

Treatment of postoperative gastric cancer with the Fuzheng Huoxue anticancer prescription

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Author contributions: All authors contributed equally to the work.

Original title: *China National Journal of New Gastroenterology* (1995-1997) renamed *World Journal of Gastroenterology* (1998-)

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Received: December 15, 1996

Revised: January 26, 1997

Accepted: February 5, 1997

Published online: September 15, 1997

Abstract

AIM: To study effects of the Fuzheng Huoxue anticancer prescription (Traditional Chinese Medicine) in treatment of gastric cancer.

METHODS: Sixty-nine patients with histologically confirmed mid- or late-stage gastric cancer were assigned to two groups. The treatment group included 35 cases (26 males and 9 females; 2 patients aged 33-40 years, 18 patients aged 41-60 years, and 15 patients aged 61-75 years; mean group age = 58.4 years). The control group included 34 cases (23 males and 11 females; 4 patients aged 33-40 years, 16 patients aged 41-60 years, and 14 patients aged 61-75 years; mean group age = 56.8 years). The two groups were not significantly different in sex, age, their clinical and pathological stages of disease or operation mode. The two groups of patients were given similar treatments; however, patients in the treatment group were given the Fuzheng Huoxue anticancer prescription. In animal studies, SGC-7901 gastric cancers cells were inoculated into the backs of 30 nude mice under sterile conditions. After inoculation, the nude mice were randomly allocated to a control group, a traditional Chinese medicine group, and a chemotherapy group ($n = 10$ mice per group). The total weight of the 10 mice in each group was similar. Each nude mouse in the control group received 0.5 mL of saline solution each day. Mice in the traditional Chinese medicine group received 0.5 mL of the Fuzheng Huoxue anticancer prescription (containing 1.5 g crude drug) each day, while mice in the chemotherapy group were

intraperitoneally injected with 1 mg of 5-Fu once a week for 8 wk.

RESULTS: Prior to treatment, the mean OKT8 percentage among gastric patients in the treatment group was $45.94\% \pm 8.45\%$, the mean OKT4/OKT8 ratio was 0.89 ± 0.19 , the mean AT-III concentration was 29.9 ± 7.9 mg/dL, the mean Fa value was $50.4\% \pm 24.4\%$, and the mean β -TG concentration was 91.0 ± 25.9 ng/dL. Prior to treatment, the mean percentage of OKT8 cells among patients in the control group was $49.21\% \pm 6.60\%$, the OKT4/OKT8 ratio was 0.94 ± 0.20 , the AT-III concentration was 32.3 ± 7.2 mg/dL, the mean Fa value was $57.3\% \pm 24.6\%$, and the mean β -TG concentration was 87.5 ± 34.2 ng/dL. After treatment, the mean OKT8 percentage among patients in the treatment group was $33.52\% \pm 7.80\%$, the mean OKT4/OKT8 ratio was 1.47 ± 0.51 , the mean AT-III concentration was 38.8 ± 5.5 mg/dL, the mean Fa value was $102.6\% \pm 31.6\%$, and the mean β -TG concentration was 62.3 ± 15.1 ng/dL. After treatment, the mean OKT8 percentage among patients in the control group was $42.22\% \pm 7.07\%$, the mean OKT4/OKT8 ratio was 1.12 ± 0.24 , the mean AT-III concentration was 30.9 ± 8.0 mg/dL, the mean Fa value was $64.6\% \pm 26.9\%$, and the mean β -TG concentration was 67.0 ± 42.1 ng/dL. These data indicate that after treatment, the immunologic function of the T lymphocytes of gastric cancer patients in the treatment group was significantly improved ($P < 0.01$). Additionally, the hypercoagulability in the treatment group was also improved ($P < 0.001$), and the mean OKT4/OKT8 ratio, antithrombin III (AT-III) concentration, and fibrinolytic activity, etc. had all become normalized. The one-year (86%), 3-year (69%), and 5-year (40%) survival rates in the treatment group were all higher than those in the control group ($P < 0.05$). The mean tumor weights in the control, traditional medicine, and chemotherapy groups were 0.895 ± 0.289 g, 0.433 ± 0.177 g, and 0.357 ± 0.142 g, respectively. The tumor-inhibition rates in the traditional Chinese medicine group and chemotherapeutic group (51.6% and 60.1%, respectively) were significantly better than that in the control group ($P < 0.001$). The mean tumor weight in the traditional Chinese medicine group (24.68 ± 1.93 g) was significantly higher than that in both the treatment group (22.96 ± 1.87 g) and control group (22.47 ± 2.18 g).

