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*Source / Izvornik:* **Collegium Antropologicum, 2011, 35, 5 - 8**

**Journal article, Published version**

**Rad u časopisu, Objavljena verzija rada (izdavačev PDF)**

*Permanent link / Trajna poveznica:* <https://um.nsk.hr/um:nbn:hr:105:293979>

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*Download date / Datum preuzimanja:* **2024-11-15**



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# The Influence of the Different Morphological Changes on Gastric Mucosa on Somatostatin Cell Number in Antrum Mucosa and Serum Somatostatin

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## ABSTRACT

*The aim of our paper was to investigate the influence of the different morphological changes on gastric mucosa on somatostatin D-cell number in antral mucosa and serum Somatostatin. We analyzed according to Sydney classification to what extent the severity of gastritis affect the observed hormonal values. somatostatin D-cell number in antral mucosa and serum Somatostatin values were compared between three groups of patients; mild, moderate and severe chronic gastritis. The average number of somatostatin cell in biopsy sample of antrum mucosa was  $30.41 \pm 35.38$  ( $N=17$ ) in the case of middle form,  $18.69 \pm 26.65$  ( $N=56$ ) in moderate and in severe case of chronic gastritis  $5.23 \pm 5.93$  ( $N=7$ ) cells in  $\text{mm}^2$  of mucosa. The level of somatostatin in the serum of middle form gastritis were  $26.43 \pm 28.76$ , moderate  $19.95 \pm 35.93$  and severe  $17.88 \pm 17.66$   $\text{pg/mL}$ . In order to determine the number of somatostatin cells in antrum mucosa and serum somatostatin with present morphological changes of mucosa, it might helpful to exclude the patients with non-ulcer dyspepsia, but with the higher risk of premalignant and malignant changes.*

**Key words:** chronic gastritis, somatostatin D-cell, serum somatostatin

## Introduction

Somatostatin is a hormone significantly participating in regulation of stomach secretion<sup>1</sup>. Released somatostatin in antrum mucosa has an inhibitory influence on gastric cells, preventing the gastric acid secretion<sup>2,3</sup>. Chronic gastritis is as well characterized by inflammatory cell infiltration of lamina propria, accompanied by atrophy of glandular epithelium<sup>4,5</sup>. Initially, the reaction is rather superficial, but an intense inflammation might infiltrate

the whole mucosa causing the development of chronic atrophy gastritis<sup>6-8</sup>. This type of gastritis can provoke metaplastic changes which are associated with occurrence of intestinal stomach carcinoma<sup>9,10</sup>. Therefore, we investigated influence of pathological changes, like different gastritis types, and different morphological changes on the number of somatostatin D-cells in stomach antrum, and serum somatostatin.

## Subjects and Methods

### Subjects

The study includes 80 patients underwent endoscopies due to dyspeptic problems like: epigastric pain, heartburn, nausea and vomiting. The patients with acute and chronic organic disease, as well as those taking antibiotics, inhibitory protonic pump or inhibitory histaminic receptor drugs in the last month were excluded.

### Endoscopy and biopsy

The endoscopic examination included the bioptic samples, taken on an empty stomach without premedication. The total number of 4 bioptic samples were taken, 1 from the side of the antrum greater curvature and 1 from the side of antrum lesser curvature 2 cm from pylorus, 1 from the side of body of the stomach greater curvature and 1 from the side of body of the stomach lesser curvature for coloring according to Giemsa.

### The number of somatostatin D-cells

In order to determine number of somatostatin cells in stomach mucosa, we have used biopsy sample of greater curvature of antrum, taken 1 cm from pylori and the result has been expressed as the number of cells in mucous mucosa millimeter. The histological material was treated with ANTI-SOMATOSTATIN, Dako LSAB kit (CODE NO. N 1551). The primary antibody was 7 mL of rabbit antiserum on somatostatin in 0,05 M Tris pufern pH 7.6. The further methods of sample analysis strictly followed the producer's guidelines (DACO). The cells were counted using computer program for automatic picture processing, VANS, Zagreb Applications form<sup>11</sup>. First of all, we have measured the sample surface and then counted the somatostatin cells, in order to obtain an exact number of somatostatin cells in mm<sup>2</sup> of antrum mucosa. The cells were counted in two samples and presented as an average number of cells for both samples.

### Radioimmunoassay of serum somatostatin

In the assay procedure we used a protocol which is similar to previously described by Arimura et al.<sup>11</sup>. This kit is standardized with Synthetic Somatostatin (SS-14), (INCSTAR Corporation-Stillwater, Minnessota, USA).

### Statistics

We have used Mann-Whitney U-test (Wicoxon Scores), Medijan test for independent samples, Kruskal-Wallis test and Komogor-Smirna test, whereas we have applied Savage Scope test for analysis of homogeneity. The statistical data analysis was done according to the program packages of SAS (SAS Institute) and Mathematical (Wolfran Research).

### Ethical considerations

All patients have signed written consent to our study. The study was approved by the Ethics Committee of the Internal Clinic, »J. J. Strossmayer« University.

## Results

Applying Sydney classification, patients with chronic gastritis were divided in three types; mild moderate and severe case. The average number of somatostatin cell in biopsy sample of antrum mucosa was  $30.41 \pm 35.38$  (N=17) in the case of mild form,  $18.69 \pm 26.65$  (N=56) in moderate and in severe case of chronic gastritis  $5.23 \pm 5.93$  (N=7) cells in mm<sup>2</sup> of mucosa (Figure 1). The results show that the number of somatostatin cells in biopsy sample significantly decreases depending on the severity of gastritis type ( $p < 0.05$ ). The diffuse gastritis type had 66 patients (84.62%) and antral type 12 (15.38%). The average number of somatostatin cells in biopsy sample of stomach antrum in the case of diffuse gastritis type was  $17.95 \pm 25.19$  and in the antral type  $32.88 \pm 41.83$  cells in mm<sup>2</sup> (Figure 2). There is a statistically significant increase of somatostatin cells in antral type in comparison to diffuse type ( $p < 0.05$ ). The level of somatostatin in the serum of middle form gastritis were  $26.43 \pm 28.76$ , moderate  $19.95 \pm 35.93$  and severe  $17.88 \pm 17.66$  pg/mL (Figure 3). The results show that value of serum somatostatin significantly decreases depending on the severity of inflammation. The occurrence of intestinal metaplasia and atrophy of stomach mucosa as a consequence of the se-

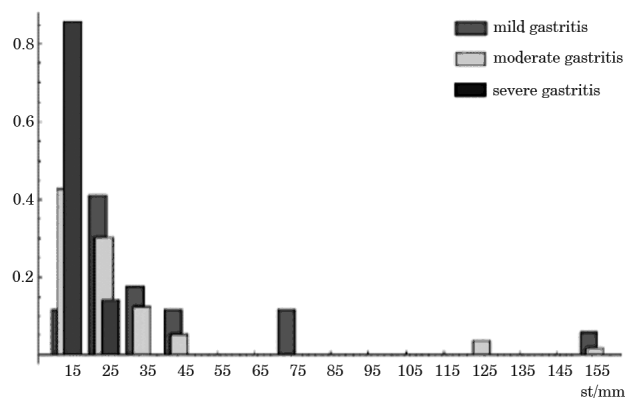


Fig. 1. Histogram of somatostatin cells in stomach mucosa according to gastritis grade.

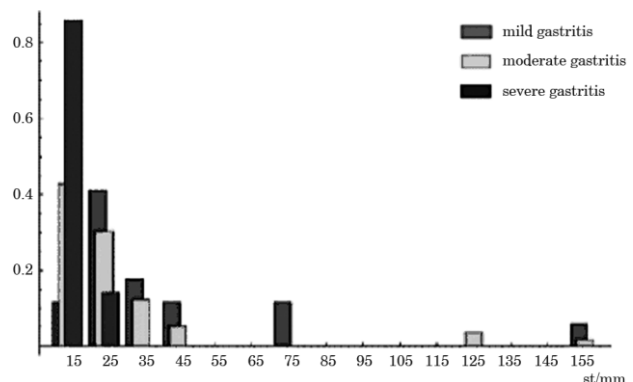


Fig. 2. Histogram of somatostatin cells in mucosa according to gastritis type.

