Abstract

Introduction

According to global statistics, cancer is one of the most important causes of death in the world. Among the known cancers, gastric cancer is one of the most deadly. Due to the high population, Asia has the highest incidence of gastric cancer and the highest mortality rate. Iran is also one of the areas where the risk of gastric cancer is high, and the World Health Organization report points to these. According to the Iranian Ministry of Health and Medical Education, due to the high cost and fatality of gastric cancer, this cancer has particular importance in Ardabil province. Existing methods and current chemotherapy drugs have not achieved satisfactory success in the treatment of gastric cancer patients and finding new drugs with high efficacy and low side effects seems unavoidable. To achieve higher efficacy and lower side effects, we conjugated the drug aspartaginase with the monoclonal antibody trastuzumab and examined its effects on gastric cancer cells

materials and methods

In the first step, the trastuzumab monoclonal antibody was activated by the 3,3′-dihydro-propionic acid (N-hydroxysuccinimide ester) (DSP) disulfide linker to link the end of lysine amino acid to the linker. The asparaginase enzyme was then added to it with a molar ratio of antibody. The mixture was kept at refrigerator temperature for 48 hours and then dialysed to purify the unreacted material. Electrophoresis and dynamic light scattering were used to prove correct binding. To investigate the effects of cellular toxicity and apoptosis, acridine orange and ethidium bromide staining were used.

Results

Using polyacrylamide electrophoresis in the presence of sodium dodecyl sulfate, antibody conjugation with asparaginase was demonstrated, and dynamic light scattering showed increase in size and surface charge change after monoclonal antibody conjugation with asparaginase. The results of Acridine Orange and Ethidium Bromide staining with fluorescent microscope for apoptosis studies showed that those cells treated with trastuzumab-asparaginase conjugate showed higher apoptosis than the asparaginase alone group,trastuzumab alone group And control group.

Conclusion

Our studies showed that binding of monoclonal trastuzumab antibody to the asparaginase enzyme using disulfide linker enhances the apoptotic effect. However, these studies were performed on cultured cells and qualitively evaluated the amount of apoptosis induced by the conjugate. Subsequent studies will quantitatively evaluate the cell death caused by the conjugate in animal studies.

Keywords: Conjugate drug, Monoclonal Antibody, Asparaginase, AGS, Trastuzumab