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GASTRIN IN SERUM AND MORPHOLOGICAL STATE OF GASTRIN-SECRETING CELLS IN PATIENTS WITH GASTRIC POLYPOSIS

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Conflict of interest
The authors declare that they have no conflicts of interest

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Abstract

Numerous studies regarding gastric hormones and their regulation have been performed until now. However, the effect of the hormones on the formation and malignisation of gastric polyps still remains not clear. ***Our aim*** *was to identify the relation between the level of gastrin in the blood, gastric mucosa, polyp tissue, gastric juice and pathogenesis of gastric polyposis.*

Materials and methods. *A thorough investigation of gastrointestinal hormones in serum and gastric juice, in polyp's tissue and mucosa, gastrin-secreting cells and proteolytic activity of gastric juice was carried out in 40 patients with gastric polyps. These patients were divided into groups, depending on the location, number, and malignancy of the polyps. As a control group, 10 healthy individuals were used to determine the normal values of the studied indicators.*

Results: *A significant increase (more than two times) in the gastrinemia level before the surgery was noted in patients with polyp recurrence, and gastrin level increased to more significant digits of 227.0+37.4 pg/ml ($p<0.05$) in one year after polypectomy.*

Conclusion. *Gastrin is apparently involved in the process of polyp formation since polyp's growth is accompanied by elevation of serum gastrin. This is confirmed by a response of gastrin in the blood to a test meal in individuals with different duration of the disease: a marked increase in gastrinemia appears in patients suffering from gastric polyposis for more than three years. Therefore, evaluation of gastrin level in the patients' blood can be used to predict a recurrence potential of polyps. This is evidenced by more pronounced hypergastrinemia before polypectomy in patients who had a further recurrence of the disease within one year after the surgery.*

Keywords
serum gastrin, gastric secretion, gastric polyps, polypectomy, polyp recurrence

Асқазан полипозы бар науқастардың қан сарысуындағы гастрин құрамы және гастрин шығаратын жасушалардың морфологиялық жағдайы

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Аңдатпа

Бүгінгі күні асқазан гормондары мен олардың реттелуіне қатысты көптеген зерттеулер жүргізілді. Алайда, гормондардың асқазан полиптерінің пайда болуына және қатерлі ісікке әсері әлі түсініксіз. ***Біздің мақсатымыз*** *қандағы, асқазанның шырышты қабатындағы, полип тіндегі, асқазан сөліндегі гастрин деңгейі мен асқазан полипозының патогенезі арасындағы байланысты анықтау болды.*

Материал мен әдістер. *Асқазан полиптері бар 40 науқаста қан сарысуы мен асқазан сөліндегі, полип тіндеріндегі және шырышты қабаттардағы, гастрин шығаратын жасушалардағы асқазан-ішек жолдары гормондарын және асқазан сөлінің протеолитикалық белсенділігін мұқият зерттеу жүргізілді. Бұл науқастар полиптердің орналасуына, санына және қатерлі ісіктеріне байланысты топтарға бөлінді. Бақылау тобы ретінде зерттелген параметрлердің қалыпты мәндерін анықтау үшін дені сау 10 адам зерттелінді.*

Нәтижелер. *Қайталанатын полипі бар науқастарда операцияға дейін гастринемия деңгейінің едәуір жоғарылауы (екі реттен артық) болды, ал полипэктомиядан кейін бір жыл өткен соң гастрин деңгейі 227,0 + 37,4 пг/мл-ге дейін жоғарылады ($p < 0,05$).*

Қорытынды. *Гастрин полиптің пайда болуына қатысады, өйткені полиптің өсуі сарысудағы гастрин деңгейінің жоғарылауы арқылы жүреді. Бұл аурудың әр түрлі ұзақтығы бар адамдарда қандағы гастриннің сынақ тамағына реакциясы арқылы расталады: асқазан полипозы үш жылдан асқан науқастарда гастринемияның айқын жоғарылауы пайда болады. Сондықтан пациенттердің қанындағы гастрин деңгейін бағалау арқылы полиптердің қайталану мүмкіндігін болжауға болады. Операциядан кейін бір жыл ішінде аурудың қайталануы болған науқастарда полипэктомияға дейінгі айқын гипергастринемия осының дәлелі.*

Түйін сөздер
асқазан полиптері, полип, полипэктомия, полиптің қайталануы, қан сарысуындағы гастрин, асқазан секрециясы

Содержание гастрина в сыворотке крови и морфологическое состояние гастринпродуцирующих клеток у пациентов с полипозом желудка

