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Diagnostic value of serum levels of galanin and obestatin in patients with gastric cancer

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SUMMARY

OBJECTIVE: Gastric cancer ranks the third among the cancer-related deaths. It is diagnosed at advanced stage in many patients due to malignant proliferation and has a poor prognosis. Currently, no instrument or biomarker has been proven to diagnose the disease before the advanced stages. This study aimed to measure the serum levels of galanin and obestatin, which were examined in various studies including cancer studies, and to discuss their diagnostic value in gastric cancers.

METHODS: In this study, 30 adult patients with gastric cancer and 30 healthy adults in the control group were examined prospectively. The demographic characteristics and serum levels of galanin and obestatin in the patient and control groups were recorded.

RESULTS: The mean serum level of galanin in the patient and control groups was 19.73±5.04 and 35.59±10.94 pg/mL, respectively. The mean serum level of obestatin in the patient and control groups was 40.21±5.82 and 15.15±3.32 ng/mL, respectively. A significant difference was found between the groups ($p<0.001$).

CONCLUSION: Serum levels of galanin were lower and serum levels of obestatin were higher in patients with gastric cancer compared to the healthy individuals. Serum levels of obestatin and galanin can be used as potential biomarkers in the diagnosis of gastric cancer.

KEYWORDS: Obestatin. Galanin. Biomarker. Gastric cancer.

INTRODUCTION

The incidence of gastric cancer varies according to the geographical region; however, it is the fourth most common type of cancer in the world and ranks the third among the deaths associated with cancer[1,2]. Gastric cancer is a type of cancer that is diagnosed at an advanced stage in many patients due to malignant proliferation, and it has a poor prognosis[3].

Many gastric cancers are usually asymptomatic in the early stages; however, they are at an advanced stage or even at a metastatic stage when they show symptoms[4]. Since the gastric cancers at the advanced stage have high rates of recurrence after the operation, they have a poor clinical prognosis[5]. Thus, it is vital that the disease is identified and treated in the early stages. The greatest obstacle to the development of effective treatment modalities is the lack of biomarkers that will monitor the pathological progression of the disease and predict the diagnosis at early stages[6]. Many genes and factors, growth factors, and signaling targets have been indicated to play a key role in identifying the pathogenesis of gastric cancer. Nonetheless, these markers are controversial and have not been fully defied in terms of their prognostic and predictive values[6]. As a result, diagnostic methods of gastric cancer are still suboptimal today, and there is no proven biomarker that can be used in the diagnosis of gastric cancer before the disease reaches advanced levels. It is very important to find biomarkers that can diagnose the disease at the early stage. Well-defined biomarkers will guide the diagnosis and treatment of the disease.

This study aimed to discuss serum levels of galanin and obestatin peptides that can be measured from the serum in the blood, which have been investigated in recent years, particularly in cancer studies, in terms of their diagnostic value in gastric cancers in the light of current literature.

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METHODS

This study was conducted with the adult patients, who were hospitalized due to the diagnosis of gastric cancer at the General Surgery and Internal Medicine Medical Oncology Clinic of Atatürk University Faculty of Medicine Research Hospital between March 2020 and August 2020, and the healthy adults or the adult patients with benign gastric diseases, who presented to the general surgery outpatient clinic. The study included 30 patients aged over 18 years with a histopathologically diagnosed gastric cancer, and a control group of 30 healthy individuals or patients with benign gastric diseases. Cases were selected randomly. To minimize the effects on the serum levels of galanin and obestatin levels, patients with primary tumors other than gastric cancer, pregnant women, patients with significant systemic diseases, and individuals aged under 18 years were excluded from the study. Approval was obtained from the AUFM Clinical Research Ethics Committee for this study (Erzurum/Turkey). All individuals participating in the study were acknowledged about the study, and informed consents were obtained.

RESULTS

In the study, 30 patients, who were histopathologically diagnosed with malignant gastric tumor, and 30 healthy individuals with no diseases or patients who were diagnosed with benign gastric diseases under gastroscopy were examined prospectively in the patient and control groups. In the patient group of 30 patients, 19 (63.33%) were male and 11 (36.67%) were female. In the control group of 30 individuals, 19 (63.33%) were female and 11 (36.67%) were male. Adult patients aged over 18 years were included in the study.

The mean age of the patient group was 62.23±10.47, and the mean age of the control group was 61.23±7.69 (44–86); and there was no significant difference between the groups. Body mass index (BMI) was 23.98±4.7 for the patient group and 23.89±3.98 the control group, and there was no significant difference between the groups ($p>0.05$) (Table 1).

The mean serum levels of galanin was19.73±5.04 pg/mL in the patient group and 35.59±10.94 pg/mL in the control group. There was a highly significant difference between the groups ($p<0.001$) (Table 2 and Figure 1).

The mean serum levels of obestatin was 40.21±582 ng/mL in the patient group and 15.15±3.32 ng/mL in the control group. There was a highly significant difference between the groups ($p<0.001$) (Table 2 and Figure 1).

