Abstract

Genetic polymorphism of biotransforming enzymes and risk of pancreatic cancer development in Czech Republic

Objective: Pancreatic cancer represents one of the biggest challenges of present-day oncology. It effects mainly effects patients in sixth or higher decade of life and due to minimal symptoms in early stages, it is usually diagnosed in locally advanced or metastatic stage of the disease. The only modality which represents a possible chance for long term survival is radical surgical resection. Chemotherapy and possible targeted therapy have only a palliative role. Due to the above mentioned facts, it would be highly useful to identify genetic factors, which could play a role in pancreatic cancer development and create specific screening program which could identify early stages of the disease. We have focused our study on gene polymorphisms in biotransforming enzymes, which modify carcinogen and procarcinogen metabolism and may represent risk factors for pancreatic cancer.

Methods: We have included 278 pancreatic cancer patients into this study. As a control group we have chosen healthy volunteers from general practicioner clinics and healthy blood donors. We have focused on gene polymorphisms in biotransforming enzymes CYP1B1, EPHX, NQO1 GSTP1, GSTT1, GSTM1. DNA was amplified by PCR, consequently split by restriction enzymes and the restriction fragment size was identified by horizontal electrophoresis. Statistical analyses were processed by the statistical software CRAN 2.4.0. The overall survival of given groups was determined using Kaplan-Meier´s survival distribution functions. The Log-rank test was used for evaluation of different survivals among investigated groups and subgroups. Odds ratios (OR) and confidence intervals for examining the association between genetic factors and cancer risk were estimated by logistic regression.

Results: Allele dictibution assessment between cases and controls showed, that Val/Val genotype carriers in codon 432 CYP1B1 have lower risk of pancreatic cancer development then wild type carriers (OR 0,59, 95%CI 36-0,96, p=0,035). Heterozygotes have also lower risk (OR 0,69, 95%CI 0,49-0,97, p=0,033). There was an even more signficant relation in the case of histologicaly verified patients. Variant allele in GSTP1 codone 105 was associated with higher pancreatic cancer risk (OR 1,38, 95%CI 0,96-1,97), the same was found for GSTT1deletion (OR 1,56, 95%CI 0,93-2,61). The combination of GSTT1 and GSTP1 had a multiplicative effect on the risk for pancreatic cancer (OR 2,5, 95% CI 1,20-5,20). There was no statisticaly significant relation in other gene polymorphisms. Also there was no association found between studied gene polymorphisms and pancreatic cancer survival.

Conclusion: Our study was the first of its kind in The Czech Republic and further research is needed to confirm the above mentioned gene polymorphisms associations with pancreatic cancer risk and survival.