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BIOMARKERS OF EFFECT AND SUSCEPTIBILITY IN POPULATION EXPOSED TO IONIZING RADIATION.

Angelini S., 3° anno di corso Dottorato in Farmacologia e Tossicologia, XV ciclo. Durata del Dottorato in anni: 4. Sede di servizio: Department of Pharmacology, University of Bologna, Via Irnerio, 48 40126 Bologna.

Molecular epidemiology is based on the use of biological markers for the purpose of identifying causes and outcomes of disease (cancer) in humans, developing strategies for risk assessment and designing effective preventive measures. There are biomarkers of exposure, effect and susceptibility and the last one may be influenced by the genotype of polymorphic genes existing in a population.
The study of health effects of ionizing radiation has received a continuing and increasing importance because of the expanding use of radiological methods in industry, science and medicine. Even thought many studies are directed to this end, the harmful effects of ionizing radiation at low-level exposure are not well elucidated.
We used micronuclei (MN) as biomarkers of effect to investigate chromosomal damage in peripheral lymphocytes from hospital workers exposed to low-levels of ionizing radiations (0.45-141.77 mSv). The MN-test was performed using the cytochalasin B technique. Samples of peripheral blood were collected from 37 subjects (19 non smokers and 18 smokers; mean age: 43.7±8.9) working in radiodiagnostic, and 37 matched controls (20 no-smokers and 17 smokers; mean age 41.6±8.3) working in the same hospital. The influence of confounding factors like smoking status, age and gender on MN frequency was investigated by multiple regression analysis. Preliminary results showed that the MN frequencies of exposed workers did not differ from those of controls (MN/1000 binucleated cells (BN) cells: 6.78±4.92 vs 5.54±2.99, respectively). Interestingly, smoking status raised chromosomal damage among the exposed workers (smokers: 8.83±5.94 MN/1000 BN, non smokers: 4.84±2.61 MN/1000 BN; p=0.011 Wilcoxon test), but not among controls (smokers: 6.00±1.94 MN/1000 BN, no-smokers: 5.15±3.67 MN/1000 BN). This suggests that smoking and ionising radiation might exert a synergistic influence on chromosomal damage. Therefore cigarette smoking status should be carefully factored into genetic monitoring studies assessing the risk associated with low-level radiation exposure. Among both exposed workers and controls, MN frequency was found to increase with age. On the other hand, no relationship between gender and MN frequency emerged in either group.
Considering that variation in the DNA repair system could modify cellular sensitivity to DNA damaging, inter-individual variation can constitute key determining factor to predict disease in the populations. The future perspectives to complete the study are genotype analysis of common sequence variations (polymorphisms) in DNA repair genes.
The XPD gene is involved in the Nucleotide Excision Repair (NER) system, the main way in which mammalian cells remove lesions induced by UV light and some chemical mutagens. The XPD gene can exist in polymorphic loci and as a component of the NER system, may operate as a genetic susceptibility factor.
XPD genotyping was performed using a restriction analysis of a genomic PCR product of the XPD gene exon 10 from 50-100 ng genomic DNA, extracted from granulocytes. The frequency of the control population was in good agreement with that expected in according to the Hardy Weinberg equilibrium. The XPD 312 variant (Asn) allele occurred with a frequency of 0.45, which agrees with previous studies reported in literature.
Integrating biomarkers of effect and of susceptibility in population studies may contribute significantly to the refinement of risk assessment. This experimental approach should allow us to identify not only the early biological effects related to the exposure, but also the individuals heightened risk of disease, in order to be able to set preventive measures.