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Конфликт интересов
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Аннотация

До настоящего времени проведено множество исследований, касающихся гормонов желудка и их регуляции. Однако влияние гормонов на образование и малигнизацию желудочных полипов до сих пор остается неясным. ***Нашей целью*** *было выявить взаимосвязь между уровнем гастрина в крови, слизистой оболочке желудка, ткани полипа, желудочном соке и патогенезом полипоза желудка.*

Материал и методы. *У 40 пациентов с полипами желудка проведено тщательное исследование гастроинтестинальных гормонов в сыворотке крови и желудочном соке, в ткани полипа и слизистой, гастринпродуцирующих клеток и протеолитической активности желудочного сока. Эти пациенты были разделены на группы в зависимости от расположения, количества и злокачественности полипов. В качестве контрольной группы использовали 10 здоровых лиц для определения нормальных значений исследуемых показателей.*

Результаты. *У пациентов с рецидивом полипа отмечено значительное повышение (более чем в два раза) уровня гастринемии до операции, а через год после полипэктомии уровень гастрина повысился до более значимых цифр 227,0+37,4 пг/мл ($p<0,05$).*

Выводы. *Гастрин, очевидно, вовлечен в процесс образования полипов, поскольку рост полипов сопровождается повышением уровня гастрина в сыворотке крови. Это подтверждается реакцией гастрина в крови на пробный прием пищи у лиц с различной длительностью заболевания: выраженное повышение гастринемии появляется у пациентов, страдающих полипозом желудка более трех лет. Поэтому оценка уровня гастрина в крови пациентов может быть использована для прогнозирования возможности рецидива полипов. Об этом свидетельствует более выраженная гипергастринемия перед полипэктомией у пациентов, у которых в течение года после операции наблюдался дальнейший рецидив заболевания.*

Ключевые слова
полипы желудка, полип, полипэктомия, рецидив полипа, гастрин сыворотки крови, желудочная секреция

Introduction

Gastrin is one of the main regulators of acid-forming function of the stomach. Currently, there are two known ways to implement the gastrin action on hydrochloric acid secretion in gastric mucosa [1-3].

The first way is based on the notion of histamine as the final stimulator of acid secretion. It increases the activity of histidine decarboxylase, which catalyzes the conversion of histidine to histamine. The last one, interacting with the H2-receptors, activates adenylate cyclase and increases intracellular level of AMP in the parietal cells [4,5].

The second way is based on the elevation of tubular permeability of the parietal cells and increase in the flow of exogenous calcium to them [2-7].

In any case, the effect of gastrin on the secretion of hydrochloric acid is caused by the interaction of the hormone with a specific gastrin receptor of the parietal cell membranes.

These processes are carried out in close contact with other biologically active substances with very narrow relationship between them [8].

Besides the influence on the secretion of hydrochloric acid, gastrin is able to stimulate smooth muscle contraction of the lower esophageal sphincter, stomach, small intestine, gall bladder [2,6,9], to increase blood flow to the stomach, small intestine, pancreas [4,8].

Trophic effects of gastrin on the various parts of digestive tract and pancreas were noted in clinical and experimental studies. Thus, mucosal thickening of stomach fundus and duodenum was revealed in patients with Zollinger-Ellison syndrome. The stimulatory effect of gastrin on the cells' growth was noted in a tissue culture of duodenal mucosa during the investigation [10,11].

Experimental data on the trophic action of gastrin is contradictory. Trophic effects of exogenous gastrin on the gastrointestinal tract mucosa, including esophagus and antrum, were marked in a number of papers, while other evidence suggests that injection of gastrin leads to the increase of mitosis number and DNA synthesis in the fundic mucosa, but not in the antral mucosa [12].

Experiments in which found that gastrin increases DNA synthesis and mitotic activity in the fundic gland cells and histamine does not cause such effect, became the basis for hypothesis on the trophic activity of gastrin [13,14]. Consequently, endogenous hypergastrinemia has trophic effect on the fundic mucosa, which is not observed after gastrectomy with antrum elimination. In humans, injection of pentagastrin contributed to the inclusion

of urinating leucine to the protein components of the gastric mucosa, but not of the duodenal mucosa [15-18]. Trophic effect of gastrin observed in the works of many authors [16,19-21]. At the same time, there is doubt about the physiological nature of trophic effect of exogenous gastrin [22-24].

Material and methods

A total of 40 patients (17 men, 23 women) with gastric polyps admitted to the Regional Oncologic Dispensary were included in the study. Age of the patients ranged from 25 to 79 years.

26 (65%) patients were examined in the hospital, 14 (35%) patients underwent examination and treatment in outpatient conditions. 10 healthy volunteers took part in the clinical trial as a control group.

Outpatient and clinical records of patients were the source of statistical data. These records included all the information on the results of endoscopy, radioimmunoassay, histological examination and surgical management, along with a long-term endoscopic follow-up of patients.

Most patients were aged 41 to 60 years when gastric polyps are frequently found. These findings should be considered in the examination of patients because the blastic transformation of polyps especially increased in individuals aged 41 to 60 years.

Upper gastrointestinal endoscopy and target biopsy of gastric tissue and surrounding mucosa was performed in all patients. Polyps were divided into two main groups depending on the histological structure of biopsy sample: 1) benign polyps – in 31 (77.5%) patients; 2) malignant polyps – in 9 (22.5%) patients. Based on the World Health Organization (WHO) classification of gastric polyps, we ranged adenomatous and hyperplastic polyps with various dysplasia rates, chronic gastritis related polypoid focal hyperplasia of mucosa and fibrous inflammatory polyps in a group of clinically benign growths. Solitary polyps were observed in 21 (52.5%) patients, multiple – in 19 (57.5%).

Biopsy was obtained from the polyp, in its area and away from it (2-3, 5-6, 8-10 cm) under the control of the camera. 8-10 tissue specimens were sampled from 40 patients during each procedure. Specimens were put in 10% formalin solution for several hours in form of immersion fixation. Furthermore, they were embedded into liquid paraffin, and 5-өm-thick sections were prepared. Hematoxylin-eosin (PAS-reaction) was used as a general stain.

To obtain serum gastrin levels, 5 ml of venous blood was collected in the morning while the patient was fasting for 12 hours. Samples were centrifuged instantly at 4 ˚C and stored at -75 ˚C until required. Serum gastrin response to a test meal (100g of cooked meat) was recorded in 10 healthy individuals and in 40 patients with gastric polyps. Changes in serum gastrin were registered in 15, 30, 45, and 60 min after the test meal. Serum gastrin levels were identified using GASK-PR-US radioimmunoassay kit (CIS Bio International, France).

We also assessed the basal serum gastrin levels in patients with polyps before the polypectomy procedure and one year after it, taking into account the presence or absence of the disease recurrence. Gastrin levels were also measured in stomach mucosa, polyp tissue, and in gastric juice in patients with antral and fundic polyps.

Total acidity and free hydrochloric acid were identified in order to determine the cause of hypergastrinemia in patients and to get normal values in control group.

Statistical data processing was performed on a computer using “Statistica 10” software package for analysis of digital data. We applied Student’s t-test to compare means equality in two samples at the value of $p<0.05$.

Results

The results of the study of basal serum gastrin and gastric acidity in patients with polyposis, depending on the nature of the polyps and changes of the gastric mucosa, are presented in Table 1, from which it appears that significant (in 2.6 times) increase in the basal level of gastrin with marked reduction in gastric acidity was observed in patients with atrophic gastritis. In patients with atrophic hyperplastic gastritis, content of serum gastrin does not differ from that in healthy individuals, although they had clearly reduced acidity of gastric juice.

Thus, the level of basal gastrin was different at the same severity of achylia in patients with gastric polyposis, depending on the nature of changes in the gastric mucosa.

Gastrin in serum was 1.8 times higher in patients with solitary gastric polyps than in healthy individuals, and it was two times as great as in patients with multiple polyps. The significant difference between this indicator in patients with solitary and multiple polyps was not found. At the same time, there is a pronounced reduction in the acidity of gastric juice in both groups of patients, and no difference in severity of achylia.

Basal serum gastrin was two times higher in patients with benign gastric polyps than that in the control group. The indicator was not much different in patients with malignant polyps, compared with healthy individuals. A marked reduction of gastric acidity was noted in both groups.

So, level of basal gastrin was different at the same severity of achylia in patients with gastric polyposis, depending on the nature of changes in the gastric mucosa, the amount and nature of pol-

Table 1.
Basal level of serum gastrin (pg/ml) and gastric acidity in patients with gastric polyposis, with changes in the gastric mucosa

No.	Survey sample	Number of surveyed patients	Basal level of gastrin (M ± m)	Gastric acidity	
				Total acidity (M±m)	Free hydrochloric acid (M±m)
1	Control group	10	87,42±2,8	53,21±1,9	26,4±0,88
2	Atrophic gastritis	24	230,2±34,3	14,5±1,3 p <0,05	0,9±0,3
3	Atrophic hyperplastic gastritis	16	97,8±15,4	15,2±1,5 p< 0,05	3,9±0,8
4	Solitary gastric polyps	21	155,0±26,7 p > 0,05	14,8±1,9 p<0,05	2,5±0,7
5	Multiple gastric polyps	19	176,3±28,3 p<0,02	I7,1±1,5 p<0,05	2,8±0,6
6	Benign gastric polyps	31	174,4±17,9 p<0,05	15,6±0,9 p <0,05	2,9±0,5
7	Malignant gastric polyps	9	87,99±9,4	13,8±1,6 p<0,05	2,7±1,2

yps. Consequently, determining the level of basal gastrin allows in some cases to identify a violation of hormonal regulation of gastric acid secretion in patients with gastric polyposis.

A more detailed analysis can be obtained in the study of gastrin after standard test meal. The results of these studies are shown in Table 2, from which it appears that significant increase of 80% in serum gastrin was noted within 30 minutes after the test meal in patients with atrophic gastritis, compared to basal level.

After 45 and 60 min, the indicator was higher by 89% and 86% than the basal level, respectively. At all stages of the study, gastrin level significantly exceeds in patients with atrophic gastritis than that of healthy individuals. Increase in gastrin level in this group of patients after the test meal is more pronounced and prolonged than in the control group (100g of cooked meat as a standard test meal).

Discussion

In patients suffering from polyposis combined with atrophic hyperplastic gastritis, standard test meal leads to a significant increase in gastrin level by 79% in 30 minutes, compared with the basal level. A further increase by 125% and 175% was recorded in 45 and 60 min, respectively, while this indicator in 15, 30 and 45 min in said group of patients is not very different from that of the control group. After 60 min, serum gastrin level was 2.6 times higher than in healthy individuals, test meal in this cohort of patients leads to a more pronounced and prolonged increase in gastrin levels compared with those in the control group.

Comparison of changes in the serum gastrin levels in patients with atrophic and atrophic hyperplastic gastritis after the test meal demonstrates that this indicator is higher in atrophic gastritis at all stages of the study. At the same time, an increase in the gastrin level was noted in 45 and 60 min after the test meal in patients with atrophic hyperplastic gastritis, compared to the basal level, which is less pronounced in patients with atrophic gastritis.

Thus, the standard test meal in patients with gastric polyposis reveals significant differences in the nature and severity of the changes in the serum gastrin compared with the control group, which is characterized by a more pronounced and prolonged hypergastrinemia. Test meal reveals inappropriate secretion of gastrin in patients with gastric polyposis, combined with atrophic hyperplastic gastritis and normal level of basal gastrin.

Table 2.
Change in the concentration of gastrin (pg/ml) in the blood of patients with atrophic and atrophic hyperplastic gastritis after the standard test meal

No.	Survey sample	Number of surveyed patients	Basal level of gastrin (M±m)	Level of gastrin after the test meal			
				In 15 min	In 30 min	In 45 min	In 60 min
1	Control group	10	87,4±2,8	87,0±9,2	127,5±17,1	122,4±16,5	108,8±16,9
2	Atrophic gastritis	24	230,2±34,3 p_2<0,05	2,82±41,9 p_2<0,05	414,2±71,2 $p_{1<}$0,05 p_2<0,05	434,1±74,0 $p_{1<}$0,05 p_2<0,05	427,2±76,2 p_1<0,05 p_2<0,05
3	Atrophic hyperplastic gastritis	16	97,8±26,7 p_2<0,05	133,6±28,9 p_2<0,05	175,0±30,9 p_1<:0,05	219,7±41,8 p_1<0,05	268,6±66,3 p_1<:0,05 p_2<0,05

Note: p_1 – statistical significance, compared to baseline; p_2 – statistical significance, compared to control group.

Table 3.
Change in the concentration of serum gastrin in patients with single and multiple gastric polyps after the standard test meal (pg/ml)

No.	Survey sample	Number of surveyed patients	Basal level of gastrin (M±m)	Level of gastrin after the test meal			
				In 15 min	In 30 min	In 45 min	In 60 min
1	Control group	10	87,4±2,8	87,0±9,2	127,5±17,1	122,4±16,5	108,8±16,9
2	Solitary gastric polyps	21	155,0±26,7 p_2<0,05	208,0±34,1 p_2<0,05	202,0±34,0 p_2<0,05	230,0±40,1 p_2<0,05	236,0±37,8 p_2<0,05
3	Multiple gastric polyps	19	176,3±28,3 p_2<0,02	204,4±29,1 p_2<0,05	378,7±77,8 p_1<:0,05 p_2<0,02	420,6±82,0 p_1<:0,05 p_2<0,01	457,6±89,7 p_1<:0,05 p_2<0,0

Note: p_1 – statistical significance, compared to baseline; p_2 – statistical significance, compared to control group.

