PO Box 2345, Beijing 100023, China
www.wjgnet.com
wjg@wjgnet.com

ELSEVIER

World J Gastroenterol 2005;11(29):4604-4606
World Journal of Gastroenterology ISSN 1007-9327

• *BRIEF REPORTS* •

Alterations of serum cholinesterase in patients with gastric cancer

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

Shan-Zhi Gu, Xin-Han Zhao, Ping Quan, Sheng-Bin Li, Key Laboratory of Environment and Genes Related to Diseases of Ministry of Education , Medical College of Xi'an Jiaotong University, Xi'an 710061, Shaanxi Province, China
Bo-Rong Pan, Department of Oncology, Xijing Hospital, Fourth Military Medical University, Xi'an 710032, Shaanxi Province, China
Co-first-authors: Shan-Zhi Gu and Xin-Han Zhao
Correspondence to: Xin-Han Zhao, Key Laboratory of Environment and Genes Related to Diseases of Ministry of Education, Department of Medical Oncology, First Hospital of Xi'an Jiaotong University, Xi'an 710061, Shaanxi Province, China. zhxinhan@pub.xaonline.com
Telephone: +86-29-85324136 Fax:+86-29-82655472
Received: 2004-10-09 Accepted: 2004-11-26

Abstract

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, $P = 0.0003$). Age was significantly associated with the incidence of gastric caner.

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

Key words: Cholinesterase activity; Gastric cancer

Gu SZ, Zhao XH, 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[1-4], existing *in vivo* in multiple forms of isozyme[5-7]. The decrease of serum CHE activity is often observed in patients with organic phosphorus poisoning[8] and damage of parenchymal cells[9-12]. 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 Rules for Gastric Cancer Study in Surgery and Pathology in Japan. The control group included 80 patients (44 males and 36 females) with non-malignant tumor hospitalized during the same period. Their age ranged 26-86 years with an average age of 57.7±15.3 years. Patients with organic phosphorus poisoning or damage of parenchymal cells were excluded.

Methods

All the patients were fasted for more than 12 h, then venous blood was taken. After centrifugation, serum was subjected to detection on the same day. Serum CHE activity was measured by the velocity method with Hitachi 7170 full automatic biochemical instrument and Hitachi 7170 special reagent. The normal reference value was 75-217 μkat/L.

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 χ^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 χ^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 ($F = 79.069$,

$P = 0.0004$). 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, χ^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 (111.4±25.8 μkat/L, Figure 1).

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

Sex	Group	*n*	Average	Standard error	95%CI	
					Lower limit	Upper limit
Male	Gastric cancer	61	81.6	31.5	77.2	86.1
	Control	44	114.8	30.8	108.9	120.6
Female	Gastric cancer	20	85.0	34.5	76.2	93.9
	Control	36	111.4	25.8	106.2	116.7

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

Sex	Variation source	Df	Mean square root	*F*	*P*
Male	Within group	1	849 712 857.157	256.718	0.000
	Age (yr)	4	6 116 906.471	18.481	0.000
	Between groups	1	261 709 135.862	79.069	0.000
	Error	79	3 309 902.711		
	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	3 129 425.453	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.

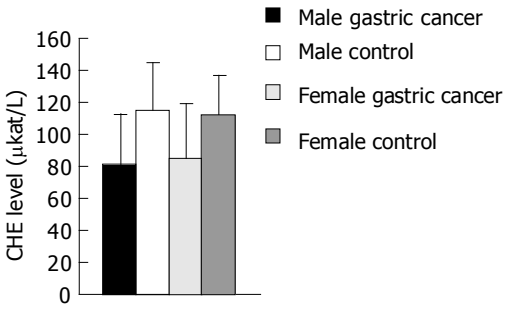

Figure 1 Different CHE levels in gastric cancer patients.

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[13,14], red cells[15], sera[16], livers[17], kidneys[18], intestines, white mass of brain[19], *etc*. In the activity center on the surface of the molecules of CHE protein, there are two places to be combined with acetylcholine, 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[20-22]. Organophosphorus toxicant is a powerful inhibitor of ACHE and PCHE [23-26]. 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*[27] discovered that the serum CHE activity in hepatitis B patients is relatively low. Khan *et al*[28] 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[29]. A number of studies have been conducted on the relation between serum CHE activity and acute leukemia and cervical cancer[30,31].

