Assessment of the Synergism Effect of Imatinib and Temozolomide on Serum Levels and Activities of Matrix Metalloproteinases 2 and 9 (MMP2, 9) in U87-Mg Glioma Cell Line

Mohsen kahrariayn[a], Khadije Najafi[a], Maryam Hosseinpour[a], Amir Kiani [b]*

Abstract

Introduction: One of the most dangerous brain tumors is Glioblastoma multiforme (GBM).The MMPs are very important biomarker in pathologic conditions and be known as metastatic factor. Temozolomide is an oral alkylating agent, and has a good effect on GBM. Gefitinib is a low–molecular weight tyrosine kinase inhibitor that is used in tratmeant of tumor.

Methods and Results: The human GBM cell line, U87 mg was obtained from Pasteur Institute of Iran. Cells grown in RPMI 1640 supplemented with 10% fetal bovine serum in a humidified incubator at 37^{0C} with 5% CO2. Cell viability after treatment, was measured by MTT test. MMP-2, MMP-9, Quantikine® ELISA kits (R&D systems, Minneapolis, USA) were used to measure supernatants MMPs. Effect of the drugs on the enzyme activity of MMP-2 and MMP-9 was assessed by gelatin zymography. Synergism of Temozolomide and Imatinib can reduce the IC50 of temozolomide. Our results show that combination of Imatinib and Temozolomide decreased the level and activity of MMP-2 and MMP-9 in supernatant of culture medium versus to control cells when only Temozolomide or Imatinib was added to their culture medium.

Conclusion: Combination of Imatinib as a tyrosine kinase inhibitor and Temozolomide as an alkylating agent is more potent than Temozolomide and it can reduce IC50 and decrease level and activitity of MMP-2 and MMP-9.The current strategies for treatment of glioblastoma are not beneficial enough. Combination therapy probably can reduce the dose of drug, cost of treatment, adverse effects and increase the survival rate of life.

Keywords: Temozolomide, Glioblastoma multiforme, Imatinib, MMP 2, MMP 9

Authors' Affiliations:

[a] Research Committee, School of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran

[b] Pharmaceutical Sciences Research Center, School of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran.

Abstract Presenter:

Mohsen kahrariayn, Student Research Committee, School of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran

E.mail : mohsen.kr91@gmail.com

****Correspondence:***

Amir Kiani, Pharmaceutical Sciences Research Center, School of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran