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THE PREDICTIVE ROLE OF GALANIN IN GASTRIC CANCER

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INTRODUCTION

Gastric cancer is the third most common cause of cancer-related mortality in the world.[1] In search of new approaches to diagnose or exclude gastric cancers, a number of tumor antigens have been identified, and many of these have been defined as immunotherapeutic agents.[2] However, therapeutic impacts of these agents have not been as satisfactory as expected. Galanin is a 29-amino acid COOH-terminally, highly conserved and only neuroendocrine peptide originally isolated from intestine.[3] The first 14 amino acids are fully conserved in near all species.[4] It modulates a diversity of physiologic processes, within perception, memory, sensory, pain processing, neurotransmitter, hormone secretion, and feeding behavior.[5] Various biologically active forms of galanin which have elongated or truncated NH2 terminal have been identified.[6]

Despite galanin's numerous effects, the relationship between galanin and gastric cancer has not been established. An article has showed that the presence of galanin in colon cancer and that may be used as a biomarker for the early detection of colon cancer.[6] In our study, we measured the level of galanin in the serum of 50 healthy donors and 90 patients with gastric cancer and searched for any relation between serum galanin level and gastric cancer.

Materials and Methods

Samples were taken from all patients with an informed consent authorized by the local ethical committee of the Acibadem University. Blood samples were taken in Acıbadem University Atakent Training Hospital, Department of Gastroenterology. In this study, a total of 140 blood serum, 90 from patients with gastric carcinoma and 50 from healthy volunteers, were analyzed. The samples were allowed to clot and then stored at -20°C until analysis. ELISA was used to analyze sera.

Statistical Analysis

The normality analysis was done by Shapiro Wilk test. Results were shown by drawing histogram, Q-Q plot and box plot graphs. The data was evaluated as mean, standard deviation, median, minimum, maximum, frequency and percentage.

Variables with normal distribution between the two groups were analyzed by Independent samples t-test and Mann Whitney U test. 3 and more groups were assessed by one-way analysis of variance of Kruskall Wallis. Multiple comparisons were made with the Dunn test. Nominal variables were assessed with Chi-square test (with Yates correction). A p-value of <0.05 was considered statistically significant. Analyzes were performed using software programs of SPSS 21 and NCSS 10 (2015. NCSS, LLC, Kasville, Utah, USA).

Table 1: Some of clinicopathological variables and galanin level in gastric cancer of patient and control group.

	Control (n=50)	Patients (n=90)	P
Age years	55.3 ± 5.71	56.12 ± 6.11	>0.05
Min-Max	*44-68*	*42-70*	
Gender (M/F)	*27/23*	*56/34*	
Total galanin (ng/mL)	2.57 ± 0.34	41.96 ± 11.76	<0.001
Min-Max	*1.9-3.1*	*10-58.6*	
Percentile 50 median		*44.60*	

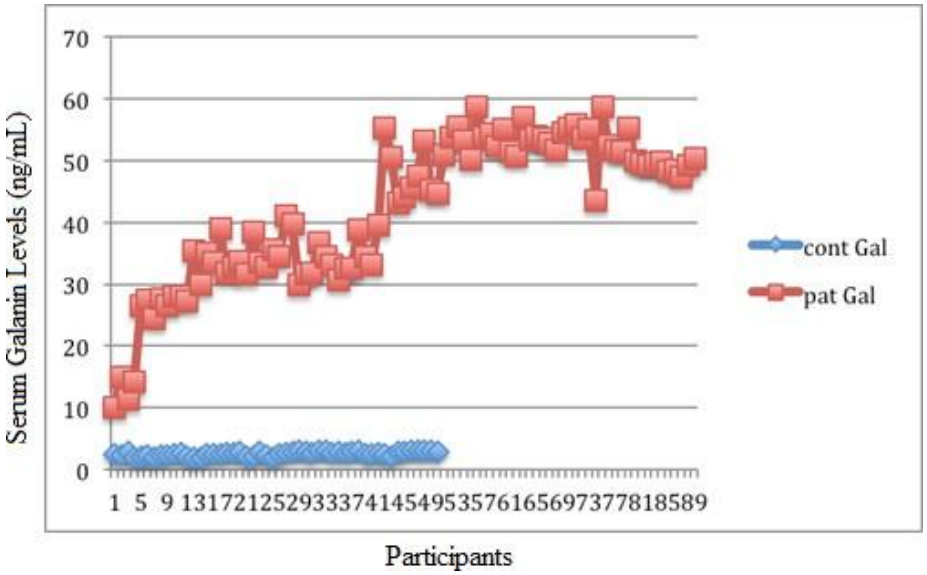

Figure 1: The histogram of the serum Galanin levels of the control and all patients.