CONCLUSION: The Fuzheng Huoxue anticancer prescription can not only replenish vital functions (Zhengqi), correct a hypercoagulatory state, improve immunologic function, and extend patient survival times, but may also directly inhibit gastric tumor growth without producing toxic side effects.

Key words: Stomach neoplasms/TCM therapy; Fuzheng Huoxue; survival rate; T lymphocyte subsets; Medicine Chinese traditional

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Zhou AG, Huang DW, Ding YX, Jiang H, Tang ML. Treatment of postoperative gastric cancer with the Fuzheng Huoxue anticancer prescription. *World J Gastroenterol* 1997; 3(3): 189-191. Available from: URL: <http://www.wjgnet.com/1007-9327/full/v3/i3/189.htm> DOI: <http://dx.doi.org/10.3748/wjg.v3.i3.189>

Table 1 Comparison of T lymphocyte subgroup levels before and after treatment (mean ± SD)

Groups		<i>n</i>	OKT3 (%)	OKT4 (%)	OKT8 (%)	OKT4/OKT8
Treatment	Before	15	56.10 ± 8.54	41.81 ± 6.18 ^a	45.94 ± 8.45 ^b	0.89 ± 0.19 ^b
	After	20	58.68 ± 9.98	41.89 ± 8.70 ^a	33.52 ± 7.80 ^d	1.47 ± 0.51 ^d
Control	Before	13	61.87 ± 5.01	46.61 ± 6.79	49.21 ± 6.60 ^b	0.94 ± 0.20 ^b
	After	12	56.11 ± 8.50	46.24 ± 6.10	42.22 ± 7.07 ^{bd}	1.12 ± 0.24
Healthy person		15	61.66 ± 6.42	48.11 ± 8.51	31.02 ± 4.96	1.57 ± 0.32

^a*P* < 0.05; ^b*P* < 0.001 as compared with the healthy subjects group; ^c*P* < 0.05; ^d*P* < 0.001 as compared with pretreatment.

Table 2 Changes in hypercoagulatory parameters before and after treatment in the two groups (mean ± SD)

Groups		<i>n</i>	AT-III (mg/dl)	FA (%)	β-TG (ng/dl)
Treatment	Before	35	29.9 ± 7.9 ^b	50.4 ± 24.4 ^b	91.0 ± 25.9 ^b
	After	35	38.8 ± 5.5 ^d	102.6 ± 31.6 ^d	62.3 ± 15.1 ^{bd}
Control	Before	34	32.3 ± 7.2 ^a	57.3 ± 24.6 ^b	87.5 ± 34.2 ^b
	After	34	30.9 ± 8.0 ^b	64.6 ± 26.9 ^b	67.0 ± 42.1 ^{bc}
Healthy persons			36.4 ± 8.3 (59)	90.3 ± 24.3 (30)	25.0 ± 8.2 (103)

^a*P* < 0.05, ^b*P* < 0.01 as compared with healthy subjects; ^c*P* < 0.05, ^d*P* < 0.001 as compared with pretreatment. The number of individuals is shown in parentheses.

INTRODUCTION

From July 1986 to July 1995, we used the Fuzheng Huoxue (strengthening the body resistance and promoting blood circulation) anticancer prescription to treat postoperative patients with mid- or late-stage gastric cancer, as well as nude mice with transplanted human gastric cancers. The treatment results are reported below.

CLINICAL INVESTIGATION

Clinical data

This study enrolled 69 patients with histologically confirmed mid- or late-stage gastric cancer, and who were being treated at Renji Hospital, affiliated with the Shanghai Second Medical University. The patients were assigned to two study groups. The treatment group included 26 males and 9 females; (two patients aged 33-40 years, 18 patients aged 41-60 years, and 15 patients aged 61-75 years; mean group age = 58.4 years). The control group consisted of 23 males and 11 females, (4 patients aged 33-40 years, 16 patients aged 41-60 years, and 14 patients aged 61-75 years; mean group age = 56.8 years). The pathological stage of each patient was determined according to the TNM classification system, as modified by the Chinese Cooperative Group in Gastric Cancer^[1]. In the treatment group, 8 cases were stage II, 15 were stage III, and 12 were stage IV. Twenty-seven cases underwent a palliative operation and 11 cases underwent a radical operation. In the control group, 11 cases were stage II, 11 cases were stage III, and 12 cases were stage IV. Twenty-three cases received a palliative operation, and 11 cases received a radical operation. The two groups showed no significant difference in sex, age, clinicopathologic stage or operation mode. The healthy individuals were recruited from staff at the Shanghai Second Medical University and its affiliated hospitals.

