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Title: B2-adrenoceptor genotype16 influences airway calibre but not hyperresponsiveness in asthmatics using regular B2-agonist in addition to inhaled corticosteroids

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Body: Background: Asthmatic patients receiving inhaled corticosteroids (ICS) may take frequent add-on short acting beta agonist (SABA) despite on-demand prescription. B2-adrenoceptor (B2ADR) genotype 16 may influence this. Methods: A randomised double-blind triple crossover study comparing 2 weeks regular inhaled racemic salbutamol (200µg qid); levosalbutamol (100µg qid); or placebo on diurnal PEF and 6h trough methacholine PC20 in 30 persistent asthmatics (15 homozygous Arg16 and Gly16) all receiving ICS. Results: Active SABAs improved evening PEF in both Gly16 ($p<0.001$) and Arg16 patients ($p=0.006$); morning PEF did not improve with either SABA in Arg16 patients ($p=0.5$) compared to improvement in Gly16 patients ($p=0.04$)

There was no worsening of airway hyper-responsiveness (AHR) at trough to methacholine after 2 weeks regular exposure to either racemic ($p=0.53$) or levosalbutamol ($p=0.84$) compared to placebo; nor between genotypes as doubling dilution (dd) difference in methacholine PC20 from placebo. Conclusion: B2ADR genotype 16 influenced differential improvements in morning pre-bronchodilator PEF when using regular SABA in addition to ICS. There was no worsening of trough AHR at 2 weeks by genotype or active SABA compared to placebo.