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Study of sEGF level in chronic atrophic gastritis with either Chinese traditional medicine or western medicine

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Abstract: This study was aimed to investigate the level of sEGF in CAG with different therapies of either Chinese traditional medicine or western medicine. Patients were divided into spleen-reinforcing Ⅰ, spleen-reinforcing Ⅱ, dampness-resolving and western medicine group by Differentiation Syndrome. Healthy volunteers acted as controls. The sEGF was investigated before and after treatment. The level of sEGF in CAG was higher than that in control group($P < 0.01$). In patients of spleen-reinforcing Ⅰ group and spleen-reinforcing Ⅱ group, the symptoms and pathological manifestations were improved dramatically ($P < 0.01$) and sEGF dropped markedly after treatment($P < 0.01$ and $P < 0.05$). The level of sEGF in the dampness-resolving group increased after treatment ($P < 0.05$). But the level of sEGF in the western-medicine group dropped a little after treatment ($P > 0.05$). The inflammation of gastric mucosa may cause the elevation of sEGF in CAG reflectively. After being effectively treated with Chinese traditional medicine, the symptoms of CAG improved simultaneously with the return of sEGF. SEGF is a sensitive index to prognosis of CAG.

Key words: Epidermal growth factor (EGF), Chronic atrophic gastritis (CAG), Chinese traditional medicine
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INTRODUCTION

The WHO in 1978 considered chronic atrophic gastritis (CAG) to be a precancerous disease of gastric carcinoma. The morbidity of CAG is high in China, and about 8% develop gastric cancer in 10-20 years(Chen et al., 1996). CAG requires effective clinical treatment to reverse its progress. However, the standard plan of treatment and the objective index of evaluation after treatment are not well understood. Previous studies indicated that EGF is high in CAG and possibly plays a role in its development (Si et al., 1998; Land et al., 1983). There are only limited studies on EGF in CAG. Is it possible to prognosis CAG by changes in EGF levels? What is the effect of Chinese traditional medicine on EGF level in CAG? To date these question are still unanswered.

This study investigates the the level of EGF in CAG patients treated with different Chinese traditional medicines or with western medicine.

METHODS

Experiment group: 70 cases averaging 50.91 ± 13.47 years old. All subjects were GI clinic patients diagnosed by gastroscopy and biopsy as having CAG. Diseases of salivary gland, small intestine, pancreases, kidney and liver cirrhosis or cancer were excluded.

Control group: 37 subjects averaging 45.08 ± 15.03 years old, were GI clinic outpatients diagnosed by gastroscopy and biopsy as having "roughly normal mucosa" and no other organic disease was detected at the same time.

Patients who had CAG were divided into

three groups (based on differentiation of symptoms and signs of traditional Chinese medicine) given spleen-reinforcing, dampness resolving and western medicine, respectively. The sEGF's level before and after treatment were compared (Chen et al., 1996). Spleen-reinforcing group of 30 patients were divided into spleen-reinforcing I, spleen-reinforcing II by different treatments according to the indication of dysfunction of the spleen. Spleen-reinforcing I patients treated by replenishing qi were stronger than those in the other group The medicinal ingredients used were dangshen, astragalus, fuling, bighead atractylodes rhizoue, Chinese yam(as main ingredients). The indications were moderate to severe dysfunction of the spleen, tongue showing no abnormal changes, no stagnation of the liver-qi, indigestion, disturbance of the spleen-yang due to dampness, exopathogen, etc. The other group took fuling, big head atractylides rhizoue, and Chinese yam as main medicines. Indications: minor dysfunction of the spleen or accompanied with stagnation of the liver qi, indigestion disturbance of the spleen-yang due to dampness. Dampness-resolving group (Si et al., 1998): 15 patients treated with the treatment of dampness-resolving. The ingredients of medicines included atractylodes, rhizome, big head atractylodes rhizome, pinellia tuber, magnolia bark, amomum fruit. Western medicine group(Land et al., 1983): 24 patients treated with folic acid 5 mg and vitamin E 100 mg, both for 3 times a day. The course of treatment was three months.

