World Academy of Science, Engineering and Technology
International Journal of Bioengineering and Life Sciences
Vol:15, No:07, 2021

The Effect of Metformin in Combination with Dexamethasone on the CXCR4 Level in Multiple Myeloma Cell Line

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Abstract : Background: CXCR4, as a chemokine receptor, plays well-known roles in various types of cancers. Several studies have been conducted to overcome CXCR4 axis acts in multiple myeloma (MM) pathogenesis and progression. Dexamethasone, a standard treatment for multiple myeloma, has been shown to increase CXCR4 levels in multiple myeloma cell lines. Herein, we focused on the effects of metformin and dexamethasone on CXCR4 at the cellular level and the migration rate of cell lines after exposure to a combination compared to single-agent models. Materials and Method: Multiple myeloma cell lines (U266 and RPMI8226) were cultured with different metformin and dexamethasone concentrations in single-agent and combination models. The simultaneous combination doses were calculated by CompuSyn software. Cell surface and mRNA expression of CXCR4 were determined using flow cytometry and the quantitative reverse transcription-polymerase chain reaction (qRT-PCR) assay, respectively. The Transwell cell migration assay evaluated the migration ability. Results: In concurred with previous studies, our results showed a dexamethasone up-regulation effect on CXCR4 in a dose-dependent manner. Although, the metformin single-agent model could reduce CXCR4 expression of U266 and RPMI8226 in cell surface and mRNA expression level. Moreover, the administration of metformin and dexamethasone simultaneously exerted a higher suppression effect on CXCR4 expression than the metformin single-agent model. The migration rate through the combination model's matrigel membrane was remarkably lower than the metformin and dexamethasone single-agent model. Discussion: According to our findings, the combination of metformin and dexamethasone effectively inhibited dexamethasone-induced CXCR4 expression in multiple myeloma cell lines. As a result, metformin may be counted as an alternative medicine combined with other chemotherapies to combat multiple myeloma. However, more research is required.

Keywords : CXCR4, dexamethasone, metformin, migration, multiple myeloma
Conference Title : ICII 2021 : International Conference on Immunotherapy and Immunology
Conference Location : Stockholm, Sweden
Conference Dates : July 15-16, 2021