

Normal Hematopoietic Stem Cell and the Toxic Effect of Parthenolide

Authors : Alsulami H., Alghamdi N., Alasker A., Almohen N., Shome D.

Abstract : Most conventional chemotherapeutic agents, which are used for the treatment of cancers, not only eradicate cancer cells but also affect normal hematopoietic Stem cells (HSCs) that lead to severe pancytopenia during treatment. Therefore, a need exists for distinct approaches to treat cancer without or with minimum effect on normal HSCs. Parthenolide (PTL), a herbal product occurring naturally in the plant Feverfew, is a potential chemotherapeutic agent for the treatment of many cancers, such as acute myeloid leukemia (AML) and chronic lymphocytic leukemia (CLL). In this study we investigated the effect of different PTL concentrations on the viability of normal HSCs and also on the ability of these cells to form colonies after they have been treated with PTL in vitro. Methods: Normal 24 bone marrow and cord blood samples were included in this study after obtaining informed consent. The mononuclear cells were isolated using density gradient separation. Cells were cultured with different PTL concentrations for 24 hours. Post-culture cell viability was assessed using 7ADD in a flow cytometry-based test. In addition, a colony-forming unit assay (CFU) was carried out to assess the effect of PTL on HSCs. the expression of NF κ B was also assessed using a PE-labeled anti-pNF κ BP65 antibody. Results: This study showed that there was no statistically significant difference in the percentage of cell death between untreated and PTL-treated cells with 5 μ M PTL ($p = 0.7$), 10 μ M PTL ($p = 0.4$) and 25 μ M ($p = 0.09$) respectively. However, at higher doses, PTL caused a significant increase in the percentage of cell death. These results were significant when compared to untreated control ($p < 0.001$). The response of cord blood cells ($n=4$), on the other hand, was slightly different from that for bone marrow cells in that the percentage of cell death was significant at 100 μ M PTL. Therefore, cord blood cells seemed more resistant than bone marrow cells. Conclusion: At concentrations ≤ 25 μ M, PTL has a minimum or no effect on HSCs in vitro. Cord blood HSCs are more resistant to PTL compared to bone marrow HSCs.

Keywords : stem cell, parthenolide, ALL, NF κ B

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