Ácido betulínico pode ser útil no tratamento do mieloma: inibe ciclo celular e aumenta a apoptose

[Effect of betulinic acid on inducing apoptosis of human multiple myeloma cell line RPMI-8226].

[Article in Chinese]
Cheng YQ, Chen Y, Wu QL, Fang J, Yang LJ.

Department of Hematology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430022, Hubei Province, China.

Abstract

The aim of this study was to investigate the effect of betulinic acid on inducing apoptosis of human multiple myeloma RPMI-8226 cell line. The inhibitory effect of betulinic acid on proliferation and its inducing apoptosis effect, influence on cell cycle and induced morphological changes of RPMI-8226 were evaluated by MTT, flow cytometry Annexin-V/PI double staining, flow cytometry with PI staining and fluorescence microscopy with Hoechst33258 staining, respectively. The transcription level changes of bcl-xl gene and caspase 3 which are two kinds of apoptosis related protein gene were determined by RT-PCR. The results showed that within a certain range of concentration (0, 5, 10, 15, 20 microg/ml), IC50 of betulinic acid to RPMI-8226 at 24 hours was 10.156+/-0.659 microg/ml, while the IC50 at 48 hours was 5.434+/-0.212 microg/ml, and its inhibiting effect on proliferation of RPMI-8226 showed both time-and dose-dependent manners. Flow cytometry with Annexin-V/PI double staining revealed that apoptotic rate of RPMI-8226 cells increased as betulinic acid concentration increased. Flow cytometry with PI staining showed that the ratio of cells in G0/G1 phase increased, while it in S phase decreased, and ratio of cells at G2/M phase did not present a significant change. Morphological differences were typical and obvious between cells in treated and control groups under fluorescence microscope using Hoechst33258 staining. RT-PCR detection of caspase 3 gene indicated that its transcription level showed an increasing trend as the concentration of betulinic acid increased, while the bcl-xl showed the opposite trend. It is concluded that the betulinic acid can induce apoptosis of RPMI-8226 within a certain range of concentration in a time- and dose-dependent manners. This phenomenon may be related to the transcriptional level increase of
caspase 3 gene and decrease of bcl-xl. Betulinic acid also affects G1/S in cell cycle which arrests cells at phase G0/G1.

PMID:19840455