Impact of Early Childhood Antibiotic Use on NK Cell Phenotype and Function in Atopic Dermatitis and Asthma

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Introduction: Atopic Dermatitis (AD) is a common skin disorder that often precedes asthma, with nearly 50% of children with AD developing asthma. The etiology is multifactorial, involving genetic, biological, and environmental contributors. AD is considered a T-cell driven disease, while Natural Killer (NK) cells may have a counterregulatory role. In mice, IL-15 therapies that expand NK cells have been beneficial, yet lesional sites in AD patients show NK cell enrichment, suggesting altered NK cell function. $CD56^{dim}$ NK cells express the Fc receptor CD16, which mediates antibody-dependent cellular cytotoxicity (ADCC), and we observed a progressive decline in CD16 expression within this subset in sensitized children with AD. Given reports linking antibiotic use to AD severity, our study aimed to examine whether early antibiotic exposure influences CD16 and TNF-α expression in $CD56^{dim}$ NK cells and whether these changes are associated with asthma risk.

Methods: The MPAACH cohort was developed to understand the progression from atopic dermatitis to asthma. This cohort (n = 682) was used for data analysis in our study. At each visit, biospecimens are collected from participating children. Specifically, our data is derived from the first three visits, and our cohort contains (n=124) randomly selected children. Sensitization was determined by skin prick test, and AD severity (SCORAD) by validated scoring. Antibiotic use was assessed by questionnaire as Yes/No within 12 months prior to each visit. NK cell CD16 and percentage TNF-α expression were determined by flow cytometry. The Wilcoxon Rank Sum test was used to determine significance for comparisons between TNF-α and antibiotic usage, as well as CD16 and antibiotic usage. The Spearman correlation test was used to assess significance for comparisons of SCORAD and CD16 with and without antibiotic usage. A Kruskal–Wallis test with Dunn's post-hoc was used to determine significance for CD16, SCORAD, and antibiotic comparisons, as well as for CD16, asthma status, and antibiotic usage comparison. Data analysis was performed by RStudio, p-values <0.05 were considered significant.

Results: Among children who had taken antibiotics, SCORAD was inversely correlated with CD16 expression ($p = 0.017$, $\rho = -0.272$). When stratified by AD severity, children with moderate AD who had taken antibiotics showed significantly reduced CD16 expression compared to both mild AD without antibiotics ($p = 0.038$) and moderate AD without antibiotics ($p = 0.033$).

Conclusion: Our analysis suggests that antibiotic early childhood usage may alter NK cell function in children with atopic dermatitis. Specifically, antibiotic exposure was associated with reduced CD16 expression on $CD56^{dim}$ NK cells, particularly in children with moderate AD. These findings highlight a potential immunological mechanism linking antibiotic use, NK cell dysregulation, and AD severity. Experiments are ongoing.

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