Bovine lactoferrin improves bone status of ovariectomized mice via immune function modulation

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Bone
Volume 48, Issue 5 , Pages 1028-1035, 1 May 2011

Received 1 September 2010; received in revised form 28 January 2011; accepted 1 February 2011. published online 09 March 2011.

Abstract

We have previously shown that bovine lactoferrin (bLF) supplementation can have a beneficial effect on postmenopausal bone loss by modulating bone formation and resorption. A direct effect of bLF on bone metabolism is support by its presence in mice blood. Moreover we know that LF plays a key role in innate immunity and recent studies have shown its ability to modulate adaptive immunity. In particular bLF ingestion prevents recruitment and activation of immune cells at inflammatory sites. We propose that LF through its ability to modulate maturation and differentiation of leucocytes can participate to abolish the deregulation induced by estrogen deficiency on T cells. This study evaluated the effects of bovine lactoferrin on immune function in ovariectomized mice. We investigated whether bLF ingestion could prevent bone loss via modulation of immune function. Three-month-old female C3H mice were either ovariectomized or sham-operated and fed for 1, 2 or 4 months with a control diet (AIN-93M) or the same diet including 10 g bLF/kg diet. Bone mineral density was determined using a Lunar Piximus densitometer. The immune parameters were assessed by flow cytometry. In addition, Real-Time PCR was performed to quantify TNFα expression and plasma cytokines were measured at 4 months with Luminex. Ovariectomy induced significant changes on bone parameters and increased recruitment of macrophages, dendritic cells, and B and T cells associated with T lymphocyte activation in bone marrow. Compared to the control diet, ingestion of bLF-enriched diet for 2 months prevented T cell activation and restored dendritic and B cell populations in the bone micro-environment in ovariectomized mice. Furthermore, TNFα expression in bone was decreased by bLF supplementation after 2 and 4 months. Similarly, a decreased plasma level of TNFα was observed concomitantly to an increase of IL-10 level. In conclusion, these experiments suggest that bLF can mediate the prevention of lymphocyte activation and cytokine release in the bone micro-environment. Dietary bLF supplementation could have a beneficial effect on postmenopausal bone loss by modulating immune function.

Research Highlights

► Modulation of bone status by bovine lactoferrin through the immune function has never been shown. ► Evolution of immune parameters after mice ovariectomy have never been evaluated. ► Correlation between bone mineral density, immune parameters and osteoclast functions are shown for the first time. ► Clear demonstration of bone status improvement through modulation of immune function can by a new therapeutic approach.

Abbreviations: LT, lymphocyte T, LB, lymphocyte B, DC, dendritic cell, BM, bone marrow, APC, antigen presenting cell, SHAMC, control mice, OVXC, control ovariectomized mice, SHAMLF, mice supplemented with bLF, OVXLF, ovariectomized mice supplemented with bLF

Keywords: Bone resorption, Osteoclastogenesis, Lactoferrin, Immunomodulation