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Predictors of response to rescue inhalers in adult asthma and associations with fatty acid biomarkers and weight loss

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Bronchodilator response (BDR) is variable in asthma and predictors of response are unclear.[1] A high fat meal attenuates BDR, with greater effects seen in obese subjects.[2] Further, obesity adversely impacts asthma medication use and response, lung function, and asthma symptoms, while weight loss improves these outcomes.[3] This study examines predictors of BDR in adults with asthma, including fatty acid biomarkers; and whether weight loss improves BDR. Cross-sectional analysis in adults with ($n = 111$, BDR +ve) and without ($n = 109$, BDR-ve) BDR ($\geq$ 12% or $\geq$ 200 ml Δ forced expiratory volume in 1 second (FEV_1)) to salbutamol following bronchial provocation challenge and longitudinal analysis of obese subjects who achieved weight loss through bariatric surgery ($n = 8$) or dietary modification ($n = 16$). Assessment included spirometry, hypertonic saline (4.5%) challenge with sputum induction, fraction of exhaled nitric oxide (FeNO) and asthma control. Fatty acids were measured in plasma and erythrocyte membranes (RBC) by gas chromatography. Analysis was performed with Spearman's Rank-Order correlations and Multivariate linear regression. Subjects with significant BDR had lower lung function (FEV_1 % predicted, $p = 0.001$), increased airway hyperreactivity ($p < 0.001$) and increased T2 airway inflammation (FeNO, $p = 0.001$ and % sputum eosinophils, $p < 0.001$) v. subjects who did not respond to salbutamol post challenge. There were no differences in plasma fatty acids, though higher RBC C18:0% ($p = 0.042$), lower C18:3n-3 ($p = 0.045$) and total monounsaturated fatty acids (MUFA) % ($p = 0.048$) were seen in BDR-ve subjects, while BDR was negatively associated with RBC C20:1n-9% ($R_s = -0.31$, $p = 0.003$). Predictors of BDR included female sex ($p = 0.005$), higher airway inflammation (FeNO, $p = 0.006$) and higher airway reactivity ($p < 0.001$). Following weight loss (ΔBMI: -10.9% kg/m^2, 95% CI [-28.9, -7.3], $p < 0.001$), rescue inhaler use decreased ($p = 0.008$) and asthma control improved ($p < 0.001$), with no difference in BDR. Plasma total saturated fatty acids (SFA)% ($p = 0.043$) and total plasma omega-6 polyunsaturated fatty acids (PUFA) ($p = 0.041$) decreased, while total plasma ($p = 0.002$) and RBC omega-3 PUFA % increased. Lower rescue inhaler use was associated with decreased RBC C18:0% (Rs = 0.79, $p = 0.008$) and C20:1n-9% (Rs = 0.81, $p = 0.005$). Fatty acid biomarkers did not predict BDR, and weight loss did not improve BDR. However, in erythrocyte membranes, subjects with significant BDR had lower SFA and higher n-3 PUFA, while lower SFA and MUFA concentrations were associated with reduced rescue inhaler use following weight loss. Future studies investigating whether BDR can be improved by weight loss or improving diet quality, with a focus on modifying dietary fat intake are needed.

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