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Peripheral lymphocyte subsets in infants at risk for celiac disease. Effect of milk feeding practices and HLA genotype. The PROFICEL study

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Celiac disease (CD) is characterised by small-intestinal mucosal injury and nutrient malabsorption in genetically susceptible individuals in response to the gluten ingestion. Disease pathogenesis involves the interaction among genetic, environmental and immunological factors. Environmental factors that have a role in the maturation of the immune system, such as milk feeding practices might potentially participate as risk or protection factors for CD. Therefore, the aim of this work was to assess the effect of the interaction between milk feeding practices and the HLA-DQ genotype on peripheral lymphocyte subsets and their activation markers in infants at risk for CD.

One hundred healthy newborns with at least one first-degree relative with CD were classified in different genetic risk groups by PCR-SPP DQB1 and DQA1 typing. Peripheral lymphocyte subset percentage and absolute counts were studied in these infants at the age of 4 months by flow cytometry analysis.

According to the HLA-DQ genotype, 22% infants were classified in the high risk (HR) group, 42% in the intermediate risk (IR) group and 36% in the low risk (LR) group, showing 24–28%, 7–8% and less than 1% probability to develop CD, respectively. At the moment of the immunological study 36% of the infants were exclusively breast fed (BF) and 64% of them were either receiving mixed breast feeding or formula feeding and were analysed together (FF group). Two-way ANOVA showed significant interactions between HLA genotype and milk-feeding practices on most of the T CD8+ lymphocyte subsets analysed. Post-hoc analyses within the FF group showed higher CD8+ counts, memory CD8+ (counts and percentage), CD8+CD38+ counts and lower naïve CD8+ percentage in HR infants compared to the FF-LR infants. Within the BF children no differences were observed between the HR and LR groups, however, those children in the BF-IR group showed significantly higher CD8+, CD8+CD45RA+ and CD8CD25+ counts compared to the BF-LR group. Finally, a significant interaction between milk feeding and HLA genotype was found on the CD4+CD38+ percentage, with FF-IR and FF-HR infants showing higher values than the FF-LR group. An influence of milk feeding alone was also found on CD4+CD25+ and CD8+CD38+ percentage which were lower and higher, respectively, in FF than in BF infants.

In conclusion, significant interactions exist between HLA-DQ genotype and milk feeding practices that affect the lymphocyte subset profile of infants at risk for CD. T cell changes observed might be relevant for the future immunological response to dietary gluten, and even for other responses involved in the course of infectious, inflammatory and autoimmune diseases.

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