

longitudinal sections were made. The stain used for histology was Alcian&Alizarin.

Results: The development of long bones in vitamin C deficient guinea pigs are considerably stagnant. Hyaline cartilage models are significantly shortened. Ossification in the diaphyses of carpal and metacarpal bones are absent, and the organization of the epiphyseal plates is very irregular with the reduction of number of chondrocytes. Moreover, there are numerous haemorrhagic regions and subperichondrial bleeding with separation of perichondrium.

Conclusion: Deprivation of vitamin C during inrauterine period disables normal development of long bones. Disorder of hyaline cartilage models was seen, as well as the disorder of ossification.

<http://dx.doi.org/10.1016/j.pbj.2017.07.085>

PS060

Peculiarities of expression of apoptosis markers in the tissues of primary fallopian tubes carcinoma



Franklin Unawunwa*, Natalia Hyriavenko, Anna Korobchanska, Mykola Lyndin, Vladyslav Sikora

Sumy State University

E-mail address: unawunwafranklin@yahoo.com (F. Unawunwa).

Aim: immunohistochemical analysis of apoptosis markers in the tissue of PFTC.

Introduction: Primary fallopian tubes carcinoma is a rare case among oncological diseases of female genital organs, but the mortality rate is rather high. Nowadays, the prognostic factors of this neoplasia are not fully determined. The data on the p53 and bcl2 proteins expression and their use as prognostic factors in patients with malignant tumors of many locations are contradictory.

Methods: the study was conducted on 66 samples of fallopian tubes tumor tissue. To study the apoptosis peculiarities of tumor cells the mouse monoclonal antibodies for bcl-2 (clone 100/D5) and p53 (clone SP5) were used. Mathematic calculations were done using Microsoft Excel 2010 with AtteStat 12.0.5.

Results: The high expression of p53 was found in patients of all clinical stages. Mutations of p53 increased with spreading of the neoplastic process. Strong correlation of p53 presence in tumor samples and clinical stage of the disease was determined ($r=0.77$). In contrast to the abovementioned protein the study of bcl-2 showed the moderate negative correlation between this protein and the stage of the disease ($r=-0.54$). Analysis of the dependence of p53 expression with the presence or absence of lymph nodes metastasis showed a direct correlation between the indicators ($r=0.25$). Thus the level of p53 expression in patients with N1 was $80.6 \pm 2.7\%$ compared with the N0 group ($29.7 \pm 3.6\%$). The stage of neoplasia differentiation is in moderate direct correlation with p53 expression ($r=0.58$) and in inverse with - bcl-2 ($r=-0.64$).

Conclusion: Expression of p53 depends on neoplasia spreading and stage of tumor differentiation. The expression of p53 is an independent prognostic marker for N-status and helps to classify the patients into "risk" groups.

Acknowledgements: Supervisor: A. M. Romaniuk, prof., doctor of medical sciences, Department of Pathological Anatomy, Medical Institute, Sumy State University.

<http://dx.doi.org/10.1016/j.pbj.2017.07.086>

PS064

Analysis of combined impact of doxorubicin and menadione on human leukaemia Jurkat T cells



Alexandru Ionut Duta*, Ioana Teodora Tofolean, Ramona Madalina Babes, Constanta Ganea, Irina Baran

"Carol Davila" University of Medicine and Pharmacy, Department of Biophysics, Bucharest, Romania
E-mail address: alexxxduta@yahoo.com (A.I. Duta).

Aim: The anti-proliferative effect and the mechanism of action of doxorubicin(DOX) in combination with menadione(MD) were studied in Jurkat T cells, a model for acute lymphoblastic leukaemia (ALL).

Introduction: Doxorubicin is a well-characterized and successful antineoplastic drug commonly used in various cancer treatments, including ALL. Menadione has proven a strong proapoptotic effect in Jurkat cells.¹⁻³

Methods: Cell cycle, apoptosis/necrosis and the oxidative status were assessed by flow cytometry on propidium iodide, Annexin V-FITC/PI and CM-H2DCFDA/7-AAD labelled cells, respectively.

Results: Oxidative stress induced within 4h by MD ($IC_{50}=11.5 \mu M$) was reduced in the presence of 500 nM DOX ($IC_{50}=22.0 \mu M$). After treatments of 18 h, DOX induced cell cycle arrest displaying a trimodal distribution; successive G2/M, S and G0/G1 blockage was produced with an IC_{50} of 49 nM, 464 nM and 1866 nM, respectively, whereas in the presence of 7.5 μM MD, increasing levels of DOX mainly induced S-phase arrest. Within 18 hours of exposure, DOX induced apoptosis in a biphasic dose-dependent manner ($K_d=335$ nM and 3.29 μM , respectively). Addition of 7.5 μM MD enhanced apoptosis at <300 nM DOX, but reduced cell death at higher levels of DOX. However, 48 h after drug removal the apoptotic rate was considerably higher in cells exposed to DOX:MD, which also showed consistent fractions of early apoptosis (up to 44%). The efficacy of DOX was doubled by MD($K_d=46.5$ nM in the presence, and $K_d=99$ nM and 143 nM in the absence of MD).

Conclusion: Data indicate that clinically relevant levels of MD and DOX in combined treatments can exert considerable cytotoxic impact on Jurkat cells, via cell cycle arrest and apoptosis induction. These findings could encourage new therapeutic strategies to improve the therapeutic index of doxorubicin in ALL treatments.

Acknowledgements: This work was supported by a fellowship of the Romanian Ministry of Education, UEFISCDI, for Young Researchers, project number 8/2016.

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<http://dx.doi.org/10.1016/j.pbj.2017.07.087>

PS068

Effect of symptom interval and demographic characteristics on initial stage of malignant tumors in children



R. Grujicic*, O. Djurmez, M. Trkulja, J. Lazić, M. Bjelić

School of Medicine, University of Belgrade, Serbia