Alternative Viewpoint Against Breast Cancer Based on Selective Serotonin Receptors 5HTR3A and 5HTR2A Antagonists that can Mediate Apoptosis in MCF-7 Cell Line

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Abstract: Background: Neurotransmitters had progressive effects on various cancers via their different type of receptors. Objective: This study was conducted to determine the pattern of serotonin receptors, respectively, 5HTR2A and 5HTR3A gene expression in MCF-7 cells and evaluate their selective antagonist effects on them. Method: RT-PCR was performed to determine the pattern of serotonin receptor gene expression in human breast cancer cell line (MCF-7). MCF-7 cells were cultured and treated via different doses of tropisetron (5HTR3A antagonist) and ketanserin (5HTR2A antagonist) for 48 hours. Oxidative and reductive enzyme activity was carried out by MTT assay. Subsequently, nuclear morphology of cells was observed by mixed dye florescent staining. To validate cell proliferation inhibition, Real time PCR was carried out for determining the descending rate of proliferating cell nuclear antigen (PCNA) gene expression in treating MCF-7 cells. Assessment of quantification of apoptosis and its discrimination with necrosis at single cell level using Flowcytometry technique was performed. Results: Results showed that 5HTR2A and 5HTR3A have expression in MCF-7 cells. Based on our finding, tropisetron and ketanserin had suppression effects on MCF-7 cells proliferation. (93.35% in tropisetron 50 µmoll¹ and 72.36% in Ketanserin 25µmoll³ concentration). Conclusion: Therefore, the use of tropisetron and ketanserin as an antagonist of serotonin receptor may be as new approaches are recommended for the treatment of breast cancer cells.

Keywords: 5HTR2A, 5HTR3A, antagonist, breast cancer, ketanserin, MCF7, tropisetron.

INTRODUCTION

Breast cancer is the most prevalent and potentially lethal disease in Iranian people and the fifth most common cause of cancer-related deaths in Iran. Its incident rate is one out of the eight in the United States and one out of thirty five people in Asia [1]. It is recognized as a multi-factor disease, whereas genetically mutation and environmental condition can lead to the breast cancer. Scientists believed that some physiological conditions such as age, sex, and environmental factors have an important role in the promotion of breast cancer [1]. Some studies have indicated the relationship between the CNS, endocrine and immune system. This process can be mediated with neurotransmitters (serotonin, norepinephrine and dopamine), neurohormons (growth hormone and prolactin) and cytokines (interleukin1, TNFα, interferon α and γ). There are strong evidences indicating that chronic stress can lead to the development of cancer cells and tumor growth in breast cancer [2, 3]. On the other hand, interaction and balance of nervous and immune systems are essential for maintaining homeostasis.