Clinical values of gastrin 17 and pepsinogen in gastric cancer and precancerous lesion screening.

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Abstract

Objective: This study aims to investigate the clinical significance of gastrin 17 and pepsinogen in gastric cancer and precancerous lesion screening.

Methods: We used ELISA to measure the levels of gastrin 17 and pepsinogen in serum from the medical examination population, which compared to endoscopic results. Then statistical analysis was performed.

Results: The classical method by testing pepsinogen (PG<70 μg/l and PGR<7) is highly specific in screening early gastric cancer and precancerous lesion, but with low sensitivity of 21.2%. Most of the population could be missed diagnosed as well as the positive predictive value is low. If we use pepsinogen combined with gastrin 17 for screening early gastric cancer and precancerous lesion, the screening positive predictive value can be improved while the specificity and sensitivity will not be changed at the same time. The disadvantage of this method is that the sensitivity is still very low. Therefore, most of the population will be missed diagnosed. If two of three indicators, PG I, PGR and G-17, is abnormal in screening early gastric cancer and precancerous lesion, the sensitivity increased from 21.2% to 79.9% while high specificity could also be kept at the same time.

Conclusions: Further examination of gastroscope for screening early gastric cancer or precancerous lesions is recommended, if two of PG I, PGR and G-17 are abnormal, making early diagnose and treatment of gastric cancer and precancerous lesions possible.

Introduction

Serological screening for gastric cancer, especially the pepsinogen (PG I and PG II and PGR) has been widely used in the detection of serological screening of gastric cancer and precancerous lesions. It has been included in the National Cancer Prevention and control program in Japan, South Korea, Finland, Norway and other countries [1-3]. Pepsinogen (PG) is an inactive precursor of pepsin. According to the biochemical and immunological characteristics, pepsin could be divided into PG I (PGA) and PG II (PGC) two subtypes. PG I was mainly secreted by the primary cells of the fundic glands and mucous neck cells, while PG II was not only secreted by the fundic glands, but also could be the gastric antrum and proximal duodenum Brunner gland secretion. PG, which is called "serological biopsy", is a valuable indicator of gastric mucosa secretion function. PG I and PGR (the value of PG I / PG II) are decreased in the patients with atrophic gastritis and gastric cancer. The diagnostic threshold can be different due to

the regional incidence of gastric cancer, types of gastric cancer and examination methods. In 2008, Asia-Pacific consensus guidelines on gastric cancer prevention, recommended threshold value is "PG I<70 g/l and PGR<3". Some domestic research suggested the application of radioimmunoassay with the threshold of "PG I<70 g/l and PGR<3", or ELISA method with the threshold of "PG I<70 g/l and PGR<7" for Chinese population [4-6].

Gastrin-17 (G-17) is one of the gastrointestinal hormones secreted by gastric antral G cells. The secretion of G-17 is mainly affected by intragastric pH value, G cell number and diet (protein is the best stimulus). It is a sensitive indicator of the secretory function of gastric antrum and plays important roles in the diagnosis and screening of atrophic gastritis and gastric cancer. Testing PG in serum combined with G-17 for distinguishing gastric cancer and other gastric diseases, which is more and more attractive for the researchers in screening gastric cancer [7-9]. Our research introduced quantitative

enzyme linked immunosorbent assay (ELISA) to detect the levels of serum pepsinogen and gastrin 17 in patients with different gastric diseases and further studied its diagnostic significance in early gastric cancer.

Materials and Methods

Materials

1300 samples of gastroenterology clinic patients were selected, which were collected in Hefei first people's Hospital from 2014 to 2016. All the patients were confirmed by gastroscopy and pathological examination, with no special medication history two weeks before detection. The acute upper digestive tract hemorrhage patients who should be treated immediately were excluded.

Method

3 ml fasting blood were taken to detect PG I, PG II and G-17 in serum. The segregated serum was frozen and stored in -20. The kit bought from Finland BIOHIT was used to perform the Quantitative ELISA assay.

Trial grouping

This study was divided into 4 groups: A, B, C, D. **Group A:** According to 2008 Asia-Pacific consensus guidelines on gastric cancer prevention, PG I<70 µg/L and PGR<7 were used as control group. **Group B:** one indicator among PG I and PGR, G-17 was abnormal. **Group C:** There were two abnormalities among PG I and PGR, G-17; **Group D:** all three of PG I and PGR, G-17 indicators were abnormal. There were 1300 samples of gastroenterology clinic patients. The crowd ratio in different group=samples in each group/1300×100%.

Note: Threshold: PG I>70 µg/l, PGR>7 and G-17: 1~15 pmol/l.

Results

According to gastroscopy and pathological analysis, these population were included in this study: 508 healthy controls, 428 *H. pylor* infected gastritis patients, 120 patients with ulcer, 98 patients with medium and severe atrophy gastritis, 66 patients with medium and severe intestinal metaplasia, 77 people with low-grade neoplasia, 3 people with high-grade neoplasia or gastric cancer in collected 1300 samples in Hefei

first people's Hospital. Severe atrophy gastritis, severe intestinal metaplasia and low-grade neoplasia were regarded as precancerous lesions. The levels of PG I, PG II, and G-17 in serum of different groups were shown in Table 1: The level of PG II and G-17 in the group with precancerous lesions was higher than that in the healthy group, while the level of G-17 was further increased in the early gastric cancer group. The level of PGR was significantly lower than the one in the healthy group, and it was further reduced in the early gastric cancer group.

Table 1. The levels of PG I, PG II, PGR and G-17 in different groups (mean ± SD).

