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Effect of a probiotic fermented milk on the thymus in a non-sever protein-energy-malnutrition model in mice

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The thymus is a primary lymphoid organ in which T lymphocyte differentiation occurs. It is considered as an organ of the endocrine system and thus an endocrine gland that secretes hormones and other soluble factors controlling the production and maturation of T lymphocytes, and regulating the activity and the interactions of T cells in peripheral tissues. It exerts a clear influence on the development and maturation of the lymphatic system and in the mucosal and systemic immune response. Protein-energy malnutrition causes a significant impairment of the immune system(1), being the thymus one of the most affected organs(2). The administration of a probiotic fermented milk can recover the intestinal barrier, histological alterations and mucosal and systemic immune functions affected by undernutrition in a non-severe malnutrition mouse model(3). This study was aimed to evaluate in the same model of malnutrition the effect of a probiotic fermented milk added to re-nutrition diet on the recovery of the thymus, analyzing histological and functional alterations caused by malnutrition. After weaning (21 days) mice were randomly divided in two control groups (well-nourished control group that received conventional balanced diet and malnourished control group)(4) and three test groups according to the dietary supplement received during re-nutrition period: milk, probiotic fermented milk or its bacterial free supernatant. Malnourished control group and mice from the three test groups were fed during 5 days with conventional diet, without restriction and after that, the malnourished period started and the animals received restricted food (25% less than well-nourished control). The malnourished control group was not re-nourished and continued with restrained ingestion during all the experiment, while mice of the test groups, when lost 25% of body weight compared to well-nourished mice, continued with the restrained ingestion, but supplemented with the dietary supplements: whole milk rehydrated 10% wt/vol, probiotic fermented milk or its bacterial free supernatant. Probiotic fermented milk was the most effective re-nutrition supplement to improve the histology of the thymus, decreasing the cellular apoptosis in this organ, and recovering the percentage of $CD4^+/CD8^-$ single positive thymocytes. Immature double positive thymocytes were increased in the malnourished control. The production of different cytokines in the thymus was increased in mice given probiotic fermented milk compared to mice that received others dietary supplement and malnourished control. The analysis of the macrophages and dendritic cells did not show significant variations comparing test and control groups. Mice given the bacterial free supernatant presented an improvement in the thymus similar to those that received milk. This is a first report demonstrating the beneficial effect of probiotic administration on thymus after a malnutrition period; which would be also responsible for the improvement of the mucosal and systemic immune response observed in previous studies using this same non severe malnutrition model. We also demonstrated the importance of the whole probiotic fermented milk supplementation on the histological and functional recovery of the thymus in a non-severe protein-energy malnutrition model. Further studies to find out the probiotic effect on different cell populations (NKT cells), and on thymic intralobular extracellular matrix (ECM) components (fibronectin), involved in the thymus maturation or cellular differentiation of malnourished mice are currently undergo.

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