortification of food with vitamin A and vitamin A supplementation should be re-examined as vitamin A status may be a risk factor for secondary osteoporosis, a disease of decreased bone mass and increased risk of fractures.

Keywords: vitamin A, retinol, osteoclasts, osteoblasts, cortical bone, osteoporosis