Association of PON1 Genotype and Phenotype with Gastric Cancer Risk

Abstract

Background: : Stomach cancer is the most common cancer in men and the second most common cancer in women in Iran. There are many factors in our body that play the role of antioxidant and detoxification and reduce the risk of stomach cancer. One of these agents is paraoxonases. Due to their functional nature, paraoxonase family enzymes, especially *PON1*, can play an important role in various cancers. Due to the importance of these enzymes, especially in the detoxification of oxidant compounds inside the body, their role in people getting cancer has been raised. Therefore, extensive studies have been conducted from different perspectives on the role of this enzyme in carcinogenesis and cancer treatment. One of these fields of study is the effect of *PON1* genetic changes on the phenotype and enzyme activity, on the one hand, and people's lifestyle (alcohol consumption, smoking, diet and its effect on lipid profile) on the risk of cancer.

Although studies have been conducted on each of the above variables on the risk of cancer, nevertheless, it seems that the study of the effect of the above variables together has received less attention. Based on this, in this research, we decided to study the effect of the aforementioned variables on stomach cancer, which is one of the most common cancers, especially in Ardabil province.

Aim: Investigating the relationship between genotype and *PON1* enzyme activity with the risk of stomach cancer.

Materials and Methods: In this case-control study, 285 people (140 people with gastric cancer as case group and 145 healthy people as control or control group) were selected from Aras Clinic of Imam Khomeini Hospital and Gastroenterology and Liver Research Center of Ardabil. Whole blood samples

were collected from the studied subjects for DNA extraction and determination of *PON1* gene polymorphisms using the Tetra-Primer ARMS-PCR technique. In the next step, the phenotype of the samples was measured by measuring the PON1 enzyme activity in the serum of the samples using a spectrophotometer. And at the end, the results were analyzed by t-test and X2 statistical tests.

Results: After data analysis, the frequency of LM55 polymorphism in the case and control group had a significant difference ($p<0.05$). Also, after additional tests, it was found that people with TT genotype are more susceptible to stomach cancer than people with AA genotype. In addition, people with gastric cancer showed lower levels of PON1 enzyme serum activity. With further investigations, it was found that people with TT genotype have lower enzyme activity and are at a higher risk of stomach cancer.

Conclusion: In this study, it was found that the LM55 polymorphism of the PON1 gene is associated with an increased risk of stomach cancer. It can be concluded that LM55 polymorphism can play an important role as a biological marker in early diagnosis and prognosis of gastric cancer. which requires more and more extensive research. Also, it can be concluded from the present study that PON1 enzyme activity decreases in patients with stomach cancer.