	Healthy people (n=508)	Precancerous leisons (n=241)	Early gastric cancer (n=3)
PG I (µg/l)	98.1 ± 41.2	112.8 ± 38.6	94.0 ± 46.5
PGII (µg/l)	8.2 ± 6.1	13.4 ± 9.5*	22.4 ± 21.3*
PGR	14.8 ± 6.3	10.5 ± 5.1*	7.1 ± 6.4*
G-17 (pmol/l)	3.5 ± 5.8	12.4 ± 11.2*	16.5 ± 17.7*

*Compared with the healthy people, P<0.01

The screening results of early gastric cancer and precancerous lesions were shown in Table 2: In group A (PG<70 µg / l and PGR<7), there were 124 people accounting for 9.54% of the total samples, and the positive predictive value of the diagnosis for early gastric cancer and precancerous lesions was 31.3%. The specificity was 91.18%, and the sensitivity was 21.2%. In group B (one abnormal indicator in PG I and PGR, G-17), there were 104 people accounting for 8.1% of the total samples, and the positive predictive value of the diagnosis for early gastric cancer and precancerous lesions was 16.45%. The specificity was 59.1%, and the sensitivity was 91.2%. In group C (there were two abnormalities in PG I and PGR, G-17), there were 86 people accounting for 6.6% of the total samples, and the positive predictive value of the diagnosis for early gastric cancer and precancerous lesions was 32.5%. The specificity was 87.7%, and the sensitivity was 79.6%. In group D (all three PG I and PGR, G-17 indicators were abnormal), there were 46 people accounting for 3.5% of the total samples, and the positive predictive value of the diagnosis for early gastric cancer and precancerous lesions was 63.17%. The specificity was 91.9%, and the sensitivity was 21.2%.

Table 2. The comparison of different methods to diagnose early cancer and precancerous lesions.

	The positive predictive value	Sensitivity	Specificity	The crowd ratio
Group A (n= 124)	31.30%	21.20%	91.20%	9.50%
Group B (n= 104)	16.5%*	91.4%*	59.1%*	8.10%
Group C (n= 86)	32. 5%	79.6%*	87.70%	6.60%
Group D (n= 46)	63.2%*	21.20%	91.90%	3.50%

*Compared with group A, P<0.01

According to the results, it's found that the traditional pepsinogen (PG<70 µg/l and PGR<7) screening works well for early gastric cancer and precancerous lesion specificity. However, the sensitivity is very low (22.2%). Most of the population can be missed diagnosed and the positive predictive value is not high enough. If pepsinogen is used combined with gastrin 17 (Group D) for screening early gastric cancer and precancerous lesion, the screening positive predictive value could be greatly improved while specificity and sensitivity are maintained at the same time. The disadvantage is that the sensitivity is still very low. Most of the group will still be missed diagnosis. If there were two abnormal indicators in PG I, PGR and G-17 to screen early gastric cancer and precancerous lesion (Group C), the sensitivity increased from 21.2% to 79.85% while high specificity of the results was maintained at the same time.

Discussions

The concept of gastric function "serology test" is using the samples of serum to detect the secretions of gastric mucosal cells, such as enzymes, hormones and so on, then evaluate the functional status of gastric mucosa, the site of infection and lesion. The core examination indicators refer to the pepsinogen and gastrin-17. Gastric mucosal atrophy may lead to the downregulation of PG I. However, when one is infected with H.p or suffers from peptic ulcers, the expression of PG I will be up-regulated. The level of PG II will increase when infected with H.p, but it drops quickly after the eradication therapy. There was a positive correlation between the progressive decrease of PG I/ PG II (PGR) and the growth of gastric mucosal atrophy [10-12]. G-17 is a sensitive indicator for gastric function. The level of G-17 decreases in the patients with complete gastric atrophy (multifocal atrophy), while the level unusually increases or decreases in the patients with gastric cancer [13,14].

The method using PG I≤70 µg/l and PG I/PG II≤7.0 to screen early gastric cancer and precancerous lesion has been widely accepted worldwide. In the past, it was known that the disadvantage of this method was high crowd positive rate. But this might not be a real sign of early cancer and precancerous lesion. In this study, the results of testing 1300 samples from gastroenterology department showed that the method using PG I≤70 µg/l and PG I/PG II≤7.0 to screen early gastric cancer and precancerous lesion has a better specificity and the positive predictive value does not seem to be high. But the worst weakness is that the sensitivity of 22.2% is very low. Most of the patients will be missed diagnosed. So it's not applicable in China.

In this study, we used different groups which were divided by PG I, PGR and G-17 levels to screen early gastric cancer and precancerous lesion. We took advantage of one abnormal indicator, two abnormal indicators, and all three abnormal indicators to analysis the specificity, the sensitivity, and the

positive predictive value, respectively. It turned out that if pepsinogen was used combined with G-17 (Group D) in early gastric cancer and precancerous lesion screening, the screening positive predictive value could be greatly improved while maintaining specificity and sensitivity at the same time. The disadvantage was the low sensitivity. Most of the patients could still be missed diagnosed. If there were two abnormal indicators in PG I, PGR and G-17 in early gastric cancer and precancerous lesion screening (Group C), the sensitivity increased from 21.2% to 79.9% while maintaining the high specificity of the result at the same time. Therefore further endoscopy for early gastric cancer or precancerous lesions will be recommended, when at least two of three indicators (PG I, PGR and G-17) were unusual, making early diagnose and treatment of gastric cancer and precancerous lesions possible.

Conclusions

In a word, if pepsinogen was used combined with G-17 (Group D) in early gastric cancer and precancerous lesion screening, the screening positive predictive value could be greatly improved while maintaining specificity and sensitivity at the same time. Further examination of gastroscope for screening early gastric cancer or precancerous lesions is recommended, if two of PG I, PGR and G-17 are abnormal, making early diagnose and treatment of gastric cancer and precancerous lesions possible.

Conflict of Interest

None

Acknowledgement

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