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

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	0.002		

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 is 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 **Fukumoto 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 cells andits exosomes transfected with mRNA of gastric cancer cells in tumor-carriedmice. *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 low- and high-resolution mass spectrometry coupled with 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 acetylcholineste- rase 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 XZ, You SL, Hu LP, Zou ZS, Mao YL, Huangpu YS. Correlation of clinical features with pathology in chronic viral hepatitis. *Zhonghua Shiyan He Linchuang Bingduxue Zazhi* 2003; **17**: 88-90

10 **Pepin JL,** Myressiotis S, Ceulemans S. Prevention of dementia: is it possible? *Rev Med Liege* 2003; **58**: 220-224

11 **Androne AS,** Hryniewicz K, Goldsmith R, Arwady 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,** Getsios D, Caro JJ, 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. *Am J Geriatr Psychiatry* 2004; **12**: 420-431

14 **Loewenstein DA,** Acevedo A, Czaja SJ, Duara R. Cognitive rehabilitation of mildly impaired Alzheimer disease patients on cholinesterase inhibitors. *Am J Geriatr Psychiatry* 2004; **12**: 395-402

15 **Darvesh S,** Arora RC, Martin E, Magee D, Hopkins DA, Armour JA. Cholinesterase inhibitors modify the activity of intrinsic cardiac neurons. *Exp Neurol* 2004; **188**: 461-470

16 **Zdrazilova P,** Stepankova S, Komers K, Ventura K, Cegan A. Half-inhibition concentrations of new cholinesterase inhibitors. *Z Naturforsch* 2004; **59**: 293-296

17 **Van Dyck CH.** Understanding the latest advances in pharmacologic interventions for Alzheimer's disease. *CNS Spectr* 2004; **9**(7 Supp 5): 24-28

18 **Eskenazi B,** Harley K, Bradman A, Weltzien E, Jewell NP, Barr DB, Furlong CE, Holland NT. Association of in utero organophosphate pesticide exposure and fetal growth and length of gestation in an agricultural population. *Environ Health Perspect* 2004; **112**: 1116-1124

19 **Arai H.** Current therapies in dementia. *Nippon Ronen Igakkai Zasshi* 2004; **41**: 310-313

20 **Kurz A,** Van Baelen B. Ginkgo biloba Compared with Cholinesterase Inhibitors in the Treatment of Dementia: A Review Based on Meta-Analyses by the Cochrane Collaboration. *Dement Geriatr Cogn Disord* 2004; **18**: 217-226

21 **Fu G**, Wang GB, Lu XM, Huang QX, Zheng H. MAPK signal transduction and apoptosisof human gastric carcinoma cells induced by liposomes of survivin antisense oligonucleotide. *World Chin J Digestol* 2004; **12**: 1034-1039

22 **Khang P,** Weintraub N, Espinoza RT. The Use, Benefits, and Costs of Cholinesterase Inhibitors for Alzheimer's Dementia in Long-Term Care. Are the Data Relevant and Available? *J Am Med Dir Assoc* 2004; **5**: 249-255

23 **Sormani MP,** Oneto R, Bruno B, Fiorone M, Lamparelli T, Gualandi F, Raiola AM, Dominietto A, Van Lint MT, Frassoni F, Bruzzi P, Bacigalupo A. A revised day +7 predictive score for transplant-related mortality: serum cholinesterase, total protein, blood urea nitrogen, gamma glutamyl transferase, donor type and cell dose. *Bone Marrow Transplant* 2003; **32**: 205-211

24 **Lu CJ,** Tune LE. Chronic exposure to anticholinergic medications adversely affects the course of Alzheimer disease. *Am J Geriatr Psychiatry* 2003; **11**: 458-461

25 **Pang YP,** Kollmeyer TM, Hong F, Lee JC, Hammond PI, Haugabouk SP, Brimijoin S. Rational design of alkylene-linked bis-pyridiniumaldoximes as improved acetylcholinesterase reactivators. *Chem Biol* 2003; **10**: 491-502

26 **Tariot PN,** Jakimovich L. Donepezil use for advanced Alzheimer's disease-a case study from a long-term care facility. *Am Med Dir Assoc* 2003; **4**: 216-219

27 **Anic K,** Ivandic A, Volaric M, Peric L, Getto L, Bacun T. Cholinesterase in the differential diagnosis of parenchymal and obstructive icterus and in the differentiation between malignant and benign obstruction. *Wien Med Wochenschr* 1999; **149**: 355-358

28 **Khan SA,** Stewart AK, Morrow M. Does aggressive local therapy improve survival in metastatic breast cancer? *Surgery* 2002; **132**: 620-626

29 **Cabello G,** Juarranz A, Botella LM, Calaf GM. Organophosphorous pesticides in breast cancer progression. *J Submicrosc Cytol Pathol* 2003; **35**: 1-9

30 **Yi Z,** Wang Z, Li H, Liu M. Inhibitory effect of tellimagrandin I on chemically induced differentiation of human leukemia K562 cells. *Toxicol Lett* 2004; **147**: 109-119

31 **Bradamante V,** Smigovec E, Bukovic D, Geber J, Matanic D. Plasma cholinesterase activity in patients with uterine cervical cancer during radiotherapy. *Coll Antropol* 2000; **24**: 373-380

Science Editor Wang XL and Guo SY **Language Editor** Elsevier HK