

CHAPTER 39

MEDICAL SCIENCES BIOCHEMISTRY

Doctoral Theses

01. GHANSHELA (Rashmi)
Risk Factors of Urinary Bladder Cancer in North-Indian Population: A Gene-Environment Interaction Study.
Supervisors: Prof. Basu Dev Banerjee and Prof. Sanjay Gupta
Th 28181

Abstract

Urinary Bladder Cancer (UBC) is a polygenic and multifactorial disease encompassing an individual's genetic status and gene-environment interaction. Tobacco smoking is the main risk factor for UBC, followed by exposure to environmental carcinogens like organochlorine pesticides (OCPs). OCPs are highly persistent and cause oxidative DNA damage. They are metabolized by Xenobiotic metabolizing enzymes (XME). XPA and XPG genes are involved in DNA repair. Polymorphisms in XMEs and DNA repair genes have been implicated in inter-individual and inter-ethnic differences in cancer susceptibility. AIM: The present study aims to investigate the association of OCPs with genetic polymorphism and expression of XME and DNA damage repair gene in patients with UBC from North-India. METHODS: OCPs levels were estimated by Gas Chromatography, genetic polymorphism was studied by allele-specific PCR/RFLP methods, gene expression was studied by RT-PCR, protein expression was studied by Western Blotting and DNA damage was analysed by comet assay. The study included 100 cases and 100 age-matched controls. RESULTS: Blood level of isomers of HCH, p,p'-DDT and its metabolites and Endosulfan-II were found to be significantly higher in UBC cases compared to controls. The GSTP1 AG, XPA GG and XPG CC genotypes were significantly associated with UBC risk. The mRNA and protein expression of CYP1B1, GSTP1, XPA and XPG was significantly associated with UBC risk. Higher levels of DNA damage were detected in cases compared to controls. Significant correlation between OCPs, gene expression, gene polymorphism, DNA damage, tumour stage and grade, and UBC risk was found. Gene-environment interaction was found between the various genotypes and OCPs. CONCLUSION: OCP exposure, altered expression and genetic polymorphism of xenobiotic metabolizing and DNA repair genes, DNA damage and the interaction between these variables act as risk factors of UBC in the North-Indian population.

Contents

1. Introduction
 2. Review of literature
 3. Aim and objectives
 4. Materials and methods
 5. Results
 6. Discussion
 7. Bibliography
- Appendices (publications and annexures).