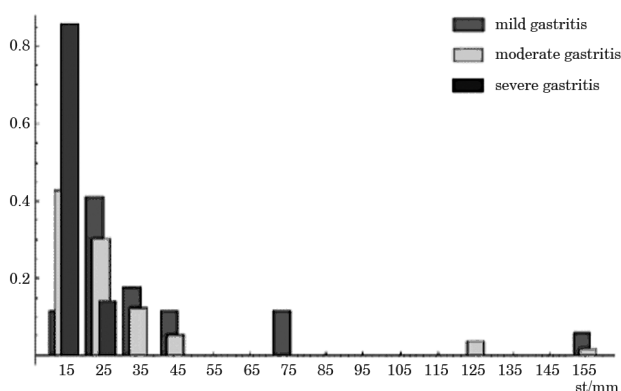


Fig. 3. Histogram of serum somatostatin according to gastritis grade.

verity of gastritis type were tightly monitored. Two patients (11.8%) with a mild gastritis type, had atrophy of stomach mucosa, but not intestinal metaplasia. However, 11 patients (19.3%) suffering from moderate gastritis type had atrophy of stomach mucosa and 5 had intestinal metaplasia. In the case of severe gastritis type, 7 (100%) patients had atrophy of stomach mucosa and 5 (71%) intestinal metaplasia. The results suggest a significant tendency of intestinal metaplasia and atrophy of stomach mucosa depending on the type of gastritis.

## Discussion

The gastric acid has an extremely aggressive influence on stomach mucosa, what was recognized at the beginning of the last century and therefore so many studies have done pathophysiological analysis of stomach secre-

tion disorders<sup>13-15</sup>. Analyzing numerous studies, Calam has concluded that gastric G-cells are under the constant control, actually suppressed by somatostatin D-cells of antrum mucosa and its special products<sup>16-18</sup>. Several studies have analyzed alteration of antrum somatostatin D-cell number depending on endoscopically visible changes like: erosion, tumor or ulcers<sup>19-21</sup>. Our study is focused on the changes occurring among the patients with dyspepsia. Applying Sydney classification<sup>22</sup> of chronic gastritis, we have investigated influence of the grade and the type of gastritis on somatostatin cell number of stomach antrum and serum somatostatin. The results indicate a strong impact of gastritis severity on somatostatin cell number in antrum. The similar results were obtained by Konturek and Bjelanski<sup>23</sup>. The chronic inflammation of stomach mucosa reduces the number of somatostatin cells and serum somatostatin values, but increases serum gastrin value and stimulates stomach acid secretion<sup>24</sup>. Furthermore, we would have an increase of intestinal metaplasia and stomach mucosa atrophy, as described by Sipponen and Kuipers<sup>25,26</sup>. Therefore, preventing the deterioration of gastritis type is very important as well as early detection and prevention of potential premalignant changes<sup>4,5,9,10,27</sup>. The number of somatostatin cells in antrum mucosa in diffuse gastritis type<sup>28,29</sup> is much smaller than in antral gastritis type, what can be explained with the fact that antral gastritis is milder type in comparison to diffuse type which infiltrates bigger surface, provoking bigger pathophysiological changes. In order to determine the number of somatostatin cells in antrum mucosa with present morphological mucosal changes, it might be helpful to exclude the patients with non-ulcer dyspepsia, but with the higher risk of premalignant and malignant changes.

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## **UTJECAJ RAZLIČITIH MORFOLOŠKIH PROMJENA ŽELUČANE SLUZNICE NA BROJ SOMATOSTATINSKIH STANICA U SLUZNICI ANTRUMA ŽELUCA I VRIJEDNOSTI SOMATOSTATINA U SERUMU**

### **S A Ž E T A K**

U ovom radu istražili smo utjecaj različitih morfoloških promjena želučane sluznice na broj somatostatinskih D stanica sluznice antruma želuca i serumski somatostatin. Prema Sydneyskoj klasifikaciji gastritisa analizirali smo koliko jačina upalnih promjena sluznice želuca utječe na promatrane vrijednosti hormona. Broj somatostatinskih D stanica u sluznici antruma želuca i vrijednosti serumskog somatostatina uspoređivali smo kod tri grupe pacijenata: s blagim, umjerenim i teškim kroničnim gastritisom. Prosječni broj somatostatinskih stanica u bioptičkom uzorku sluznice antruma bio je  $30,41 \pm 35,38$  ( $N=17$ ) u blagom gastritisu,  $18,69 \pm 26,65$  ( $N=56$ ) u umjereno teškom i  $5,23 \pm 5,93$  ( $N=7$ ) stanica u  $\text{mm}^2$  sluznice. Vrijednosti serumskog somatostatina u blagom gastritisu bile su  $26,43 \pm 28,76$ , umjerenom  $19,95 \pm 35,93$  i teškom obliku  $17,88 \pm 17,66$  pg/mL. Određivanje broja somatostatinskih stanica sluznice antruma želuca i serumskog somatostatina kod određenih morfoloških promjena želučane sluznice može nam pomoći da izdvojimo pacijente s neulcusnom dispepsiom te one koji imaju veliki rizik od razvoja premalignih i malignih promjena.