Alterations of serum cholinesterase in patients with gastric cancer

Shan-Zhi Gu, Xin-Han Zhao, Ping Quan, Sheng-Bin Li, Bo-Rong Pan

AIM: To understand the correlation of serum cholinesterase (CHE) activity with gastric cancer and to assess their clinical significance.

METHODS: The velocity method was adopted to detect the activity of serum CHE in patients with gastric cancer and in patients with non-malignant tumor as controls.

RESULTS: The serum CHE activity in the treatment group was significantly lower than that in the control group with a very significant difference between the two groups (83.3 ± 113.1, \( \chi^2 = 0.0003 \)). Age was significantly associated with the incidence of gastric cancer.

CONCLUSION: Serum CHE activity has a close relation with the incidence of gastric cancer.

© 2005 The WJG Press and Elsevier Inc. All rights reserved.

Keywords: Cholinesterase activity; Gastric cancer

Gu SZ, Zhao KH, Quan P, Li SB, Pan BR. Alterations of serum cholinesterase in patients with gastric cancer. World J Gastroenterol 2005; 11(29): 4604-4606

http://www.wjgnet.com/1007-9327/11/4604.asp

INTRODUCTION

CHE is a type of glycoprotein, existing in vivo in multiple forms of isozyme. The decrease of serum CHE activity is often observed in patients with organic phosphorus poisoning and damage of parenchymal cells. In clinical practice, we have discovered that there is a decrease of serum CHE activity in patients with gastric cancer. This study aimed to detect the serum CHE activity in patients with gastric cancer, and to observe the correlation of serum CHE activity with the incidence of gastric cancer.

MATERIALS AND METHODS

Subjects

The treatment group included 81 patients (61 males and 20 females aged 30-80 years with an average age of 58.8 ± 12.0 years) with gastric cancer hospitalized from January 1998 to June 2002. The disease was confirmed by gastroscopic examination and/or pathological examination. Clinical and pathologic classifications followed the General

Statistical analysis

All the data were fed into a computer. The SPSS10.0 software package was employed for analysis and processing. The chi-square test was conducted. With the CHE difference between the gastric cancer group and the control group, \( F \) test was adopted. For the purpose of reviewing the relation between sex, age and CHE, the multi-factor regression analysis was conducted with respect to the above three factors. The statistical significance level was defined as \(<0.05\) with two-sided detection.

RESULTS

Serum CHE activity in gastric cancer

The age of the gastric cancer group and control group both expressed abnormal distribution with the mid-value being 60.5 and 61.5 years respectively. The \( \chi^2 \) was performed (\( \chi^2 = 22.265, P = 0.0002 \)), suggesting that the age distribution in the two groups was overbalanced. The result from the \( \chi^2 \) detection for the sex distribution was \( \chi^2 = 25.138 \) and \( P = 0.0003 \), showing that the sex distribution in the two groups was out of balance as well. Tables 1 and 2 respectively show the co-variance analysis results.

The age and nature of gastric cancer patients had a linear correlation with the CHE level (\( r = 0.8, P = 0.031 \)), suggesting that the difference in CHE level between gastric cancer patients and controls was significant (\( F = 79.069, \)
The serum CHE level of gastric cancer patients (81.6±31.5 μkat/L) was significantly lower than that in the control group (114.8±30.8 μkat/L), indicating that age was also an important factor affecting the incidence of gastric cancer ($F = 18.481$, $P = 0.0003$).

With the age distribution, $\chi^2$ was performed ($\chi^2 = 5.281$, $P = 0.383$), showing that the age was evenly distributed. In gastric cancer patients and controls, CHE had a normal distribution and the variance was in order. Therefore, single-factor variance analysis could be made. The average value, standard deviation and single-factor variance are listed in Tables 1 and 2.

The difference in CHE levels of the two groups was significant ($F = 29.884$, $P = 0.0006$). The serum CHE level in gastric cancer patients (85.0±34.5 μkat/L) was significantly lower than that in the control group (114.8±30.8 μkat/L), Figure 1).

