Normal antioxidative enzyme activities in several genes are associated with less Bronchial hyperresponsiveness (BHR) among young Danes.

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Aim

BHR might be associated to the oxidative defense. We hypothesize that genotypes coding for normal antioxidative enzyme activity (AEA) influence the occurrence of BHR.

Methods

Study population:
In a cross sectional study 7,271 subjects aged 20-44 year (73% response rate) were recruited using an asthma screening questionnaire. All subjects with asthma (n = 460) and a 20% random sample (n= 728) were clinically investigated, including a bronchial provocation test, a blood sample, and skin prick test (SPT) with 13 aeroallergens. For house dust mites (HDM) groups were calculated according to the size of the SPT. BHR was defined as at least 20% drop in baseline FEV_1.

Variants in the following genes were genotyped:
Glutathione peroxidase, GPX1 (Pro198Leu, rs1050450), manganese superoxide dismutase, SOD2 (Ala16Val, rs4880) and 3 glutathione S-transferases; GSTP1 (Ile105Val, rs1695), GSTT1 (gene copy nr(1)) and GSTM1 (gene copy nr(1)).

Genes coding for normal AEA (2): GPX1 Pro/Pro, SOD2 Val/Val, GSTP1 Ile/Ile, GSTT1 two copies, GSTM1 two copies

References

(1) Brasch-Andersen C, Christiansen L, Tan Q, Haagerup A, Vestbo J, Kruse TA. Possible gene dosage effect of glutathione-S-transferases on atopic asthma: using real-time PCR for quantification of GSTM1 nd GSTT1 gene copy numbers. Hum Mutat 2004 September;24:208-14.

(2) Malling TH, Sigsgaard T, Brasch-Andersen C, Frischknecht L, Andersen HR, Kruse TA, Sherson D, Skadhauge LR, Thomsen G, Baelum J, Omland Ø. Genetic polymorphisms in antioxidative enzymes are associated to forced expiratory volume in 1 s (FEV1) in smokers independently of asthma. Clin Respir J. 2012 Jan;6(1):46-55.

Results

Table 1 shows characteristics of study population in the 917 subjects fulfilling all criteria in the analysis

	Random sample (n=618)	Case sample (n=375)
Female gender, n (%)	319 (52)	222 (59)
Mean age, years (SD)	35.3 (7.3)	34.1 (7.4)
BHR, n (%)	91 (15)	156 (42)
Atopy, n (%)	194 (32)	207 (55)
Any positive HDM, n (%)	84 (14)	112 (30)
Current smokers, n (%)	177 (29)	120 (32)
Nr. of genes coding for normal AEA, 0, 1, 2, 3, 4+	73, 195, 221, 105, 24	49, 113, 144, 63, 6
Mean FEV_1, l (SD)	3.77 (0.75)	3.57 (0.77)
Mean height, m (SD)	1.74 (0.09)	1.73 (0.10)

Logistic regression models showed a negative association between being BHR and having at least 4 genotypes coding for normal AEA compared to no normal genotype. Table 2 shows OR's in a model adjusted for smoking, FEV_1, sex, atopy, height^2 and SPT-size of HDM. The result were similar after further adjustments for BMI, county and sample (random/case), OR 0.25 (0.06-1.06) for at least 4 genotypes coding for normal AEA. OR's for BHR were decreased for 1 – 3 genotypes with normal AEA compared to no normal genotype, but not significantly so and no clear dose-response relations were seen.

Table 2

Number of genes coding for normal AEA	Adjusted OR's
0 (n=118)	1
1 (n=285)	0,74 (0,43 - 1,28)
2 (n=335)	0,79 (0,47 - 1,34)
3 (n=151)	0,72 (0,39 - 1,32)
4+ (n=28)	0,24 (0,059 - 0,94)

Conclusions

This study suggests, that a combined effect of several genotypes coding for normal AEA might be a protective factor for BHR among young adults.