Study results of serum gastrin levels in patients with single and multiple polyps after the test meal are presented in Table 3.

The results demonstrate that gastrin level in patients with solitary gastric polyps significantly exceeds the indicator in the control group in response to the test meal during the entire study. At the same time, the level of this hormone undergoes further slight fluctuation, reaching 208.0 + 34.1 pg/ml at 15 min after the test meal.

When multiple gastric polyps, a significant increase by 115% in serum gastrin level is registered after 30 min as a response to the test meal compared to the basal level. Its level increased by 139% and 160% after 45 and 60 min, respectively. Gastrin level in these patients was significantly higher than that in healthy individuals at the appropriate time at all stages of the study. It was noted a more pronounced and prolonged increase in the gastrin level in patients with multiple polyps in response to the standard test meal, compared to healthy individuals.

Comparing changes in the content of serum gastrin in patients with solitary and multiple gastric polyps after the test meal, we have found its significant increase after 30, 45 and 60 min in patients with multiple polyps.

Consequently, the standard test meal leads to distinct changes in the dynamics of gastrin level in patients with solitary and multiple gastric polyps, compared with control group. If the basal gastrin level in one or another group of patients is almost identical, then it changes differently in response to test meal. Thus, the response to test meal is negligible in patients with solitary polyps, while there is a pronounced and long lasting hypergastrinemia in patients with multiple polyps. It may indicate a different nature of the regulatory function changes in the gastrin producing cells in patients with solitary and multiple gastric polyps.

We determined the basal level of gastrin in patients with polyposis before polypectomy and one year after it, depending from the presence or absence of the disease recurrence (Table 4).

It was revealed that basal serum gastrin before surgery was higher than control level by 88% in patients without recurrence of polyp formation in one year after polypectomy. So, one year after surgery it was decreased to 101.0 + 18.9 pg/ml, which is only slightly higher than gastrin level in healthy individuals. In these patients, the acidity of gastric juice was reduced as before the surgery, so after it.

Significant increase (more than two times) in the gastrinemia level before the surgery was noted in patients with disease recurrence, and one year after polypectomy gastrin level increased to more significant digits of 227.0+37.4 pg/ml (p<0.05).

That is, performing the polypectomy is not accompanied by normalization of the basal gastrin level in the blood of patients with gastric polyposis,

Table 4.
Basal level of serum gastrin (pg/ml) in patients with gastric polyposis before and after polypectomy, with the disease recurrence and without it, within one year after surgery

No.	Survey sample	Number of surveyed patients	Basal level of gastrin
1	Control group	10	87,4±2,8
2	Patients with polyposis before the surgery without following recurrence	24	154,6±34,6 p> 0,05
3	Patients with polyposis within one year after the surgery without recurrence	10	101,0±18,9 p > 0,05
4	Patients with polyposis before the surgery with recurrence	16	182,3±37,0 p<0,05
5	Patients with polyposis within one year after the surgery with recurrence	13	227,0±37,4 p<0,05

Table 5.
Change in gastrin concentration (pg/ml) in the blood of patients with gastric polyposis before polypectomy and within one year after it without recurrence in response to the standard test meal

No.	Survey sample	Number of surveyed patients	Basal level of gastrin	Level of gastrin after test meal			
				In 15 min	In 30 min	In 45 min	In 60 min
1	Control group	10	87,4±2,8	87,0±9,2	127,5±17,1 p_1<:0,05	122,4±16,5 p_1<:0,05	108,8±16,9
2	Patients with polyposis before the surgery	24	154,6±34,6 p>0,05	188,0±40,1 p_2<0,05	246,1±41,6 p_2<0,05	275,0±49,1 p1<:0,05 p_2<0,05	404±90,5 p1<:0,05 p_2<0,05
3	Patients with polyposis within one year after the surgery	10	101,0±18,9 p>0,05	128,9±32,2 p >0,05	145,0±24,7 p > 0,05	185,0±43,7 p> 0,05	184,4±45,8 p> 0,05

Note: p_1 – statistical significance, compared to baseline; p_2 – statistical significance, compared to control group.

despite the presence or absence of polyp recurrence. However, if there is a reducing trend of this indicator while no recurrence, then a trend of its increase is revealed during recurrence. The level of achylia was expressed almost equally in all patients during all periods of determination.

