عنوان مقاله:

(Dimethylaminoparthenolide (DMAPT) as an alternative approach for treatment of Familial Mediterranean Fever (FMF

محل انتشار:

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خلاصه مقاله:

Objective(s): Familial Mediterranean Fever (FMF) is a hereditary auto-inflammatory disorder that is caused by mutations in the Mediterranean fever (MEFV) gene and is associated with an increase in pro-inflammatory cytokines, such as interleukin-۱β (IL-۱β) and interleukin-۱۸ (IL-۱۸), leading to excess inflammation. Colchicine is a common drug widely used for treatment of FMF attacks, but about ۵–۱۵% of the patients show resistance to the regular colchicine treatment. In this study, we used dimethylamino-parthenolide (DMAPT), as a small molecule inhibitor of Nuclear factor-κB (NF-κB), NLR family Pyrin domain containing ۳ (NLRP۳), and cysteine-aspartic acid protease ۱(Caspase-۱) on FMF-derived peripheral blood mononuclear cells (PBMCs).Materials and Methods: The effects of DMAPT and colchicine on metabolic activity and apoptosis of FMF-derived PBMCs were evaluated by MTT and Annexin V/PI assays, respectively. Also, the expression levels of NF-κB, NLRP۳, MEFV, CASP۱, and IL-۱β mRNA were investigated using a TaqMan real-time PCR, and the protein levels of IL-۱β, IL-۱۸, and IL-۳۷ were assessed via an enzyme-linked immunosorbent assay (ELISA) in LPS/ ATP-stimulated PBMCs.Results: DMAPT decreased the expression levels of NFκB (۰.۳۸±۰.۰۹۶, P<۰.۰۰۰۱), NLRP۳ (۰.۳۹±۰.۱۲, P<۰.۰۰۱), MEFV (۰.۳۸۴±۰.۱۴۵, P<۰.۰۰۱), CASP۱ (۰.۴۸±۰.۱۳, P=۰.۰۰۲۳), and IL-۱β (۰.۰۹±۰.۰۹, P<۰.۰۰۰۱) and reduced the secretion levels of IL-۱β (۸.۹۲±۵.۳ vs. ۱۴۹.۸۵±۲۰.۹۲, P<۰.۰۰۰۱), IL-۱۸ (۱۳۵±۳۲.۱ vs. ۱۹۲±۲۲.۱۸, P=۰.۰۱), and IL-۳۷ (۲۷.۵±۶.۳ vs. ۷۸.۱۹±۱۴.۳, P<۰.۰۰۰۱) as compared to untreated cells.Conclusion: Given the obtained results in comparison with previous research, the future clinical development of DMAPT could result in the expansion of new anti-inflammatory therapeutics for FMF disorder.

کلمات کلیدی:

CASP۱, Dimethylamino-arthenolide, Familial Mediterranean fever, IL-۱β, IL-۱۸, MEFV, NFκB, NLRP۳