The evaluation of the effect of P2X7 receptor inhibitor at macrophages induced OX-LDLon expression of NOX1, MMP-3 and

Abstract

Background: Foam cells are macrophages filled with fat that play an important role in the development of atherosclerosis. Foam cells promote the development of atherosclerosis by increasing the expression of inflammatory factors and also by increasing the oxidative stress caused by increasing the activity of NADPH oxidase and other inducing enzymes. Also, by increasing the activity of metalloproteinase enzymes, it causes plaque instability and vascular damage. P2X7 receptor is part of purinergic receptor, non-selective cation channel, expressed in immune cells, especially inflammatory macrophages.

Aim: In the present study, we have investigated the effect of P2X7 receptor antagonist on the expression of genes involved in the process of creation and development of atherosclerosis in macrophages induced by oxidized LDL (the main factor in foam cell formation).

Materials and methods: The studied groups include group 1 (control): THP-1 cells treated with PMA, group 2: THP-1 cells treated with PMA and ox-LDL, group 3: THP-1 cells 1 is treated with PMA, OX-LDLand P2X7 inhibitor. In this study, THP1 cells (monocyte progenitor cells) were transformed into macrophage cells by PMA. Then macrophage cells were treated with oxidized LDL to form foamy cells and also to investigate the effect of P2X7 receptor, macrophages were treated with oxidized LDL along with P2X7 antagonist. Oil Red O (ORO) staining was used to confirm the formation of foamy cells. Then, after RNA extraction and cDNA synthesis, the expression of NOX1, MMP3 and TGF β genes were checked by qPCR technique.

Result: The results of ORO show the ability of P2X7 to reduce the production of foam cells from OX-LDL. RT-PCR results show the ability of P2X7 to decrease the expression of NOX1 gene compared to the group treated with OX-LDL($P<0.001$) and decrease the expression of the MMP3 gene compared to the group treated with OX-LDL($P<0.001$) and decrease the TGF gene. will be b was the ratio of the group treated with OX-LDL($P<0.0001$).

Conclusion: The results of this study showed the positive effects of inhibiting the P2X7 receptor to suppress the formation of foam cell and the significant effects on inhibiting the expression of atherogenic genes. In general, therefore, this combination can be used as a practical option for further investigations.

Keywords: Macrophage,Foam cell, MMP3,TGF-B,OX-LDL,P2X7,NOX1,