Table 5 shows the results of determination of the serum gastrin concentration in patients with gastric polyposis before and one year after surgery without recurrence of the disease under the influence of the test meal. It was noted that test meal before polypectomy leads to the increased gastrinemia already in 15 minutes after it, reaching significant level in 45 minutes.

We observed no significant changes of gastrin level in the blood in response to test meal in patients within one year after polypectomy in the absence of disease recurrence.

Thus, significant hypergastrinemia develops in response to test meal in patients with gastric polyposis without the disease recurrence, and one year after surgery gastrin level reaches close to that of healthy individuals.

Gastrin level in the blood increased within 15 minutes after test meal in patients with gastric polyposis and the disease recurrence before the polypectomy performance, reaching a valid value of 281.6+37.0 pg/ml after 30 minutes, which is much higher than gastrin concentration in the control group at the same moment (Table 5).

Test meal within one year after surgery in patients with recurrent disease caused a distinct increase in gastrin level not only compared to its initial level, but also to its control concentration. The changes were noted at all stages of its determination. If gastrinemia level was decreasing already after 45 min in healthy individuals, then in this group of patients it was continuing to grow even after one hour after the test meal.

Therefore, the tendency to recurrence of polyp formation is evident in the increasing the level of gastrin in the blood of patients (before and after the operation) under the influence of the standard test meal.

In the context of the investigation data of gastrin level in patients within one year after polypectomy, it was interesting to estimate the level of gastrinemia after test meal in patients within one year after gastrectomy for polyposis (Table 6).

Thus, gastrectomy in patients with polyposis reduces the basal level of gastrin by 1.8 times as compared to control level. And, standard test meal causes a slight increase in gastrin level in the blood within one year after the gastric resection. Even the

Table 6.
Changes in gastrin concentration (pg/ml) in the blood of patients with gastric polyposis with recurrent disease before surgery and within one year after it, in response to the test meal

No.	Survey sample	Number of surveyed patients	Basal level of gastrin	Level of gastrin after test meal			
				In 15 min	In 30 min	In 45 min	In 60 min
1	Control group	10	87,4±2,8	87,0±9,2	127,5±17,1 p_1<:0,05	122,4±16,5 p_1<:0,05	108,8±16,9
2	Patients with polyps before the surgery	16	182,3±37,0 p_2<0,5	227,0±54,9 p_2<0,5	281,6±37,0 p_1<:0,05 p_2<0,05	284,0±37,0 p_1<:0,05 p_2<0,05	258,0±32,0 p_1<:0,05 p_2<0,02
3	Patients with polyps within one year after the surgery	13	207,0±37,4 P2<0,05	326,8±40,0 p_2<0,05	337,0±28,5 p_1<:0,05 p_2<0,05	385,0±26,6 p_1<:0,05 p_2<0,05	423,0±41,0 p_1<:0,05 p_2<0,05

Note: p_1 – statistical significance, compared to baseline; p_2 – statistical significance, compared to control group.

Table 7.
Changes in gastrin concentration (pg/ml) in the blood of patients after gastric resection in response to the test meal

No.	Survey sample	Number of surveyed patients	Basal level of gastrin	Level of gastrin after test meal			
				In 15 min	In 30 min	In 45 min	In 60 min
1	Control group	10	87,4±2,8	37,0±9,2	127,5±17,1	122,4±16,5	108,3±16,9
2	Patients after gastric resection	3	47,0±9,2 p<0,05 1	47,7±2,5 p<0,05	45,3±4,3 p<0,05	48,7ұ5,1 p<0,05	60,0±9,9 p< 0,05

Table 8.
Mucosal gastrin in different parts of the stomach in patients with polyposis, in the polyp tissue (μg/g) and in the gastric juice of the patients (pg/ml)

Mucosal gastrin concentration (μg/g)		Concentration of gastrin in the tissue of gastric polyp ((μg/g)	Concentration of gastrin in the gastric juice (pg/ml)
in antrum	in fundus		
81.2±8.1	42.6±7.5	3.6±0.6	69.5±7.8

highest level of gastrin did not reach the basal level in healthy individuals at this moment (Table 7).

Thus, gastrectomy in patients with polyposis causes a sharp decline in the serum gastrin and no reaction to the test meal.

