Clinical and experimental studies on stomach carcinoma treated with Yangwei Kangliu granules

Wen-Ping Lu, Gui-Zhi Sun, Bing-Kui Piao, Hai-Tao Dong, Zong-Yan Yang, Hong-Sheng Lin

Wen-Ping Lu, Gui-Zhi Sun, Bing-Kui Piao, Hai-Tao Dong, Zong-Yan Yang, Hong-Sheng Lin, Department of Tumor, Guangmumen Hospital, China Academy of TCM, Beijing 100053, China

Dr. Wen-Ping Lu, female, born on 1968-10-23 in Chengde City, Hebei Province, graduated from the China Academy of TCM as a postgraduate in 1995, currently Physician-in-Charge, having 3 papers published.

Author contributions: All authors contributed equally to the work.

Key project in The 8th five-year plan supported by the State Administrative Bureau (No. 85-919-01-02).

Correspondence to: Dr. Wen-Ping Lu, Department of Tumor, Guangmumen Hospital, China Academy of TCM, Beijing 100053, China

Telephone: +86-10-63013311-303

Received: January 12, 1997
Revised: June 3, 1997
Accepted: June 28, 1997
Published online: December 15, 1997

Abstract

AIM: To study the anti-cancer mechanism of Yangwei Kangliu (YWKL) granules from the view point of red blood cell (RBC) immunity and to investigate the relationship between RBC immunity and T lymphocyte immunity.

METHODS: Fifty patients with advanced gastric carcinoma were treated with a combination of YWKL granules and chemotherapy. Venous blood samples were obtained before treatment and after one course of treatment. The rosette rate of c-3b-receptor (RBC-C-3bRR), tumor and red cell (RRTR) and RBC immune complex (RBC-ICR) were measured under microscopy by counting the rosettes formed by sensitized or unsensitized yeast adherence. The T lymphocyte subset was observed by the method of APAAP. Control patients were treated with chemotherapy alone (n = 20). In addition, mouse tumor studies were performed to investigate the dynamic changes of RBC-C-3bRR, RRTR and RBC-ICR in response to treatment with YWKL granules (n = 30). Mice treated with chemotherapy alone (n = 30) or water alone (n = 30) were used as controls.

RESULTS: The clinical therapeutic effect of combination treatment with YWKL granules and chemotherapy (i.e. the treatment group) was markedly superior to that of chemotherapy alone (i.e. the control group) (P < 0.01). In the treatment group, the rosette rates of RBC-C-3bRR and of RRTR were significantly increased (P < 0.01) after treatment, the rate of RBC-ICR was markedly decreased (P < 0.01), and the ratio of CD4 to CD8 was obviously elevated (P < 0.01). Moreover, CD8 was much lower (P < 0.01) and the ratio of CD4 to CD8 was much higher (P < 0.01) than that in the control group. The RRTR rate was positively correlated with the ratio of CD4 to CD8. In mice, on day 9 of bearing cancer, the tumor weight in the group treated with YWKL granules alone was much lower than that of the tumors in the control mice groups; in addition, the YWKL treated mice showed higher RBC immune function than the mice of the two control groups. On day 13 of bearing cancer, however, the differences in both tumor weight and RBC immune function had disappeared.

CONCLUSION: The anti-cancer mechanism of YWKL granules may involve enhancement of RBC immunity and of T lymphocyte immune function, which is supported by the finding of RBC immune function being correlated with T lymphocyte immune function.

Key words: Stomach neoplasms; Yangwei Kangliu granules; RBC immunity

© The Author(s) 1997. Published by Baishideng Publishing Group Inc. All rights reserved.

Lu WP, Sun GZ, Piao BK, Dong HT, Yang ZY, Lin HS. Clinical and experimental studies on stomach carcinoma treated with Yangwei Kangliu granules. World J Gastroenterol 1997; 3(4): 266-268. Available from: URL: http://www.wjgnet.com/1007-9327/full/v3/i4/266.htm DOI: http://dx.doi.org/10.3748/wjg.v3.i4.266

INTRODUCTION

Several studies have provided experimental and clinical data demonstrating that the immune system plays a key role in controlling the occurrence and development of tumors. As a result, red blood cell (RBC) immunity has emerged as a new subdiscipline in the modern field of immunology[21]. Since then, studies have identified a close correlated between RBC immunity and prognosis of tumors, and have characterized the functions as involving clearance of the immune complex in circulation, controlling and regulating other immune cells and effector-like actions.

The current study was designed to investigate the anti-cancer effects of Yangwei Kangliu (YWKL) granules and its function of strengthening body resistance by supporting a healthy qi and dispelling blood stasis and toxic material; specifically, its effects on RBC immune activity were studied in humans and a mouse model system.