A statistically significant and negative correlation was found between the measured serum levels of obestatin and galanin ($r= -0.585$ and $p<0.001$) (Figure 1).

DISCUSSION

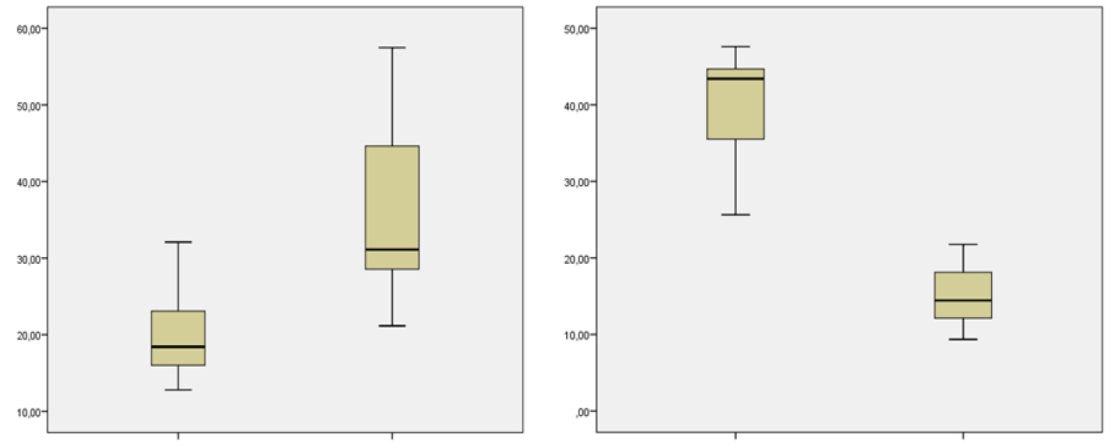
Gastric cancer is the fourth most common cancer in the world, and it has been identified as an international public health issue[7]. Biomarkers are needed for indicating the diagnosis and prognosis of such a disease[8]. In recent years, various hormones have been defined related to the physiology and cancers of the gastrointestinal system. These may be the hormones or markers that can be used in the diagnosis, prognosis, or even treatment of the disease. Galanin is known for its orexigenic effects, and obestatin is known for its anorexigenic effects. They are known as the peptide biomarkers, as proved in one study[9]. The stomach is a tissue that is rich in both of the two hormones and their receptors.

Table 1. Characteristics of the patient and control groups

	Male		Female		Mean age	BMI	Total	
	n	%	n	%	years	kg/m²	n	%
Patients	19	63.33	11	36.67	62.23±10.47	23.98±4.7	30	100
Control	11	36.67	19	63.3	61.23±7.69	23.89±3.98	30	100
Total	30	50	50	50	61.73±9.08	23.93±4.34	60	100

Table 2. Index of variability of obestatin and galanin levels measured in the patient and control groups.

	N	Obestatin (ng/mL) (min–max)	Galanin (pg/mL) (min–max)	p-value
Patient group	30	40.21±5.82 (25.63–47.61)	19.73±5.04 (12.80–32.08)	<0.001
Control group	30	15.15±3.32 (9.36–21.77)	35.59±10.94 (21.15–57.48)	<0.001



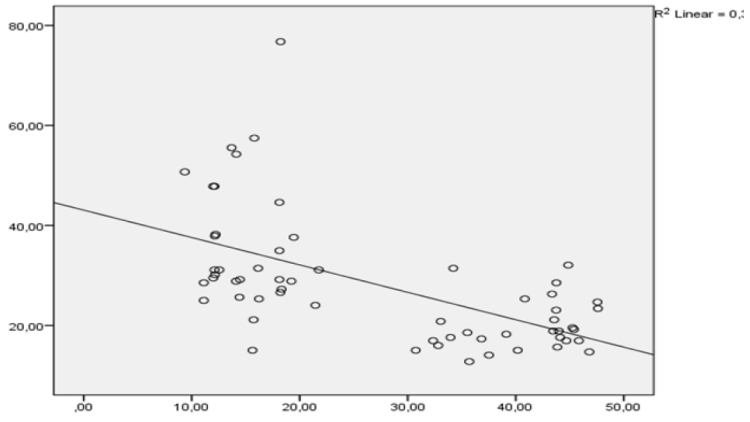


Figure 1. Statistics of galanin and obestatin levels.

The levels of galanin and obestatin in the body are affected by weight[9]. Serum levels of galanin were found to be higher in the obese patients[10]. In contrast, an inverse relationship was found between weight and obestatin in the study on obestatin[11]. The levels of obestatin were found to be higher in individuals with anorexia nervosa compared to the individuals in the healthy group[12].

In terms of weight, no significant difference was observed between the BMI values of the study groups, despite the fact that the patients were selected randomly in our study. Accordingly, investigating the effect of biomarkers used on cancer without being affected by weight contributed to the significance of our study.