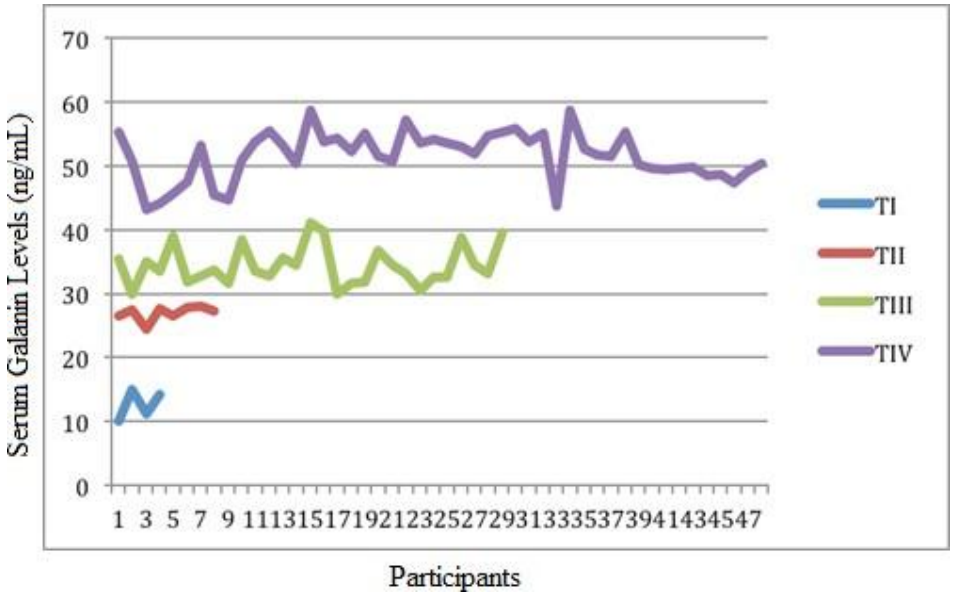

Figure 2: The histogram of the serum Galanin levels of the TI-TIV Stages.

RESULTS

Patient group consisted of 56 (62.9%) men and 34 (37.1%) women, with a mean age of 56.12 years **(**range: 42-70 years). According to the TNM classifications and histopathologic grading system of the International Union Against Cancer, there were 4 patients with stage I, 8 with stage II, 29 with stage III, and 49 with stage IV tumors. And the patients classified into three groups according to their tumor grading as such: 4 patients had well differentiated tumor, 9 patients had moderately differentiated tumor and 77 patients had poorly differentiated tumor. The mean age of the donors (control group) was 55.3 years (range: 44-68 years).

The average galanin level in the serum of the gastric cancer patients was 41.96 ng/mL, with a range of 10-58.6 ng/mL. This was a significantly higher than what was measured from the serum of healthy donors. (p=0.001).

The clinical profiles of patients with a serum galanin level above the cut off level (1 ng/mL) are shown in Table 1. Statistical analysis of the relationship between the serum galanin levels and clinicopathological parameters revealed that the serum galanin was not significantly affected by age or gender. However, patients with distant metastasis tended to have higher serum galanin levels (p=0.001), and stage IV patients also expressed higher galanin levels than the early-stage patients (p=0.001). Thus, the elevation with serum galanin levels appears to be closely associated with the malignant progression of gastric cancer. We showed a significant correlation between serum galanin levels and tumor size, as a significantly higher level of galanin was detected in patients with tumor bigger than 3 cm tumor in size (p=0.004), and between serum galanin levels and T stages. (p=0.001). Also, the serum galanin levels were correlated significantly with histologic grade, primary tumor, lymph node metastasis, lymphatic invasion,

vascular invasion, neural invasion (p=0.004, p=0.002, p=0.001).