EGF measurement: The examined patients' sEGF before level and after the treatment were measured by RIA. The reagents were supplied by Beijing North Biological Technology Research Company. Three ml of vein blood drawn at 8 Am before breakfast were preserved at -20 ℃, and after subsequent incubation, was mixed with reagent (^{125}I – hEGF) and antibody, and incubated again at 4 ℃ for 24 hours, and then mixed in 500 μL separating agent at room temperature for 15' and then centrifuged(15 min at room temperature, 3000 r/min × 15 min) and calculated with γ counter.

Gastroscopic reexaminations and biopsy were carried out after the course of treatment.

Criteria of treatment efficiency: The symptoms were ranked according to the medical principles of clinical trial drafted by the Ministry of Health. Asymptomatic: 0 point, occasionally occurs: 1 point; usually happens but can be tolerated: 2 points; persistent and intolerable: 3 points. Pathological changes were: minor, peptic glands decreased to less than 1/3 of normal: moderate; peptic glands decreased to about 1/2 of normal : severe; left peptic glands less than1/3 of normal: three grades.

Statistical methods: sEGF was presented as $X \pm SD$ and confirmed by t test. The efficiency of treatment was rated by %. Team comparison was proven by adjust χ^2 test.

RESULTS

Before treatment the levels of sEGF in every CAG group were all-higher than the control group's ($P < 0.01$). In the spleen-reinforcing team (Ⅰ and Ⅱ), after taking the Chinese traditional medicine for spleen-reinforcing, there was a significant decrease in the sEGF ($P < 0.01$ and 0.05). After treatment with Chinese medicine for dampness-resolving sEGF did not fall but increased ($P < 0.05$). Those treated with western medicine showed a drop in sEGF, which was not statistically significant ($P > 0.05$) (Table 1).

Symptoms relieving means symptoms rank dropped more than 50%. Pathological improvement refers to favorable pathological change of more than one grade. The Chinese medicines for spleen-reinforcing for CAG were beneficial; and the effective rate of modifying of symptom and pathology were all much higher than those of the western medicine group and dampness-resolving group. Though the clinical symptoms in the dampness-resolving group were improved, the pathological improvement was not significant. In the western-medicine group, they were both not significant(Table 2).

Table 1 sEGF level in each group before and after treatment

	n	EGF before treatment ($\mu g/L$)	EGF after treatment (ug/L)	P value
Spleen-reinforcing Ⅰ	11	$4.24 \pm 1.24^{*}$	2.59 ± 0.87	< 0.01
Spleen-reinforcing Ⅱ	19	$3.33 \pm 0.99^{*}$	2.46 ± 0.77	< 0.05
Dampness-resolving	15	$3.34 \pm 1.11^{*}$	4.03 ± 0.97	< 0.05
Western-medicine	24	$3.55 \pm 0.82^{*}$	2.92 ± 0.92	> 0.05
Control-team	37	1.77 ± 0.61		

* Compared with the control team $P < 0.01$

Table 2 Comparison of symptom improvement and pathological improvement

	Case	Effective rate of symptom improv.	Effective rate of pathological improve.
Spleen-reinforcing	30	26(87%)*	24(80%)**
Dampness-resolving	15	12(80%)*	5(33%)Δ
Western-medicine	25	10(40%)	12(48%)Δ

* Compared with western-medicine group $P < 0.01$; * * Compared with western-medicine and dampness-resolving $P < 0.01$; Δ Comparison between western-medicine and dampness-resolving.

