

EXPAH: EFFECTS OF POLYCYCLIC AROMATIC HYDROCARBONS (PAHs) ON ENVIRONMENTAL POLLUTION ON EXOGENOUS AND ENDOGENOUS DNA DAMAGE – CZECH COHORT

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STUDIED GROUPS

Policemen represent a model group, which is highly exposed to ambient air pollution as well as they spend the most of their working hours outdoors. Therefore the effect of PAHs adsorbed on air particles < 2.5 mm was studied in two groups:

policemen from the center of the City spending daily > 8h outdoors

matched controls working indoors

METHODS

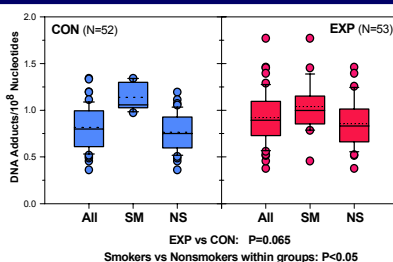
- PAHs: VAPS, Personal monitoring
- Cotinine
- Triglycerids
- Total, HDL and LDL cholesterol
- Vitamins A, C, E, folic acid
- Oxidative damage: 8-oxodG, MDA-DNA adducts
- DNA adducts by ³²P-postlabelling
- Protein p53 and p21
- Chromosomal aberrations: Conventional, FISH
- Micronuclei
- Genetic polymorphisms: CYP1A1, GSTM1, GSTP1, GSTT1, NAT2, EPHX, MTHFR, MS, p53, XRCC1, XPD, hOGG1

PAHs CONCENTRATIONS Personal monitoring

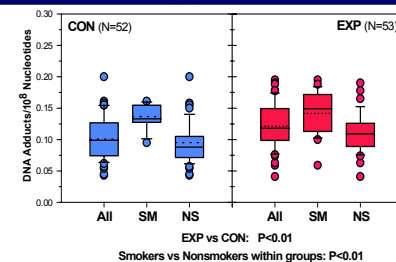
(median and range)				
Group	N	Age (years)	B[a]P ng/m ³	carcPAHs ng/m ³
EXPOSED	53	31.6 ± 7.2	1.6 (0.3 - 8.7)	9.7 (3.1 - 58.2)
Smokers	19	32.9 ± 7.0	1.6 (0.3 - 7.5)	10.8 (3.1 - 43.6)
Nonsmokers	34	30.9 ± 7.3	1.5 (0.3 - 8.7)	8.7 (3.1 - 58.2)
CONTROLS	52	29.6 ± 9.1	0.8 (0.3 - 2.8)	5.8 (3.1 - 19.3)
Smokers	7	37.6 ± 14.2	0.3 (0.3 - 1.4)	3.3 (3.1 - 8.2)
Nonsmokers	45	28.3 ± 7.6	0.9 (0.3 - 2.8)	6.1 (3.1 - 19.3)

RESULTS

TOTAL DNA ADDUCTS



„LIKE“ B[a]P-DNA ADDUCT



MULTIPLE REGRESSION ANALYSIS: DNA - PAH adducts

Model	Coefficients	Unstandardized Coefficients B	Sig.	95 % Confidence Interval for B		R	Adjusted R square	Sig.
				Lower bound	Upper bound			
1	(Constant)	1.072	0.000	0.977	1.167	0.54	0.26	0.000
	Non-exp. + non-smok	-0.277	0.000	-0.389	-0.164			
	Exp. + non-smok.	-0.211	0.001	-0.332	-0.090			
	XRCC1 (+/+)	-0.124	0.012	-0.220	-0.028			
	XPD-23 (+/+)	0.149	0.022	0.022	0.276			
Exploratory model - whole set of variables								
2	(Constant)	1.203	0.000	1.080	1.326	0.54	0.26	0.000
	Non-exp. + non-smok	-0.280	0.000	-0.394	-0.167			
	Exp. + non-smok.	-0.237	0.000	-0.359	-0.114			
	XPD-23 (-/-)	-0.122	0.013	-0.218	-0.027			
	Vit. C (µmol/L)	-0.001	0.017	-0.002	0.000			
Exploratory model - XRCC1 excluded								
3	(Constant)	1.040	0.000	0.932	1.149	0.54	0.27	0.000
	Non-exp. + non-smok	-0.286	0.000	-0.397	-0.175			
	Exp. + non-smok.	-0.199	0.001	-0.319	-0.080			
	XRCC1 (+/+)	-0.111	0.025	-0.207	-0.014			
	GSTM1 (null)	0.095	0.040	0.005	0.186			
Exploratory model - XPD-23 excluded								

MULTIPLE REGRESSION ANALYSIS: Percentage of aberrant cells (FISH)

	Bulky DNA Adducts	B[a]P-like DNA adducts	MDA -DNA Adducts
Micronuclei /1000 cells	0.190	0.004	0.180
% AB.C. (conventional)	0.623	0.871	0.590
% AB.C. (FISH)	0.069	0.045	0.807
F _G /100	0.086	0.027	0.916
t/1000	0.114	0.048	0.848

P- values for ANOVA, Kruskal-Wallis tests, Pearson and Spearman correlation coefficients

EFFECT OF DNA ADDUCTS ON CYTOGENETIC ENDPOINTS

Model	Coefficients	Unstandardized Coefficients B	Sig.	95 % Confidence Interval for B		R	Adjusted R square	Sig.
				Lower bound	Upper bound			
6	(Constant)	-0.283	-0.019	-0.518	-0.048	0.58	0.29	0.000
	Age (years)	0.012	0.000	0.007	0.017			
	CYP1A*2C (Ile/Val) (+/+)	0.144	0.024	0.020	0.268			
	B[a]P-like adducts/10+08 ncls	1.399	0.018	0.251	2.548			
	EPHX (high activity)	-0.106	0.036	-0.205	-0.007			
	Folates (nmol/l)	-0.004	0.059	-0.008	0.000			
	p53 msp1 (+/+)	-0.324	0.098	-0.709	0.061			

PIN=0.10, POUT=0.15

SUMMARY

- Predictor of total DNA adducts was smoking, vitamin C, polymorphisms of GSTM1, EPHX exon 4, XRCC1 and XPD exon 23.
- Predictor of „like“B[a]P- derived DNA adduct was smoking, exposure to carcinogenic PAHs, and polymorphisms of GSTM1, XRCC1, MTHFR.
- Predictor of the frequency of aberrant cells by convention method was polymorphisms of CYP1A1, XPD exon 6 and XPD exon 23.
- Predictor of the frequency of translocations by FISH was age, smoking, exposure to carcinogenic PAHs, folate, polymorphisms of CYP1A1, GSTM1, GSTP1, EPHX, p53, msp1 and MTHFR.

CONCLUSIONS

- Results of DNA adducts analysis and FISH analysis indicate that city policemen represent a group of the increased genotoxic risk.
- DNA adducts highly correlated with cytogenetic endpoints by FISH.
- Polymorphism of metabolic and DNA repair genes identify subjects susceptible to DNA damage by exposure to carcinogenic PAHs.

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Acknowledgement

Supported by the EC QLRT-2000-00091 and by the Czech Ministry of Environment VaV/340/2/00