

P21**Combined evaluation of expression of telomerase, survivin and anti-apoptotic Bcl-2 family members in relation to loss of differentiation and apoptosis in human head and neck cancers**

Sharma Himani¹, Sen Sudip¹, Mathur Meera²,
Bahadur Sudhir³, Singh Neeta¹

¹Biochemistry; ²Pathology; ³Otorhinolaryngology, All India
Institute of Medical Sciences, New Delhi, India

Head and neck squamous cell carcinoma (HNSCC) is one of the most common cancers which accounts for 5% of all adult cancers worldwide. Deregulation of apoptosis is seen in many human cancers whereby the antiapoptotic members of the Bcl-2 family and the Inhibitor of apoptosis (IAP) member, Survivin have been shown to play an important role. To determine whether aberrations in these anti-apoptotic proteins are related to the development of HNSCC, we compared their protein expression in tumor tissue sections of 46 HNSCC patients and 19 histopathologically normal tissues by immunohistochemistry. We also looked at the telomerase activity by PCR-ELISA whose reactivation is seen in many tumors as well as looked at the apoptotic index by TUNEL assay in these tumors. Protein expression of Bcl-2 and Survivin was significantly associated with the histological differentiation status of tumors and that of Bcl-XL with nodal metastasis. Telomerase activity was found to be upregulated in tumors as compared to the normal tissue ($p < 0.001$). Immunohistochemistry has generally been performed on paraffin embedded archival samples thereby making the sample unavailable to assay the telomerase enzyme activity. To the best of our knowledge, this is the first study of its kind whereby we have used frozen samples to simultaneously look into the correlation of the apoptotic pathway and proliferation promoting telomerase enzyme activity in relation to loss of apoptosis and differentiation in HNSCCs. Telomerase activity in these tumors was found to be correlated with Bcl-2, Bcl-XL and Survivin overexpression and with reduced apoptosis in tumors thereby suggesting that novel strategies can be developed to control cancer cell growth by co-targeting telomerase and apoptotic pathways.

P22**Chemopreventive dietary factors augment apoptosis induced by cisplatin in head and neck cancer**

Sharma Himani, Sen Sudip, Singh Neeta

All India Institute of Medical Sciences, Biochemistry, New Delhi, India

Epidemiological data suggests that nutrient factors obtained from fruits and vegetables play an important chemopreventive role, however, current knowledge of the effect of dietary factors on toxicity of chemotherapeutic agents is limited. A better understanding of molecular mechanisms involved in process of apoptosis is needed by which chemotherapeutic drugs kill tumor cells. The objective of this study was to investigate whether efficacy of chemotherapeutic agent Cisplatin generally used for head and neck cancers can be enhanced by pretreatment with b-carotene, Retinoic acid, Quercetin and Genistein

in human laryngeal carcinoma HeP2 cells. Morphological examination, Flowcytometry and Caspase-3 assay were used for detection of apoptosis. Expression of the antiapoptotic proteins Bcl-2, Bcl-XL and Survivin, a member of Inhibitor of Apoptosis (IAP) family was seen by Western blotting. Results indicate that priming with these dietary factors for 24 hours prior to Cisplatin treatment results in an increase in apoptosis induced by Cisplatin alone. Cisplatin (2.5 microg/ml) treatment for 24 hours led to 20% apoptosis whereas pretreatment with these dietary factors for 24 hours prior to Cisplatin treatment at this dose resulted in an increase of apoptosis as seen with Cisplatin alone. The findings indicate that these dietary factors sensitize the Hep2 cells by downregulating the anti-apoptotic members of the Bcl-2 family namely Bcl-2, Bcl-XL and also Survivin, a member of the inhibitor of apoptosis (IAP) family. Cisplatin alone did not significantly reduce the levels of the antiapoptotic proteins. However the dietary factors alone and along with Cisplatin, resulted in a significant decrease in the expression of these proteins as observed by Western blotting thereby sensitizing the Hep2 cells to apoptosis. Hence, these dietary factors can be used in combination with Cisplatin to sensitize head and neck cancer cells to chemotherapy.

P23**The role of primary health care professionals in tobacco prevention**

A. Jovicevic Bekic¹, A. Dzeletovic², D. Jovicevic¹

¹Institute for Oncology and Radiology of Serbia, Department of Epidemiology and Prevention, Belgrade, Serbia and Montenegro; ²Institute for Public Health of Serbia, Center for Health Promotion, Belgrade, Serbia and Montenegro

Objective: Health professionals in primary health care are considered to have the greatest potential for influencing smoking habits in the general population and specific risk groups such as children, pregnant women etc. The objective of the study was to analyze professional attitudes of doctors and nurses in primary health care towards smoking and the impact their personal habits on their professional behaviour.

Methods: A survey on personal habits and attitudes toward tobacco use was carried out in a representative sample of primary health care centers in Belgrade.

Results: A total of 1693 primary health care professionals (general practitioners, gynecologists, pediatricians, dentists, nurses etc) completed a questionnaire. The prevalence of smokers in this group was 43%. The number of smokers was significantly higher among nurses than among doctors (48% and 35%, respectively). Although 60% of participants consider smoking extremely harmful and think they have enough knowledge on that subject, only 21% ask regularly all new patient of their smoking habits. One third of health professionals regularly advise patients smokers to stop smoking; only 12% recommend patients to visit centers specialized for cessation programs. The attitude towards smoking depends on a smoking status of a professional - doctors smokers ask and advise patients on smoking less frequently than doctors non-smokers. Ten percent of participants have participated in tobacco control programs so far. Less than half of participants (40%) expressed interest in participating in future tobacco prevention activities.