DISCUSSION

EGF is a polypeptide composed of 53 amino acid residues, mainly secreted by the submaxillary gland, pancreas and intestine, and can induce acidification of tyrosine residue in protein. It also promotes differentiating and proliferating of cells, stimulates the syntheses of mRNA, DNA and protein in epithelial cells, promotes the differentiation and proliferation of mucosa, enhances the blood supply of the mucosa and secretion of mucus and bicarbonate, inhibits the secretion of Hcl and intrinsic factor, activates omithine decarboxylase, and facilitates the regeneration of the mucosa in the gastro-intestinal tract (Elliott et al., 2000).

The increase of sEGF usually indicates inflammatory stimulation to epithelial tissue and self-secretion of epithelial carcinoma. Some drugs, as protective agent of gastric mucus can also promote the secretion of sEGF (Tarnawski et al., 1998). When there is inflammation of the gastric mucusa, EGF can stimulate the proliferation of mucus cells and facilitate healing. It had been reported that the sEGF in CAG patients was higher than that in healthy people(Si et al., 1998; Zhang et al., 1998). This study showed that inflammatory stimulation increases secretion of endogenous EGF and promotes resistance to all kinds of inflammatory factors by the renovation and proliferation of gastric mucosa. It was found in recent years that EGF not only regulated the growth and differentiation of normal cells but also played an important role in the course of malignant changes(Land et al., 1983). EGF can induce normal cells to represent the phenotype of transfer cell, let the cell-density related inhibitory activity die out, and enhance the metabolism to promote the carcinogenesis by some virus and chemical substance (Takekura et al., 1991), inhibit the function of the immune-system and induce the expression of the c-onc gene, c-fos and c-myc(Kanagihara et al., 1993). So a long period of drugs administration can promote the release of endogenous EGF or enhance the expression of EGFR, such as CBS, sucralfate, which make it of doubtful value for the treatment of CAG(Tarnawski et al., 1995; Piotrowski et al., 1993). This study proved again that CAG patients had increased sEGF, whose level fell quickly after treatment. It reflected that the increase of sEGF in CAG was probably induced by the inflammatory reaction, and sEGF level fell after the CAG improved. Our study showed that EGF was the sensitive criterion for evaluation the course of CAG in patients. On the other hand, we could use that among different plans for medicinal treatment, using Chinese medicine to reinforce the spleen had greater clinical efficiency based on correct differentiation, accompanied by decreasings the level of sEGF. These favorable changes were greater than

those of the western-medicine group. The use of dangshen, astragalus, fuling, bighead atractylodes rhizoue, and Chinese yam (as main ingredient) by the spleen-reinforcing Ⅰ had strong effect on replenishing qi. On the other hand, the spleen-reinforcing Ⅱ group used fuling, big head atractylides rhizoue, and Chinese yam (as main medicine). Although the difference in sEGF between the two groups was not significant, the difference before and after treatment in the spleen-reinforcing Ⅰ group was higher than that of the spleen-reinforcing Ⅱ. So as far as the treatment with CAG and lowering sEGF, spleen-reinforcing Ⅰ is better than spleen-reinforcing Ⅱ group. But for dampness-resolving for the treatment of CAG, although symptoms were improved after treatment, the pathological improvement was not significant; sEGF showed a reverse increase. It was concluded that the dampness-resolving approach was not ideally good for CAG, so spleen-reinforcing should be continued after dampness-resolving therapy.

In this study we tried using nonmucosa-protective agents folic acid and Vit E to treat CAG. But both clinical and pathological improvement were poor and the fall in sEGF was not significant. So considering EGF as monitoring criteria for CAG treatment, it is better not to select mucosa-protective agents to decrease the level of sEGF. Chinese traditional medicine can be chosen. If there are no accompanying symptoms, such as stagnation of the liver indigestion, disturbance of the spleen yang due to dampness, exopathogen, etc., reinforcing spleen should be the main approach. Symptoms accompanying CAG should be dealt with first, and then be followed up by rehabitating the spleen. On clinical grounds if the disturbance of the dampness to spleen is apparent, resolving dampness should be followed up with reinforcing the spleen. By doing that, prognosis of CAG was appearing to be improved.

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