

APPLICATION OF ALKALINE COMET ASSAY IN HUMAN BIOMONITORING FOR GENOTOXICITY: A STUDY ON OCCUPATIONAL EXPOSURE TO CYTOSTATICS

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Introduction

The use of cytostatics drugs in anticancer therapy is increasing. Health care workers can be occupationally exposed to these drugs classified as carcinogenic, mutagenic or teratogenic (IARC, 1987, 1997). Cytostatics drugs are a heterogeneous group of chemicals widely used in the treatment of cancer, nevertheless have been proved to be also mutagens, carcinogens and teratogens. Workers may be exposed to this drug, being in the hospital settings the main focus dwelled upon the pharmacy, and nursing personnel. Alkaline comet assay is one of the most promising short-term genotoxicity assays for human risk assessment, being recommended to monitor populations chronically exposed to genotoxic agents. DNA glycosylase (OGG1) represents the main mechanism of protecting the integrity of the human DNA with respect to 8-OHdG, the most well studied biomarker of oxidative damage.

Research Aim and Methods

This study intended to assess genotoxic effects of cytostatics occupational exposure by alkaline comet assay. The study population consisted of 46 exposed subjects working as pharmacists, pharmacy technicians, and nurses that handle cytostatics drugs and 46 unexposed control subjects. The alkaline comet assay was used to evaluate the genotoxicity towards peripheral blood lymphocytes, and the slides were stained with DAPI. Percentage of DNA in the tail and oxidative damage parameters were measured with Perceptive Instruments[®] software. The genotype of the polymorphisms *OGG1* (rs1052133) was studied by Real Time PCR using the *iCycler iQ[®] Multicolor* Real-Time PCR.

Results

Table 1 - Descriptive statistics of % DNA in tail and FPG means by gender and exposure (mean ± mean standard error, range).

Groups	Gender	N	% DNA in tail Mean ± S.E. (range)	FPG Mean ± S.E. (range)
Exposed	Females	40	14.84±1.38 (1.79-31.64)	5.31±0.61 (0.19-13.91)
	Males	6	17.43±5.96 (4.61-44.50)	5.39±1.09 (2.38-9.65)
Controls	Females	34	14.15±1.49 (2.48-30.43)	4.57±0.74 (0.02-14.46)
	Males	12	7.46±1.54 (2.79-18.49)	4.65±0.89 (0.10-9.61)

- ✓ No statistical significant differences were found in both parameters between the exposed and control groups, and the three possible *OGG1* genotypes.

Table 2 - Descriptive statistics of % DNA Tail and FPG means in the studied population (mean ± mean standard error, median, and range) by *OGG1* Ser326Cys polymorphisms and exposure, p-value of Kruskal-Wallis test.

Groups	OGG1	N	% DNA Tail Mean ± S.E. (range)	FPG Mean ± S.E. (range)
Exposed	Cys/Cys	7	13.11 2.80 (1.79 – 23.53)	5.03 1.48 (0.27 – 12.0)
	Ser/Cys	14	13.23 1.42 (2.48 – 28.19)	4.97 0.72 (0.10 – 14.46)
	Ser/Ser	25	14.26 1.38 (2.68 – 44.50)	4.94 0.51 (0.02 – 12.90)
p-value			0.777	0.647
Controls	Cys/Cys	2	14.22 9.31 (4.91 – 23.53)	7.39 4.61 (2.78 – 12.00)
	Ser/Cys	18	12.04 1.86 (2.48 – 28.19)	4.69 1.00 (0.10 – 14.46)
	Ser/Ser	26	12.52 1.74 (2.68 – 30.43)	4.30 0.73 (0.02 – 12.69)
p-value			0.906	0.682

Conclusions

Occupational exposure to cytostatics drugs is associated with genotoxic effects. In this study, the results of the comet assay analyzed parameters were higher in exposed in comparison with controls, however not significant. Also the study of the susceptibility biomarkers did not show statistical significant differences.

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