Methods and parameters of observation

The Fuzheng Huoxue anticancer prescription contained Codonopsis pilosula (Franch.) N. annf (15 g), Astragalus membranaceus (Fisch.) Bge (15 g), Atractylodes macrocephala Koidz (12 g), Poria cocos (Schw.) Wolf (12 g), Rehmannia glutinosa (Gaertn.) Lib. osch (12 g), Adenophora tetraphylla (Thunb.) Fisch (15 g), Salvia miltiorrhiza Bge (15 g), and Angelica sinensis (Oliv.) Diels (12 g). One dose of this mixture was given to patients once a day. The control prescription contained Citrus tangerina Hort. et Tanaka (12 g), Magnolia officinalis Rehd. et Wils (12 g), Amomum villosum Lour (6 g), Oryza sativa L (15 g), and Hordeum vulgare L (15 g), and was also given as a single dose, once a day.

Treatment methods

Starting at one month after an operation, decoctions of the Fuzheng

Huoxue anticancer prescription, the control prescription, and FT-207 manufactured by the Shanghai No.12 Pharmaceutical Factory, (100-200 mg, three times daily) were given to the designated groups for five days.

Measurements of patient survival and assay methods

Patient survival rates were calculated by the direct method. T-lymphocyte subgroups, antithrombin III levels, fibrinolytic activity (Fa), and β-thromboglobulin (β-TG) were measured by a fluorescent immunoassay method^[2], rocket electrophoresis^[3], fibrolytic area^[4], and radioimmunoassays, respectively.

EXPERIMENTAL INVESTIGATION

Materials and methods

Materials An oral formulation of the Fuzheng Huoxue anticancer prescription with a crude medicine concentration of 3.0 g/mL was autoclaved and then stored at low temperature. Human gastric cancer cell line SGC-7901 was purchased from the Shanghai Institute of Pharmaceutics. Female nude mice aged 6-8 wk and 5-Fu (bat. No. 930712) were purchased from the Shanghai Tumor Institute, and the Shanghai Haipu Pharmaceutic Factory, respectively.

Methods SGC-7901 cells were inoculated into the backs of nude mice under sterile conditions. The mice were weighed on the next day, and then randomly allocated to a control group, a traditional Chinese medicine group, and a chemotherapy group (*n* = 10 mice per group). There was no significant difference in the total body weight of the nude mice in each group. A 0.5 mL dose of saline solution was instilled into the stomach of each mouse in the control group each day, while 0.5 mL of the Fuzheng Huoxue anticancer decoction was instilled into the stomach of each mouse in the traditional Chinese medicine group. Mice in the chemotherapy group were intraperitoneally injected with 1 mg of 5-FU once a week for 8 wk.

Observation parameters Each mouse was monitored for its body weight, tumor weight, and any tumor inhibitory effects.

Experimental results

Tumor weight and tumor inhibition The mean tumor weights in the control, traditional Chinese medicine, and chemotherapy groups were 0.895 ± 0.289 g, 0.433 ± 0.177 g, and 0.357 ± 0.142 g, respectively. While compared with tumor growth in the control group, the tumor inhibition rates in the traditional Chinese medicine group and chemotherapeutic group were 51.6% and 60.1%, respectively, (*P* < 0.001).

Body weight of the nude mice The mean body weights of the nude mice in each group before and after treatment were 21.50 ± 1.51 g and 22.47 ± 2.18 g, respectively, in the control group, 21.50 ± 0.47 g and 24.68 ± 1.93 g, respectively, in the traditional Chinese medicine group, and 21.55 ± 0.64 g and 22.96 ± 1.87 g, respectively, in the chemotherapy group. None of these differences before and after treatment were statistically significant (*P* > 0.05). However, when compared with the mean pretreatment weight, the mean body weights in the traditional Chinese medicine and chemotherapy groups were significantly higher after treatment (*P* < 0.05). Furthermore, when compared with the mean body weight in the control group, the mean body weight in the traditional Chinese medicine group showed a significant increase (*P* < 0.05).

RESULTS

Comparison of survival rates between the treatment and control groups

Among the 35 patients in the treatment group, 31 survived > 0.5 years, 30 (86%) survived > 1 year, 24 (69%) survived > 3 years, and 14 (40%) survived > 5 years. Among the 34 patients in the control group, 28 (82%) survived > 0.5 years, 22 (65%) survived

> 1 year, 14 (41%) survived > 3 years, and 6 (18%)> 5 years. The 1, 3, and 5-year survival rates in the treatment group were all significantly higher than those in the control group ($P < 0.05$).

