Results: The development of long bones in vitamin C deficient guinea pigs is considerably stagnant. Hyaline cartilage models was seen, as well as the disorder of ossification.

Conclusion: Deprivation of vitamin C during intrauterine 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

PS064

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

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

“Carol Davila” University of Medicine and Pharmacy, Department of Biophysics, Bucharest, Romania
E-mail address: alexxxduta@yahoo.com

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 pro-apoptotic 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 4 h by MD (IC50 = 11.5 μM) was reduced in the presence of 500 nM DOX (IC50 = 22.0 μM). 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 IC50 of 46.5 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(Kd = 46.5 nM in the presence, and Kd = 99 nM in the absence of MD) 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(Kd = 46.5 nM in the presence, and Kd = 99 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.

References

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. Grujićic*, O. Djurmez, M. Trkulja, J. Lazić, M. Bjelić

School of Medicine, University of Belgrade, Serbia