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Gstm1 and Gstt1 Genotypes and Chromosomal Damage in Subjects Exposed to Low Level of Formaldehyde

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Introduction

During the course of evolution, the living organisms have developed a set of enzymes able to eliminate the harmful xenobiotics present in food and in the environment (1). Among the several detoxification mechanisms (phase II) used for protection, the reduced glutathione and the glutathione-S-transferases (GSTs) is one of the most efficient systems. At least five gene families are present in humans (GSTM, GSTT, GSTP, GSTA and microsomal GST). In humans at least twenty GST enzymes with different isoenzymatic forms are present. Both GSTM1 and GSTT1, in particular, are polymorphic and there is now a considerable volume of data supporting the opinion that these polymorphisms can influence the susceptibility to cancer. In Europe the GSTM1 "null" genotype (GSTM1-) is present in about 50% of the studied populations, while the frequency of GSTT1 "null" genotype (GSTT1) ranges from 20% to 38% (2). The aim of this study was to investigate if it was possible to find a relationship between cytogenetic damage due to formaldehyde exposition and GSTT1 / GSTM1 genotypes.

Material and Methods

GSTM1 and GSTT1 genotypes were determined by PCR. The amplified products were two fragments of 273 bp and 480 bp respectively and the absence of these products was indicative of the deleted genotypes. Chromosome aberrations were analysed in peripheral blood lymphocyte cultures harvested after 48 h. For each subject, 100 complete metaphase plates were analysed, utilizing international standards for chromosome aberrations (CA) counting. Eighty individuals belonging to 4 hospitals in the Northwest of Italy, working into anatomy-pathology laboratories, constituted the sample. The exposition level was determined by a personal dosimeter, immediately before the blood venipuncture.

Results

The GSTT1 "null" genotype frequency was 22.5%, which is included in the European population range, while the GSTM1 null genotype was 28.2%, lower than the values reported in the literature for Caucasians. The CA frequency and that of cells with aberrations, analysed in 55 subjects of our sample, was respectively 3.5% and 3.1%; these values were statistically higher ($p<0.05$, χ^2 test) than our controls (historical data on hospital non exposed personnel) (3). It was not possible to find any relation between CA frequency and level of exposition to formaldehyde. The exposure level (range 1-268 μg/mc) was, in any case, lower than the limits set forth the law (270 μg/mc). As far as concerns the chromosome damage in relation to the genotype, the GSTM1 "null" subjects showed a frequency of damaged cells (DC) which was significantly higher than the frequency in the GSTM1+ individuals (4.22% vs 2.54% - $p<0.001$ χ^2 test). Instead no difference was found between GSTT1+ and GSTT1- subjects (Tab. 1). Moreover, in considering also the smoking habit, lymphocytes from smokers with the GSTM1 "null" genotype were also found to exhibit increased chromosomal damage as compared to these from smokers with GSTM1 + genotypes (χ^2 test $p<0.05$) (tab 2).

Tab 1. CA and DC frequency in GSTT1 and GSTM1 subjects

genotype	n. subjects	%CA	% DC
GSTT1 +	42	3.64	3.22
GSTT1 -	12	3.20	2.85
GSTM1 +	38	3.05	2.54
GSTM1 -	15	4.36	4.22**

Tab 2. DC frequency in GSTM1 smokers and non-smokers

	smokers	non-smokers
GSTM+	2.28	2.59
GSTM1-	4.52*	3.85

Discussion

In this study we examined the possible relation between cytogenetic damage due to low formaldehyde exposition

and GSTT1 and GSTM1 genotypes in hospital workers employed in anatomy-pathology laboratories. The CA frequency in these subjects fell in the range found in some our previous studies on hospital workers exposed to anaesthetic gases and low level ionising radiations (3, 4) and since these values were higher than those found in non exposed individuals, they could indicate a signal of early adverse biological effect. However different GSTM1 genotypes seem influence the level of cytogenetic damage since the CA frequency was statistically higher in GSTM1 "null" genotype. Moreover the smoking habit could significantly influence the damage in GSTM1 "null" individuals.

Key Words

GSTT1, GSTM1, chromosomal aberrations, formaldehyde exposure.

References

[1] Nebert D.W., Am. J. Hum. Genet., 1997. 60: 265-271.
[2] Nelson H.H., Wiencke J.K., Christiani D.C., Chang T.J., Zheng-Fa Zuo, Schwartz D.S., Byung-Kook Lee, Spitz M.R., Min Wang, Xiping Xu, Kelsey C.T., 1995. Carcinogenesis, 16: 1243-1245.
[3] Lamberti L., Bigatti P., Ardito G., Armellino F., 1989. Mutagenesis, 4: 95-97.
[4] Bigatti P., Lamberti L., Ardito G., Armellino F., 1988. Mutation Res., 204: 343-347.