The numbers of different T lymphocyte subgroups in the peripheral blood of subjects in the two groups before and after treatment are shown in Table 1. The immunologic function of subjects in both groups showed significant improvement after treatment.

Changes in the hypercoagulatory parameters of subjects in both groups before and after treatment are shown in Table 2. While both groups were in a hypercoagulatory state before treatment, the hypercoagulatory state of the treatment group showed significant improvement after treatment. The values for AT-III and Fa in the treatment group did not significantly differ from those in healthy individuals ($P > 0.05$). The control subjects remained in a hypercoagulatory state.

DISCUSSION

Patients with mid- or late-stage gastric cancer are usually deficient in Zheng qi, and have an impaired immunologic response^[5]. The immunologic state of a human is closely correlated with tumor occurrence and development; furthermore, immune responses mediated by T lymphocytes play a major role in tumor immunity.

Our study showed that prior to treatment, the suppressor T lymphocytes of gastric cancer patients were hyperactive and the patients showed a poor immune response. Zhengxu (weakened body immunity) decreases a patient's anticancer response as well as their ability to tolerate chemotherapy. The Fuzheng method is widely used to treat tumors by practitioners of traditional Chinese medicine or combined traditional and Western medicine, and especially in Beijing, Shanghai, Tianjing, and Fujian^[6,7], China.

Gastric cancer is associated with blood stasis, and the extent of blood stasis is correlated with the severity and outcome of the disease^[8]. AT-III is the most important anti-agglutination agent found in plasma. Fa directly reflects the activity of proplasminogen, and β -TG directly reflects the extent of blood stasis. The results of our study showed that prior to treatment, the patients with gastric cancer were in a state of hypercoagulation, and this was the basis for our clinical use of the Huoxue Huayu method. Zhengxu and

blood stasis are basic characteristics of patients with mid- or late-stage gastric cancer. In addition to the Fuzheng method, the Huoxue method can also be used to treat such patients. The Fuzheng Huoxue anticancer prescription produced better clinical effects in treating postoperative patients with mid- or late-stage gastric cancer as compared with the effects shown in control patients. The immunologic function and hypercoagulation status of the patients improved significantly. These results suggest that the Fuzheng Huoxue anticancer prescription can not only replenish Zheng qi, enhance the anticancer response of patients, and reduce the side effects of chemotherapy, but can also improve blood stasis and circulation, as well as immunologic function, and is thus beneficial for treating tumors and extending patient survival times. Our animal studies proved that the Fuzheng Huoxue anticancer prescription inhibited tumor growth without producing any significant toxic side effects or affecting the body weights of the nude mice. Based on these results, we feel the Fuzheng Huoxue anticancer prescription has a bright future for use in cancer management. While the Fuzheng Huoxue anticancer prescription may directly inhibit or kill gastric tumor cells, these activities require further confirmation.

REFERENCES

- 1 Xu GW. Gastric cancer. 1st ed. Beijing: People Health Publishing House 1987: 85-89
- 2 Zheng WF. Medical immunomethod. Ed 1. Beijing: People's Health Publishing House 1989: 128
- 3 Zhou BZ. Practical techniques in electrophoresis and immunoelectrophoresis. Wuhan: Hupei Science and Technology Publishing House 1988: 155-163
- 4 Harmis BD, Likewood D. Experimental methods in gel electrophoresis of protein. Beijing: Science Publishing House 1986: 161
- 5 Wang GT, Zhu JS, Xu JY. Activity detection of subgroup of T lymphocyte, NK cell and interferon in peripheral blood of patients with advanced gastric cancer. *Shanghai Medical Journal* 1995; **18**: 109-110
- 6 Yu GQ, Liang FY. Development of study in treating tumor with Fuzheng Peiben. *China Tumor Information* 1990; **3**: 10-13
- 7 Li PW. The prospect of the treatment of tumor with integrated traditional Chinese and western medicine through the changes in papers on tumor of recent 16 years. *Chinese Journal of Integrated Traditional and Western Medicine* 1993; **13**: 45-46
- 8 Zhou AG, Huang DW, Ding YX, Chen MF, Li DH, Jiang SJ. Investigation on blood stasis syndrome of patients with gastric malignant tumor before and after operation and before death. *Chinese Journal of Integrated Traditional and Western Medicine* 1990; **10**: 540-541

S- Editor: Filipodia L- Editor: Jennifer E- Editor: Hu S



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ISSN 1007-9327