### Table 1 Serum CHE distribution in gastric cancer patients (μkat/L)

| Sex Group       | n  | Average (μkat/L) | Standard error | Lower limit | Upper limit |
|-----------------|----|-----------------|----------------|-------------|-------------|
| Male Gastric cancer | 61 | 81.6            | 31.5           | 77.2        | 86.1        |
| Male Control    | 44 | 114.8           | 30.8           | 108.9       | 120.6       |
| Female Gastric cancer | 20 | 85.0            | 34.5           | 76.2        | 93.9        |
| Female Control  | 36 | 111.4           | 25.8           | 106.2       | 116.7       |

### Table 2 Covariance analysis results of CHE in gastric cancer patients and controls

| Sex Group       | Df | Mean square root | $F$   | $P$   |
|-----------------|----|-----------------|-------|-------|
| Male Within group | 1  | 849.712 857.157 | 256.718 | 0.000 |
| Age (yr)        | 4  | 616.906 471    | 18.481 | 0.000 |
| Between groups  | 1  | 261.705 135.862| 79.069 | 0.000 |
| Error           | 79 | 330.902 711    |       |       |
| Total           | 85 |                 |       |       |
| Female Within group | 1  | 93.519 230.733 | 29.884 | 0.000 |
| Age (yr)        | 3  | 732.546 506    | 16.372 | 0.000 |
| Between groups  | 1  | 3329.425 453   | 54.081 | 0.000 |
| Error           | 61 | 430 763 233    |       |       |
| Total           | 66 |                 |       |       |

### Multi-factor logistic regressive analysis

The three variables (sex, age, and CHE) were put into the Logistic model. After being fitted with the backward method, the final model was expressed (Table 3). The factors put into the model were only sex and CHE. The adaptive regressive equation was $P (1) = 1/[1+e^{-0.129+2.542X1+1.006X3}]$ or CHE = 12.701. Therefore, after removing the influence of other factors, the reduction of the CHE activity was a dangerous factor for gastric cancer.

### Table 3 The Logistic analysis of sex and CHE

| Variable | B   | SE  | Wald | df  | Sig. | Exp (B) | 95.0% CI for Exp (B) |
|----------|-----|-----|------|-----|------|---------|----------------------|
|          |     |     |      |     |      |         | Lower               | Upper               |
| Sex      | 1.066 | 0.234 | 20.825 | 1  | 0.000 | 2.905   | 1.837                | 4.592               |
| CHE      | 2.542 | 0.313 | 66.131 | 1  | 0.000 | 12.701  | 6.883                | 24.435              |
| Constant | 16.129 | 0.697 | 77.303 | 1  | 0.000 | 6.883   | 4.592                | 10.000              |

### DISCUSSION

Cholinesterase can be divided into true cholinesterase (acetylcholinesterase, ACHE) and pseudocholinesterase (PCHE). ACHE exists mainly in the vesicles of cholinergic nerve peripheral synapse where there is a comparatively large amount of ACHE in the folding of the terminal synapse back membranes. It also exists in the cholinergic neurons, red cells, sera, livers, kidneys, intestines, white mass of brain, etc. In the activity center on the surface of the molecules of CHE protein, there are two places to be combined with acetycholine, namely the anion place with negative charges and the place with ester decomposition. The place with ester decomposition has an acidic action point formed by serine hydroxide and an alkaline action point formed by histidine imidazole ring. They are combined by means of hydrogen bonds. PCHE reduces when the parenchymal cells are damaged, as the liver synthesizes PCHE. Organophosphorus toxicant is a powerful inhibitor of ACHE and PCHE. Measuring serum CHE activity can help diagnose organophosphorus poisoning and evaluate the condition after recovery. The results of this experiment indicate that human serum CHE activity has a significant correlation with gastric cancer.

Anic et al. discovered that the serum CHE activity in hepatitis B patients is relatively low. Khan et al. detected serum CHE and lactic dehydrogenase (LDH) activity in 40 cases of mammary cancer patients, 25 cases of benign tumor patients and 30 cases of healthy persons, and found that there is a significant difference in serum CHE activity between malignant and benign tumor patients.