Our studies have shown that functional state of gastrin producing cells of the stomach, which determines the gastrinemia level in patients with polyposis, plays an important role in the pathogenesis of gastric polyposis. However, it could not base only on an assessment of the gastrin level in the blood of patients. It was necessary to determine the concentration of the hormone in the mucosa of different parts of the stomach, in the polyp tissue and in the gastric juice of the patients with polyps. Such a study could let to assess more adequately the role of gastrin in the pathogenesis of polyp formation. Therefore, we analyzed the content of gastrin in the mucosa, polyp tissue and gastric juice in 7 patients with antral (5) and fundic (2) polyps of the stomach. The results obtained are shown in the Table 8.

As it can be seen from the above data, the highest level of gastrin was observed in the antral mucosa, which amounted to 81.2+ 8.1 μg/g. At the same time, if to focus on the results obtained in determining the level of gastrin in the mucosa of healthy individuals, then the estimated indicator in these patients was almost twice higher than in healthy individuals.

Gastrin level was two times lower in the mucosa of fundic polyps than in the antral polyps. Due to lack of own information and literature data on the gastrin level in the fundic mucosa in healthy people, it was difficult to assess the significance of gastrin concentration in patients with fundic gland polyps.

Gastrin content in the polyp tissue appeared negligible compared with its content in the gastric mucosa and amounted to 3.6±0.6 μg/g.

Our results showed that the content of gastrin in gastric juice in patients with polyposis was slightly lower (69.5±7.8 pg/ml) than in healthy individuals which is amounted to185±28 pg/ml

Thus, an increase in the gastrin level in the gastric mucosa was noted in patients with gastric polyposis. It obviously provides a higher basal gastrin level in the blood of these patients without significant impact on the gastrin content in the gastric juice. Gastrin level in the polyp tissue was low and independent of the polyp localization.

There are various endocrine cells in the gastric epithelium that produce nearly all known peptide hormones. It is important to determine the amount of gastrin producing G-cells in the gastric mucosa, which can be done by immunohistochemistry methods [25-27]. Change in their number and staining intensity may indirectly indicate the gastrin level in the blood, which has a paracrine effect on nearby cells.

At the same time, there were large enough difficulties in interpreting the results of immunochemical studies. Thus, increasing the number of cells may be the result not only of their actual increase, but also can be caused by increased synthesis of the corresponding peptide or delay of its secretion.

But an immunohistochemical study of various types of endocrine cells and the relation between them can be used to determine the role of their peptide products in the origin and development of various diseases of the digestive system. The most interesting is the change of G-cells in patients with precancerous diseases of the stomach. Unfortunately, information about the G-cells and the concentration of immunoreactive gastrin in biopsy specimens of gastric mucosa in chronic gastritis and gastric polyposis is not enough.

The effect of neuro-humoral factors in the regulation of motor and secretory function of the stomach must be evaluated to provide each method of surgical treatment of gastric polyposis. It was, therefore, necessary to examine the quantitative and functional status of gastrin producing cells of the antral mucosa, as well as their relationship with the level of gastrin in the blood and the connection with gastric secretion in polyposis.

Table 9.
Basal level of gastrin in the blood and G-cells quantity in stomach mucosa of patients with gastric polyposis

No.	Survey sample	Number of surveyed patients	Basal level of gastrin in the blood (pg/ml)	G-cells quantity in stomach mucosa		
				Antrum	Stomach body	Polyp
1	Control group	10	87,4±2,8	293,0±27,0	0±0	-
2	Patients with gastric polyps	17	317,1±25,3	338,9±22,7 p>0,05	5,8±1,8 p<0,05	2,9±0,9

Gastrin level in the blood and tissues depends not only on the change of functional state of G-cells, but also on their mass in the gastric mucosa. The last one is very important to find in patients with gastric polyposis.

We counted G-cells in the mucosa of antrum and stomach body, as well as in the polyps' mucosa in 17 patients with polyposis (Table 9).

In the presence of severe basal hypergastrinemia in patients with gastric polyposis, the number of G-cells in 1 mm^2 of antral mucosa reached 338.9±22.7. This value is slightly higher than the indicator in apparently healthy individuals, which is equal to 293.0±27.0.

G-cell number was determined in the mucosa of stomach body in 7 patients. The number of G-cells in these patients was significantly lower than in the antrum. G-cells were not defined in this part of the stomach in the control group.

G-cells were found in the polyps' mucosa in only 12 of 17 patients, their number was equal to only 2.9±09.

Since the level of gastrin in the blood and tissues of the gastric mucosa, as it was shown by our study, depended on the location of polyps, therefore, the number of G-cells in the gastric mucosa was determined in patients with polyposis of antrum and stomach body (Table 10).

