XRCC3241 POLYMORPHISM INFLUENCE ON GENOTOXICITY BIOMARKERS FREQUENCY IN WORKERS OCCUPATIONALLY EXPOSED TO FORMALDEHYDE

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Introduction

Formaldehyde (FA) is ubiquitous in the environment and is a chemical agent that possesses high reactivity. Occupational exposure to FA has been shown to induce nasopharyngeal cancer and has been classified as carcinogenic to humans (group 1) on the basis of sufficient evidence in humans and sufficient evidence in experimental animals. The exposure to this substance is epidemiologically linked to cancer and nuclear changes detected by the cytokinesis-block micronucleus test (CBMN). This method is extensively used in molecular epidemiology, since it determines several biomarkers of genotoxicity, such as micronucleus (biomarkers of chromosomes breakage or loss), nucleoplasmic bridges (biomarker of chromosome rearrangement, poor repair and / or telomeres fusion) and nuclear buds (biomarker of elimination of amplified DNA).

The gene X-ray repair cross-complementing group 3 (XRCC3) is involved in homologous recombination repair of cross-links and chromosomal double-strand breaks and at least one polymorphism has been reported in codon 241, a substitution of a methionine for a threonine.

Aim of the Study

Determine whether there is an *in vivo* association between genetic polymorphism of *XRCC3* and the frequency of genotoxicity biomarkers – MN, NPB, NBUD and MN in buccal cells, in occupationally workers exposed to formaldehyde.

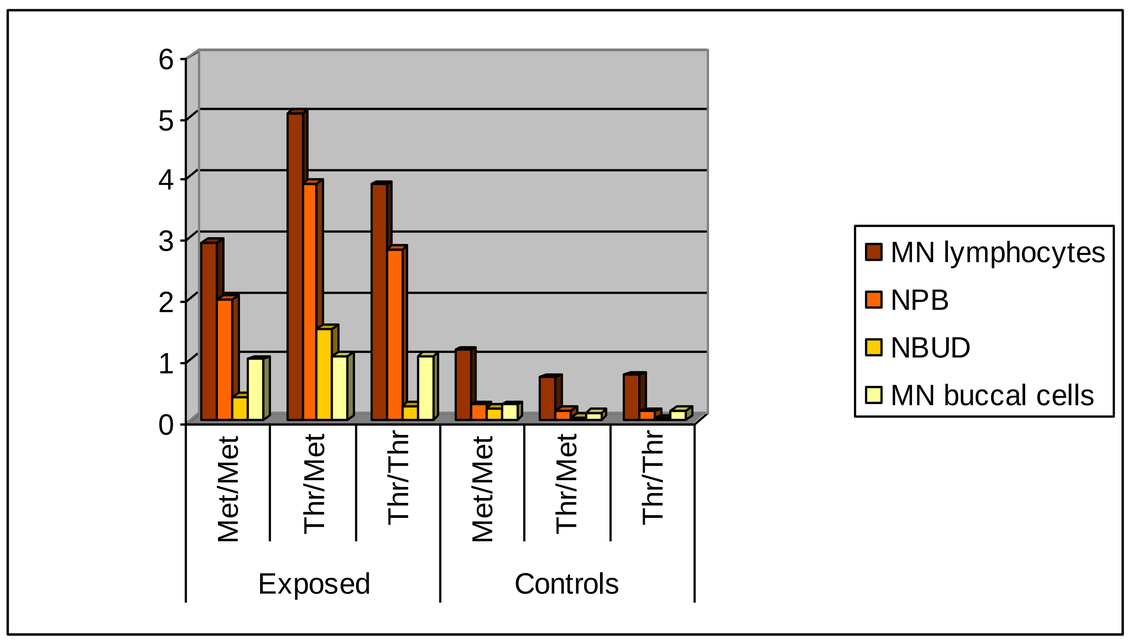
Methodology

We compare a sample of 52 workers exposed to FA in pathological anatomy laboratories with 82 controls, in order to investigate whether exposure to FA and of genetic polymorphism of *XRCC3* is associated with the frequency of the genotoxicity biomarkers in study. The evaluation of genotoxic effects was measured by CBMN. All samples were coded and analysed under blind conditions and the criterion of scoring the cells was the same as the described in *The Human MicroNucleus Project.* DNA was isolated from PBL and the XRCC3 241 genotype study was performed by Real Time PCR, using the iCycler iQ® Multicolor Real-Time PCR Detection System (BIO-RAD).

Table 1 – Descriptive statistics for genotoxcity biomarkers means according to XRCC3 Thr241Met polymorphisms

Groups	XRCC3	N	Mean MN lymphocytes ± S.E.	Mean NPB± S.E.	Mean NBUD± S.E.	Mean MN buccal cells ± S.E.
Exposed	Met/Met	13	2.92±0.930 (0-12)	2.00±1.138 (0-15)	0.38±0.180 (0-2)	1.00±0.707 (0-9)
	Thr/Met	22	5.05±0.979 (0-14)	3.91±0.840 (0-13)	1.50±0.334 (880-2)	1.05±0.381 (0-5)
	Thr/Thr	17	3.88±0.848 (0-12)	2.82±0.944 (0-13)	0.24±0.953 (0-2)	1.06±0.491 (0-8)
Controls	Met/Met	20	1.15±0.460 (0-7)	0.25±0.123 (0-2)	0.2±0.092 (0-1)	0.25±0.143 (0-2)
	Thr/Met	27	0.70±0.296 (0-6)	0.15±0.116 (0-3)	0.04±0.037 (0-1)	0.11±0.82 (0-2)
	Thr/Thr	35	0.74±0.233 (0-6)	0.14±0.073 (0-2)	0.03±0.29 (0-1)	0.17±0.096 (0-2)

Figure 1 – Distribution of the genotoxcity biomarkers according to XRCC3 Thr241Met polymorphisms



Conclusions

The exposed workers carrying the Thr/Met *XRCC3*241 genotype were found to have higher MN mean than Met/Met and Thr/Thr *XRCC3* 241 genotypes. Moreover, the values were higher when compared with their control counterparts. Binary logistic regression analysis indicated that the exposure to formaldehyde was an important variable affecting the genotoxic response ($p<0.001$), but the polymorphisms of XRCC3 at codon 241 were not found statistically significant with exception to NBUD ($p<0.05$). Understanding the complexity of the relationships between exposure, DNA repair and genotoxicity biomarkers frequencies probably require larger scale studies and complementary biomarkers. Chromosomal instability has been associated to XRCC3 gene mutation and other genes involved in repair. Manifold studies suggest a direct role of XRCC3 Thr241Met polymorphism maybe associated, but not significant, to a reduce capacity of DNA repair. This study was verified that carriers of Thr241Met polymorphism have higher means of genotoxicity biomarkers in exposed workers.

References

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