DISCUSSION

As far as we know, this is the first study to show the significance of galanin level in gastric cancer. We hypothesize that the increased serum galanin level of gastric cancer patients may be due to the secretion of this neuropeptide by cancer cells. However, the physiology behind the secretion of galanin by the other cell types or tissues remains unknown and should be further researched. Elevated levels of galanin have been established within neoplastically altered tissues originated from neuroectoderm, such as pheochromocytoma, pituitary adenoma, neuroblastoma, and squamous cell carcino. Kim et al also showed that the colon cancer patients exhibited elevated serum galanin concentration compared to the healthy controls.[6] However, the resource of the elevated serum galanin levels was not discovered.[6]

The presence of galanin in the serum of gastric cancer patients may be associated with the function of galanin as a regulator of epithelial secretion and proliferation.[11] Galanin interacts with galanin receptor-1 to activate the mitogen-activated protein kinase signaling pathway and enhances the mitogenic activity of these cancer cells. Despite these findings, it has been also demonstrated that galanin may parade a protective function in head and neck squamous cell cancer (HNSCC) since galanin receptor-1 and 2 inhibit the proliferation of HNSCC cells via extracellular signal- regulated kinase mediated effects on cell-cycle control proteins.[12]

In conclusion, current study shows that serum galanin levels are overexpressed in gastric tumors, notably in those with metastatic potential, and ELISA with anti-galanin can serve as a promising diagnostic tool for gastric cancer.

REFERENCES

1. Rawla, P, Barsouk, A. Epidemiology of gastric cancer: global trends, risk factors and prevention.Prz Gastroenterol, 2019; 14: 26-38.
2. Lee DH, Yang Y, Lee SJ, Kim KY, Koo TH, Shin SM, Song KS, Lee YH, Kim YJ, Lee JJ, Choi I, Lee JH. Macrophage inhibitory cytokine-1 induces the invasiveness of gastric cancer cells by up-regulating the urokinase-type plasminogen activator system. Cancer Res, 2003; 63: 4648-4655.
3. Tatemoto K, Rokaeus A, Jornvall H, McDonald TJ, Mutt V. Galanin-a novel biologically active peptide from porcine intestine. FEBS Lett, 1983; 164: 124-128.
4. Schmidt WE, Kratzin H, Eckart K, et al. Isolation and primary structure of pituitary human galanin, a 30-residue nonamidated neuropeptide. Proc Natl acad Sci USA, 1991; 88: 11435-11439.
5. Floren A, land T, Langel U. Galanin receptor subtypes and ligand binding. Neuropeptides, 2000; 34: 331-337.
6. Kim KY, Kee MK, Chong SA, Nam JM. Galanin is up-regulated in colon adenocarcinoma. Cancer Epidemiology Biomarkers & Prevention, 2007; 16(11): 2373-78.
7. Bauer FE, Hacker GW, Terenghi G, Adrian TE, Polak JM, Bloom SR. Localization and molecular forms of galanin in human adrenals. Elevated levels in pheochromocytomas. J Clin endocrinol Metab, 1986; 63: 1372-1378.
8. Grenback E, Bjellerup P, Wallerman E, Lundblad L, Anggard A, Ericson K, Amman K, Landry M, Schmidt WE, Hökfelt T, Hulting AL. Galanin in pituitary adenomas. Regul Pept, 2004; 117: 127-139.
9. Tuechler C, Hametner R, Jones N, Jones R, Iismaa TP, Sperl W, Kofler B. Galanin and galanin receptor expression in neuroblastoma. Ann NY Acad Sci, 1998; 863: 438- 441.
10. Sugimoto T, seki N, Shimizu S, Kikkawa N, Tsukada J, Shimada H, Sasaki K, Hanazawa T, Okamoto Y, Hata A. The galanin signaling cascade is a candidate pathway regulating oncogenesis in human squamous cell carcinoma. Genes Chromosomes Cancer, 2009; 48: 132-142.
11. Lang R, Gundlach AL, Holmes FE, Hobson SA, Wynick D, Hökfelt T, Kofler B. Physiology, signaling and pharmacology of galanin peptides and receptors: Three decades of emerging diversity. Pharmacol Rev, 2015; 67: 118-175.
12. Kanazawa T, Misawa K, Misawa Y, Uehara T, Fukushima H, Kusaka G, Maruta M, Carey TE. G-protein-coupled receptors: next generation therapeutic targets in head and neck cancer? Toxins (Basel), 2015; 7: 2959-2984.