Conclusion: Health professionals in primary health care, particularly those that are smokers, are not engaged enough in promoting health behavior among their patients. Medical school curriculum and continual medical education programs for physicians and nurses should be strengthened to help reduce smoking rates among health professionals and change their attitudes towards tobacco control.

Experimental and Geographic Pathology/Epidemiology

P26

Esophageal cancer in Iran: Is the pattern different with the western countries?

R. Bijarchi¹, M.R. Sohrabi², M.Y. Juibari³, A. Yoonessi³
¹Hamedan University of Medical Sciences, School of Medicine, Hamedan, Iran; ²H pital Paul Brosse, Service de biochimie et biologie mol culaire, Paris, France; ³Digestive Disease Research Center, Cancer Genetics Study Branch, Tehran, Iran

Iran is one of the countries in the category of the Asian esophageal cancer belt. Until now, there has been suggested that the ratio of esophageal adenocarcinoma to the squamous cell carcinoma (E/S ratio) has been increased. During 10 years from 1991 to 2001 all patients with esophageal cancer which diagnosis has been established by pathology were prospectively included in this study. All the data about demographic information, smoking habits, family history of esophageal cancer in first-degree relatives was collected. We scrutinized the trend in the E/S ratio in Iran as compared to the western countries. 224 cases [49 Adenocarcinoma (64.02 years, 38 males), 175 Squamous Cell (58.12 years, 91 males)] were enrolled. 23.2% of the cases were under 50 years. Of these 11.5% were esophageal adenocarcinoma as compared to the 23.2% in the total population ($P < 0.05$). Positive family history in the first-degree relatives was observed in 2 adenocarcinoma and 5 of the squamous cell carcinoma. There was no significant difference between age, gender, ethnic origin and number of cigarettes per day and the type of cancer in our population. Although not significant, but there was an increasing trend in E/S ratio during these 10 years. It seems that in spite of recent publication regarding the difference in pattern of esophageal cancer between western and developing countries, this study could not provide information supporting this concept.

P27

Opportunities of an individual approach to postoperative treatment in breast cancer patients

B.G. Borzenko, H.M. Bakurova, T.N. Kuchnina, Z.M. Scorobogatova
 Donetsk Medical State University, Biochemistry, Donetsk, Ukraine

Background: In breast cancer treatment the surgical method is the basic. However frequently it is supplemented with use of

various ways of antineoplastic therapy, for example, chemotherapy. With this purpose we investigated activity of Thymidine kinase (TK)-the recognized marker of proliferation. Thymidine phosphorylase (TP) is used as the indicator of sensitivity to same chemopreparations. Activity of Adenosinedeaminase (ADA) connected with differentiation and apoptosis of a cell on which effect some preparations.

Materials and methods: Activity of TK, TP and ADA is investigated in blood serum, bioplate of tissues and in lymphocytes of breast cancer patients T3N2M0 (70 persons) before and after radical mastectomy and during medicinal treatment. Activity of enzymes in blood serum of healthy women (30 persons) is investigated aged 40-49 years.

Results: It is established, that in blood serum of breast cancer patients T3N2M0 raises activity of TK (3.44-0.51 nmol/hour/mg, control 3.03-0.20 nmol/hour/mg) and is reduced activity of TP (34.56-2.56 nmol/min/mg, control 42.36-1.25 nmol/min/mg). It is revealed, that activity of TP depends on a degree of a differentiation of a tumour. In bioplate of low differentiation tumours and in blood serum of such patients activity of TP was three times lower than norm. Activity of ADA is reduced in blood serum (5.2 times) and reduced in lymphocytes (3.4 times) in comparison with norm. After operation activity of TK and TP in blood serum practically did not change and activity of ADA has authentically decreased from 7.85-1.85 to 5.28-0.73 nmol/min/mg. Simultaneously ADA has raised in lymphocytes from 40.08-2.14 to 50.03-5.16 nmol/min/mg.

Conclusions: During chemotherapeutic treatment in patients with high differentiation of tumour in two weeks activity of TK was reduced up to 1.85-0.67 nmol/hour/mg, TP came nearer to norm (58.88 -5.12) nmol/min/mg, ADA did not change. In patients with low differentiation of tumour TK accrued up to 9.16-1.6 nmol/hour/mg, TP and ADA remained same as before treatment. In this group within 5 years high percent of lethal outcomes that speaks about low efficiency of chemotherapy. Thus, it is revealed that at treatment of breast cancer patients is necessary to take into account differentiation of a tumour and for individual treatment to use activity of TK,TP and ADA as a test of efficiency.

P28

Immunohistochemical analysis of p53 and Bcl2 in gastric cancer patients

E. Azizi¹, B. Minaee³, M.H. Ghahremani¹, S.N. Ostad¹, M. Jamali⁴
¹Molecular research Lab., Dept. of Pharmacology and Toxicology, Faculty of Pharmacy, ²Dept. of Pharmacology and Toxicology, Pharmaceutical Sciences Unit, Islamic Azad University and ³ Dept. of Anatomy and Embryology, ⁴Dept. of Pathology, Faculty of Medicine, Tehran University of Medical Sciences (TUMS), Tehran, Iran

Background: Gastric cancer is considered to be one of the most common types of cancers worldwide. Most patients are diagnosed at advanced stages, and fatal outcome is expected. Abnormal expression of proteins regulating the cell cycle, particularly p53 and Bcl2, has been reported in gastric cancers with controversial conclusions. Our aim was to study the expression of p53 and Bcl2 proteins and to correlate the obtained results