Galanin is a neuropeptide with 30 amino acids, which basically isolated in the intestines and has a wide distribution in humans, including enteric nerves in the central nervous system, endocrine system, and autonomic nervous system[13]. Galanin is synthesized in the brain and intestine. It plays a role in the regulation and learning of nutrition, and response to nerve damage and pain. It functions in intestinal contractions, gastric acid secretion, and inhibition of the release of pancreatic peptides in the gastrointestinal system[14,15].

Various studies have been conducted on galanin in patients with cancer[14-17]. In a study conducted on patients with gastric cancer, the levels of galanin measured before the surgery were found to be lower compared to the postoperative levels and the levels of the healthy individuals. In addition, the expression levels of galanin decreased more in the tumor tissue compared to the adjacent tissue without tumor[15].

Although the potential role of galanin in gastric cancer is not fully known, looking at the expression of galanin and its receptors in a series of gastric cancer cell lines, higher expression of galanin initiates apoptosis of the gastric cancer cells. This suggests that galanin may have tumor-suppressing effects in gastric cancer. Thus, a decrease is observed in the expression of galanin in gastric cancers[18].

The most emphasized issue related to the pathophysiology of galanin is that galanin and its receptors play a role in the inhibition of cell proliferation and apoptosis[19,20]. It has been stated that galanin and its receptors play a role in the inactivation of cell proliferation and apoptosis in head and neck cancers[16].

In experiments involving the transplantation of human gastric cancer cells into rats, galanin treatment has been proven to reduce the volume and weight of the tumor; however, it did not change the rates of apoptosis[21].

In addition, the anti-proliferative effects of galanin have been demonstrated in pheochromocytoma and pancreas cancer[17,22].

Despite all these studies, the role of galanin in gastric cancer has not been fully elucidated yet. The BMI values of the groups examined in our study were the same, and the levels of galanin were found to be lower in the patient group. This supports the hypothesis that the expression of galanin decreased and its tumor-suppressing gene characteristics was epigenetically silenced in gastric cancers due to the mechanism of gastric cancers. In addition, due to the anti-proliferative effects, it raises the question of whether galanin and its receptors can be used in cancer treatments. More comprehensive studies are needed on this subject matter.

Obestatin is a peptide with 23 amino acids that is synthesized from preproghrelin, which is a prohormone originated from the stomach and small intestine endocrine cells similar to ghrelin. The stomach tissue, particularly its oxyntic mucosa, is the richest tissue in obestatin[23].

Obestatin is encoded by the same gene as the ghrelin hormone, and it is known to have opposite effects on the energy homeostasis and gastrointestinal functions. It inhibits gastrointestinal motility by stimulating the vagal afferent fibers. It creates a feeling of central satisfaction due to this effect and prevents weight gain. In addition, it causes delay of gastric emptying by inhibiting jejunal contractions[23,24].

The levels of ghrelin, obestatin, and peptide YY3-36, which were measured before and after the subtotal gastrectomy in patients with early gastric cancer, were evaluated. The levels of obestatin in the early postoperative period were observed to decrease compared to the preoperative period. Thus, it is thought that intestinal hormones in the gastrointestinal system may play a role in the pathogenesis during the development of gastric cancer[25].

In our study, similar to the literature, the levels of obestatin were found to be higher in patients with gastric cancer. Since our study was not a genetic analysis study, the pathophysiology was not fully explained. However, the fact that the BMI values of the groups were equal supports the hypothesis that obestatin is more common in tumor environments, and it accelerated the mitogenesis by activating the proliferation of cell line in gastric cancer, rather than supporting the effect of obestatin on motility and appetite.

The most important limitation of this study was the small number of patients due to the expensive tests. Another limitation was the lack of comparison with the serum bloods taken after the resection of the tumor from the same patients diagnosed with gastric cancer as a control group. The other limitations may be the difference in the stages of the gastric cancers, the lack of pathological classification, and the inability of the study to reveal the relationship between the severity of the cancer and the peptide hormones.

CONCLUSION

Although gastric cancer is common among the cancers in the world, the disease is usually diagnosed in advanced stages, and it has a poor prognosis. There are no instruments that have been proven to detect gastric cancer in its early stages. Various biomarkers have been used; however, no biomarker with high diagnostic value has yet been found. Serum levels of galanin were found to be lower and serum levels of obestatin were found to be higher in patients with gastric cancer compared to the healthy individuals. Obestatin and galanin can be used as potential biomarkers in the diagnosis of gastric cancer. Studies on this subject with large patient groups will better explain the effects of these peptide hormones.

AUTHORS' CONTRIBUTIONS

FAU: Conceptualization, Data curation, Formal Analysis, Writing – original draft. **ED:** Conceptualization, Data curation, Project administration, Supervision, Writing – original draft, Writing – review & editing. **RP:** Resources, Formal analysis. **NÖ:** Resources, Formal analysis. **MİY:** Project administration, Supervision, Writing – review & editing. **YA:** Conceptualization, Formal analysis

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