If the ratio between CHE activity and serum CHE activity is less than 0.42, the malignant source should be considered. A number of studies have been conducted on the relation between serum CHE activity and acute leukemia and cervical cancer.

Among the 81 cases of gastric cancer in the present study, there were 39 cases (48.2%) whose serum CHE activity was less than 75.0 μkat/L. Among the 80 cases of...
controls, there were only five cases (6.3%) whose serum CHE activity was less than 50.0 μkat/L. In the gastric cancer group, there were 14 cases whose serum CHE activity was less than 75.0 μkat/L. However, in the control group, there were no such cases. The results suggest that if a patient with gastric pathological changes whose serum CHE activity was less than 50.0 μkat/L, sharp vigilance on the existence of gastric cancer should be maintained after organophosphorous poisoning and damages of parenchymal cells, etc., are excluded.

In conclusion, the determination of serum CHE activity is a rapid, simple, convenient, inexpensive and reliable method to diagnose gastric cancer. Its exact mechanism remains to be further explored.

REFERENCES

1. Fukimoto H, Tennis M, Locascio JJ, Hyman BT, Growdon JH, Irizarry MC. Age but not diagnosis is the main predictor of plasma amyloid beta-protein levels. Arch Neurol 2003; 60: 958-964
2. Luo ZB, Xu CP, Wang D, Wang G, Xiao SQ, Zhu GY, Fang DC. Immunotherapy of dendritic cell and its exosomes transfected with mRNA of gastric cancer cells in tumor-carried mice. World Chin J Digestol 2004; 12: 9-12
3. Valbonesi P, Sartor G, Fabbri E. Characterization of cholinesterase activity in three bivalves inhabiting the North Adriatic sea and their possible use as sentinel organisms for biosurveillance programmes. Sci Total Environ 2003; 312: 79-88
4. Pelizzi N, Puccini P, Riccardi B, Acerbi D, Catinella S. Characterization of Ganstigmine metabolites in hepatocytes by liquid chromatography. Rapid Commun Mass Spectrom 2003; 17: 1691-1698
5. Sagi Y, Weinstock M, Youdim MB. Attenuation of MPTP-induced dopaminergic neurotoxicity by TV3326, a cholinesterase-monoamine oxidase inhibitor. J Neurochem 2003; 86: 290-297
6. Luo ZB, Xu CP, Zhu GY, Zhang PB, Guo CH, Luo YH, Fang DC, Luo CJ. Immunotherapy of dendritic cells transfected with mRNA of gastric cancer cells in carried-tumor mice. World Chin J Digestol 2004; 12: 13-15
7. Marco JL, Carreiras MC. Recent developments in the synthesis of acetylcholinesterase inhibitors. Mini Rev Med Chem 2003; 3: 518-524
8. Pascuzzi RM. The edrophonium test. Semin Neurol 2003; 23: 83-88
9. Xin SJ, Zhang LX, Zhu CL, Hu JH, Duan ZX, You SL, Hu LP, Zou ZS, Mao YL, Huangpu YS. Correlation of clinical features with pathology in chronic viral hepatitis. Zhonghua Shi Yan He Linchuang Bingdu Xue Zhi 2003; 17: 88-90
10. Pepin JL, Myerissiotis S, Ceulemans S. Prevention of dementia: is it possible? Rev Med Liege 2003; 58: 220-224
11. Androne AS, Hryniewicz K, Goldsmith R, Arwoody A, Katz SD. Acetylcholinesterase inhibition with pyridostigmine improves heart rate recovery after maximal exercise in patients with chronic heart failure. Heart 2003; 89: 854-858
12. Migliaccio-Walle K, Getios D, Caro JH, Ishak KJ, O’Brien JA, Papadopoulos G. AHEAD Study Group. Economic evaluation of galantamine in the treatment of mild to moderate Alzheimer’s disease in the United States. Clin Ther 2003; 25: 1806-1825
13. Grossberg G, Irwin P, Satlin A, Mesenbrink P, Spiegel R. Rivastigmine in Alzheimer disease: efficacy over two years.