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Role of recombinant human erythropoietin loading chitosan-tripolyphosphate nanoparticles in Busulfan-induced genotoxicity: Analysis of DNA fragmentation via comet assay in cultured HepG2 cells

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Busulfan is one of the most effective chemotherapeutic agents used for the treatment of chronic myeloid leukemia. Busulfan is involved in secondary malignancy due to its genotoxic potential in normal tissues. As an alkylating agent, busulfan can cause DNA damage by cross-linking DNAs and DNA and proteins, induces senescence in normal cells via transient depletion of intracellular glutathione (GSH) and subsequently by a continuous increase in reactive oxygen species (ROS) production. Erythropoietin, a glycoprotein widely used against drug induced anemia in cancerous patients and regulates hematopoiesis, has been shown to exert an important cyto-protective effect in many tissues. Recombinant human erythropoietin has been demonstrated to directly limiting cell injury and ROS generation during oxidative stress. Furthermore, rhEPO decreased levels of pro-apoptotic factor (Bax) and also increased expression of the anti-apoptotic factor Bcl2. According to EPO' s short half-life and requirements for the frequently administration, finding the new strategies to attenuate its side effects is important. The aim of this study was to explore whether rhEPO loading chitosan-tripolyphosphate nanoparticles protects against busulfan-induced genotoxicity in HepG2 cells. For this purpose, cells were incubated with busulfan alone, regular rhEPO alone and regular rhEPO and CS-TPP-EPO nanoparticles along with busulfan in pre- and co-treatment condition. Our results showed that busulfan induced a noticeable genotoxic effects in HepG2 cells ($p<0.0001$). Both regular rhEPO and CSTPP-EPO nanoparticles reduced the effects of busulfan significantly ($p<0.0001$) by reduction of the level of DNA damage via blocking ROS generation and enhancement intracellular glutathione levels. CS-TPPEPO nanoparticles were more effective than regular rhEPO in both pre- and co-treatment conditions. In conclusion, our results show that administration of rhEPO and CS-TPPEPO nanoparticles especially in the pre-treatment conditions, significantly decreased the level of DNA damage induced by busulfan, measured with the comet assay, in HepG2 cells compared to the regular rhEPO group.

Biography

Nasrin Ghassemi Barghi is currently pursuing PhD in Toxicology at Mazandaran University of Medical Sciences, Iran. She has accomplished her MS in Toxicology from Isfahan University and BS of Laboratory Sciences from Kerman University of Medical Sciences. Her research interests include cancer chemotherapy and secondary malignancy induced by anticancer drugs, cell culture, apoptosis, nanotoxicology, synthesis of chitosan nanoparticle, western blotting, genotoxicity, comet and micronucleus assay, HPLC, in vivo organ toxicity etc. Presently, she is working on antioxidants such as melatonin and EPO and has academic accomplishments with multiple research, publications in highly prestigious journals and various presentations in both national and international conferences.

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