Genetic Polymorphisms In Antioxidative Enzymes And Phenotypes Of Asthma

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Risikofaktorer for Astma hos Voksne

Methods:

Study population
In a cross-sectional Danish case-base study of asthma (ECRHS protocol) 1164 subjects aged 20-44 years were enrolled.

Phenotypes
Eight different phenotypes defined by the combinations

Current asthma → Steroid usage, BHR, Atopy, Eosinophilia

Doctor diagnosed asthma → Eosinophilia

BHR: positive PD20 at metacholine challenge, cummulative dose 2.46 mg
Atopy: at least 1 of 13 positive skin prick test mean diameter > 3mm
Eosinoplilia: > 0.4 x 10^9 eosinophils/l blood

Genotypes
Real time PCR were used to investigate polymorphisms in Glutathione Peroxidase (GPx1: pro198leu)
Mangenese Superoxide dismutase (SOD2: ala9val)
Three Glutathione-S-Transferases (GSTT1: null, one or two copies) (GSTM1: null, one or two copies) (GSTP1: ile105val).

Table 1. Characteristics of study population n=1.191	
Mean age, years (SD)	34.7 (7.1)
Female, n (%)	609 (56)
BMI, mean (SD)	25.7 (4.9)
Doctor diagnosed asthma, n (%)	331 (30)
Current asthma symptoms, n (%)	311 (29)
Steroid, n (%)	130 (12)
BHR, n (%)	239 (25)
Atopy, n (%)	415 (39)
Blood eosinophilia, n (%)	111 (10)
Smoking	
Never, n (%)	578 (53)
Former, n (%)	185 (17)
Current, n (%)	326 (30)

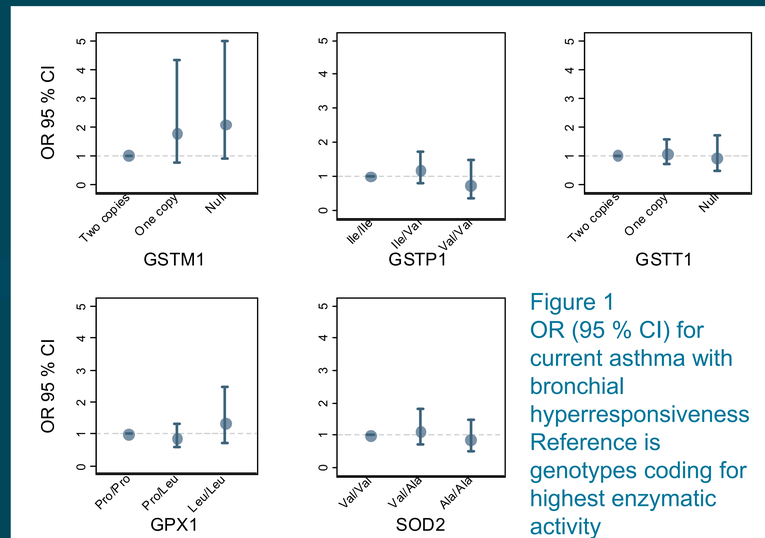

Figure 1
OR (95 % CI) for current asthma with bronchial hyperresponsiveness
Reference is genotypes coding for highest enzymatic activity

Results:

Demographic data for study population is shown in table 1 with prevalence of the investigated phenotypes between 5 % and 19 %, lowest for eosinophilic asthma and highest for atopic asthma.
Allele frequencies are shown in table 2.
Current asthma with concurrent BHR were as shown in figure 1 not associated with any of the genotypes, nor were current asthma in combination with steroid usage, atopy or eosinophilia (table 3). Similar results were shown for phenotypes involving doctor diagnosed asthma.
Neither restricting to current smokers nor ever smokers changed the estimates

Table 2
All genotypes were in Hardy-Weinberg equilibrium Allele frequencies were as follows:

GPX1 (rs1050450)	Proline	0.69	Leucine	0.31
SOD2 (rs4880)	Valine	0.49	Alanine	0.51
GSTP1 (rs1695)	Isoleucine	0.66	Valine	0.34
GSTT1	no deletion	0.64	deletion	0.36
GSTM1	no deletion	0.29	deletion	0.71

Aim:

To investigate associations between genotypes of five major antioxidative enzymes and different phenotypes of asthma

Table 3. Association between asthma phenotypes and genotypes adjusted for study area, sex, age, BMI and smoking status

		Current asthma symptoms in combination with Steroid usage	Atopy	Blood eosinophilia
GPX1	Pro/Pro	1.0	1.0	1.0
	Pro/Leu	0.8 (0.5-1.3)	1.0 (0.7-1.5)	1.0 (0.6-1.8)
	Leu/Leu	0.8 (0.4-1.6)	1.7 (1.0-2.8)	1.3 (0.5-3.0)
SOD2	Val/Val	1.0	1.0	1.0
	Ala/Val	1.0 (0.6-1.6)	1.1 (0.7-1.6)	0.6 (0.3-1.1)
	Ala/Ala	0.7 (0.4-1.3)	0.9 (0.6-1.5)	0.6 (0.3-1.2)
GSTP1	Ile/Ile	1.0	1.0	1.0
	Ile/Val	1.0 (0.6-1.5)	1.3 (0.9-1.8)	1.5 (0.8-2.6)
	Val/Val	1.1 (0.6-2.1)	0.9 (0.5-1.6)	1.5 (0.6-3.5)
GSTT1	Two copies	1.0	1.0	1.0
	One copy	1.3 (0.9-2.0)	0.8 (0.6-1.2)	1.0 (0.6-1.8)
	Null	1.1 (0.6-2.1)	1.0 (0.6-1.7)	1.0 (0.5-2.4)
GSTM1	Two copies	1.0	1.0	1.0
	One copy	0.9 (0.4-1.9)	1.6 (0.8-3.3)	0.8 (0.3-2.5)
	Null	0.9 (0.5-1.9)	1.9 (0.9-3.9)	1.6 (0.6-4.6)

Conclusion:

Asthma or any phenotype of asthma is not associated to genotypes of any of GPx1, SOD, GSTT1, GSTM1 or GSTP1. Smoking does not change the estimates

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