As it turned out, the high basal gastrin level was combined with a marked increase of G-cells in the gastric antral mucosa and reached 406.6±35.9 in patients with antral polyposis. The amount of G-cells in polyps' mucosa in these patients appeared 83 times lower than in other mucous sections of this part. Number of cells in the mucosa of stomach body amounted to 59±29 in patients with antral polyps.

In less pronounced hypergastrinemia, the number of G-cells in the stomach body in patients with gastric polyposis did not differ from that of healthy individuals and it was 1.85 times lower than in patients with antral polyposis. Level of G-cells in the polyps of stomach body mucosa in patients of this category did not differ from the indicator in the patients with antral polyposis. The number of these cells in polyps' mucosa was lower than in the rest part of the stomach body mucosa and the mucosa of antral polyps.

Thus, when antral polyposis, hypergastrinemia caused not only by increased functional activity of gastrin producing cells, but also by increasing their numbers in the antral mucosa. The number of G-cells was dramatically reduced in the mucosa of gastric polyps, especially in polyps of the gastric body. We can assume that hypergastrinemia, revealed in patients with polyposis of stomach body, is caused only by increased functional activity of gastrin producing cells.

Finally it should be noted that gastrin, having marked trophic effect in physiological conditions as well as in neoplastic processes [28,30], may participate in the formation of atrophic hyperplastic changes with focal hyperplasia in the mucosa, as it was evidenced by our findings. This pathology of mucosa appears due to the formation of the gastric polyps, and polyps are most often detected in the pyloric antrum of the stomach (63% of cases). This is confirmed by a higher concentration of gastrin in the serum of patients with multiple gastric polyps compared with those who has solitary polyps, and even more in comparison with healthy people.

According to some reports [23,31-35], a higher level of gastrin in the blood of patients with gastric carcinoma, compared to healthy individuals,

Table 10.
Basal level of gastrin in the blood and G-cells quantity in stomach mucosa of patients with gastric polyps of different localization

No.	Survey sample	Number of surveyed patients	Basal level of gastrin in the blood (pg/ml)	G-cells quantity in stomach mucosa		
				Antrum	Stomach body	Polyp
1	Control group	10	87,4±2,8	293,0±27,0	0±0	-
2	Patients with polyps of antrum	10	405,0±31,5 p_1<:0,05	406,6±35,9 p_1<:0,05	5,9±2,9 $p_{1<:}$0,05	4,9±1,5
3	Patients with polyps of stomach body	7	228,5±25,7 p_1<:0,05 p_2<0,05	220,5±27,3 p_1>0,05 p_2<0,05	5,5±1,6 p_1<:0,05 p_2 >0,05	1,0±0,4 p_2<0,05

Note: p_1 – statistical significance, compared to control group; p_2 – statistical significance, compared to patients with polyposis of antral part of the stomach.

indicates the role of gastrin in the pathogenesis of tumor development. Although in our studies, gastrinemia was less pronounced in patients with malignant polyps than in those with benign polyps. However, participation of gastrin in the process of polyp formation has no doubt because an increase in the size of the polyp accompanied by an increase in gastrinemia. This was confirmed by the assessment of gastrin concentration in the blood after test meal in patients with different duration of the disease in question: the highest gastrinemia appears in individuals suffering from gastric polyposis over three years.

Another proof of participation of gastrin in the gastric polyp formation is detectable maximum hypergastrinemia in polyps of pyloric antrum, i.e. in the areas subjected to the most frequent polyp formation.

Assessing the level of gastrin in the blood of patients can be used to predict the possible recurrence of polyp formation. This is confirmed by a more pronounced hypergastrinemia before the polypectomy in patients, who were diagnosed with a recurrence within one year after the surgery. This indicator can serve as an additional sign of polyp recurrence since gastrinemiya in recurrence is more than twice higher than that seen in patients without identified polyposis recurrence within one year after polypectomy.

Conclusion

Despite the fact, that polypectomy decreases the gastrin concentration in the blood (which indicates a decrease in the risk of the disease recurrence), yet gastric resection should be considered the most radical surgery for multiple polyps. After this surgery, even the test meal does not increase the level of gastrin and it stays equal to its basal level in healthy individuals.

Once again it should be noted that polyps are most frequently formed in the pyloric antrum that can be confirmed by a higher content of gastrin in the mucosa of this part compared to other areas of the stomach.

In conclusion, our findings suggest that polyp formation accompanied by an increased gastrin level in the blood of patients, has significant impact on the concentration of gastrin in gastric juice and influences the function of gastric acid formation in patients with polyps.

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