function (FEV₁, FEF₂₅₋₇₅, total airway resistance at 5Hz: R5) and on salbutamol FEV₁ recovery post histamine challenge. Comparisons were made between genotypes comprising one or two copies of Arg (i.e. ArgArg or ArgGly n = 15, FEV₁ = 91.1%, FEF₂₅₋₇₅ = 58.3%) vs. no copies of Arg (i.e. GlyGly n = 10, FEV₁ = 94.1% FEF₂₅₋₇₅ = 60.0%).

Results Data are shown in table as change from baseline (i.e. pre vs. post propranolol as means and SEM) within each genotype. Within the Arg genotype there were significant effects of propranolol on FEV₁, FEF₂₅₋₇₅ and R5 as well as significant blunting of salbutamol response, while in the Gly genotype only salbutamol response was significant. However when comparing the Arg vs. Gly genotypes there were no significant differences for any of the outcomes.

Conclusion Propranolol produces significant effects on pulmonary function and salbutamol response in the Arg genotype, although there were no significant differences between Arg and Gly genotypes.

P192 A PILOT STUDY TO ASSESS THE INFLUENCE OF 2-ADRENOCEPTOR POLYMORPHISM ON SMALL AIRWAY FUNCTION AND ASTHMA CONTROL

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Introduction and Objectives It is increasingly recognised that small airway dysfunction is associated with suboptimal asthma control. We have previously reported that 2-adrenoreceptor polymorphism at position 16 (i.e. Arg/Gly) is not related to FEV₁ or airway hyper-responsiveness in persistent asthmatics.¹ However effects of 2-adrenoreceptor polymorphism on the small airways are not known. This pilot study in a different cohort of patients evaluated the effects of 2-adrenoreceptor polymorphism on small airway function and asthma control. Impulse oscillometry (IOS) was used to assess small airway function along with FEF₂₅₋₇₅. IOS is an effort independent test performed during normal quiet tidal breathing and is able to discriminate between changes in central and peripheral airways. Resistance at 5 Hz (R5) and 20 Hz (R20) indicate total and central airway resistance respectively - the difference between R5 and R20 indicates peripheral airway resistance. Asthma control was assessed using the Asthma Control Questionnaire (ACQ-5).

Methods We collected spirometry, IOS and ACQ data from patients attending a secondary care asthma clinic. A total of 100

patients all taking inhaled corticosteroids (20% taking long acting beta-agonists) were included with a mean: age 39.2 year FEV₁ 88.4%, FEF₂₅₋₇₅ 55.5%, R5%162%, R5-R20 0.07 kPa/l/s, ACQ-5 1.70

Results 48% (n = 48) had 1 or 2 copies of the Arg allele (i.e. Arg/Arg or Arg/Gly genotypes) while 52% (n = 52) had no copies of the Arg allele (i.e. Gly/Gly genotype). There was no significant difference between genotypes in terms of FEV₁, FEF₂₅₋₇₅, R5, R5-R20 or ACQ. Furthermore there was no significant effect of LABA according to Arg/Gly polymorphism.

REFERENCE

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P193 A ROLE FOR ACTIVE VITAMIN D IN STEROID RESISTANT ASTHMA PATIENTS WHO HAVE ENHANCED PRODUCTION OF IL-17A AND REDUCED IL-10

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Background Steroid refractory (SR) asthma, a distinct disease phenotype, has a high morbidity and mortality and takes up a disproportional burden of healthcare cost. IL-17A is a pro-inflammatory cytokine that is essential for host defence against pathogens but can also lead to damage of the surrounding tissues associated with immune diseases and is linked with severe asthma. IL-10 has crucial immunoregulatory properties, and we have previously shown *in vitro*, that T cells from steroid refractory asthma patients fail to respond to glucocorticosteroids for the induction of IL-10 synthesis.

Methods We assessed IL-17A and IL-10 synthesis in steroid sensitive, SS, (mean% change in FEV₁ following 2 weeks of oral prednisolone 16%) versus SR (mean% change FEV₁ 0%) asthma patients and investigated their response to dexamethasone.

Results PBMC from SR individuals synthesised 7-fold higher levels of IL-17A than disease-severity matched SS patients (by flow cytometry and CBA). Interestingly IL-17A levels inversely correlated with changes in lung function following oral steroids whereas higher IL-10 levels were associated with an increase in lung function. Dexamethasone failed to inhibit IL-17A, but, surprisingly, increased protein synthesis, an effect that was also seen *in vivo*: inhaled glucocorticosteroid dosages correlated with IL-17A protein levels. This suggests the potentially detrimental effects corticosteroids might have in certain asthma phenotypes. The production of IL-10 by T cells was impaired in cultures from SR asthmatics, but not in healthy controls or SS asthma patients implying an associated impaired IL-10 response with poor asthma control. 1alpha,25-dihydroxyvitamin D3 (1,25(OH)D) not only restored the capacity of T cells to produce IL-10 upon stimulation with dexamethasone in SR asthma patients, but also inhibited IL-17A synthesis in culture independently of steroid.

Conclusion High IL-17A levels are associated with poor response to steroids and more severe asthma. Our data supports a steroid-enhancing property of 1,25(OH)D in severe asthma through inhibition of IL-17A and via enhancement of IL-10 synthesis.

Abstract P192 Table 1: Spirometry, IOS and ACQ-5 according to Arg/Gly-16 polymorphism

	Arg-Arg / Arg-Gly	Gly-Gly	p-value
FEV ₁	88 (82-94)	85 (78-91)	0.46
(% predicted)			
FEF ₂₅₋₇₅	53 (45-62)	49 (41-57)	0.48
(% predicted)			
R5	149 (132-168)	178 (147-209)	0.58
(% predicted)			
R20	142 (127-156)	146 (130-162)	0.80
(% predicted)			
R5 - R20 (kPa/L/S)	0.07 (0.05-0.09)	0.07 (0.05-0.09)	1.00
ACQ-5	1.38 (0.92-1.84)	1.96 (1.54-2.38)	0.07

Data presented as means (95% CI)