MATERIALS AND METHODS

Subjects

A total of 70 patients with pathology-confirmed gastric cancer who were admitted to our hospital or to the China-Japan Friendship Hospital for treatment were enrolled in our study and randomly divided...
Table 1 Change of red blood cell immune function in the Yangwei Kangliu treatment group (% x ± s)

| Group           | n  | C-3b-RR | Immune complex | Tumor and red cell |
|-----------------|----|---------|----------------|--------------------|
| Normal          | 30 | 17.3 ± 5.04 | 9.6 ± 1.72    | 40.6 ± 6.17        |
| Pre-treatment   | 50 | 8.8 ± 2.37  | 13.2 ± 2.88   | 29.3 ± 6.32        |
| Post-treatment  | 50 | 15.0 ± 2.71  | 8.9 ± 1.85    | 39.2 ± 1.96        |

*P< 0.01 vs pre-treatment.

Table 2 Change in T lymphocyte subset between the Yangwei Kangliu + chemotherapy (treatment) and chemotherapy only (control) group

| Group            | n  | CD3   | CD4   | CD8   | CD4/CD8 |
|------------------|----|-------|-------|-------|---------|
| Treatment group   |    |       |       |       |         |
| Pre-treatment     | 50 | 66.80 ± 6.81 | 38.00 ± 4.52 | 52.36 ± 2.91 | 11.23 ± 0.16 |
| Post-treatment    | 50 | 66.27 ± 5.55  | 39.00 ± 4.15  | 51.43 ± 2.84  | 14.8 ± 0.156 |
| Control group     |    |       |       |       |         |
| Pre-treatment     | 20 | 63.59 ± 8.32  | 38.18 ± 6.7   | 31.56 ± 2.82  | 1.26 ± 0.22  |
| Post-treatment    | 20 | 62.84 ± 9.05  | 36.37 ± 4.39  | 32.47 ± 4.89  | 2.21 ± 0.25  |

*Compared with the treatment group in pre-treatment *P< 0.01; *Compared with the treatment group in post-treatment, *P< 0.01.

and RRTR were both significantly enhanced, and the RBC-ICR was decreased as compared with those observed at the pretreatment stage (P< 0.01).

The changes in T lymphocyte immune function are presented in Table 2. After treatment, although the CD4 and CD8 levels were elevated, there were no difference from the pretreatment stage (P> 0.05). However, the level of CD4 was significantly lower (P< 0.01) and the ratio of CD4 to CD8 was significantly greater (P< 0.01) than the pretreatment levels. The control group showed no differences of these indices from the pretreatment levels to the post-treatment levels. Comparison of the post-treatment indices of the treatment group and the control group showed no differences for the levels of CD4 and CD8 (P> 0.05). However, compared to the control group, the level of CD4 in the treatment group was significantly lower (P< 0.01) and the ratio of CD4 to CD8 was also significantly higher (P< 0.01). The RRTR was positively correlated to the ratio of CD4 to CD8 (Y = 1.14 + 0.005x, P< 0.01).

**EXPERIMENTAL STUDIES**

**Materials and methods**

**Tumor model and transplantation** The fore-stomach carcinoma cell, which is a model of high pulmonary metastasis, was retrieved from storage in liquid nitrogen were thawed at 37-40 ℃ and inoculated subcutaneously into the right back of inbred 615-strain. When the resultant tumor had grown to 1.0-1.5 cm in diameter, the mice were sacrificed and the tumor tissues were resected and made into a single cell suspension. Then, this suspension was brought up to 0.2 mL with normal saline consisting of 1 × 10^6 tumor cells and was injected subcutaneously into the right back of a fresh mouse.

**Grouping** The transplanted mice were randomly divided into three groups of 30 for treatment with either TCM (administered 0.8 mL YWKL liquid, once daily, starting at 24 h after transplantation, with daily dose was equivalent to 1.4 g of raw drugs), chemotherapy (administered 25 mg/kg 5-fluorouracil, once every other day, intragastric), or control (administered 0.8 mL water, once daily, intragastric).

**Determination index** The inhibitory rates for tumor, RBC-C3-RR and RBC-ICR were determined as described above.

**Methods**

A batch of mice were sacrificed respectively on post-inoculation day 3, 9 and 11; ten mice were sacrificed for each time point. The tumors were resected and weighed, and the inhibitory rate was calculated. Blood was collected by retro-orbital puncture and used to test the RBC-C3-RR and RBC-ICR.

**RESULT**

Data for the dynamic changes of tumors in mice are shown in Table 3. After the latent stage (3-5 d of bearing tumors), the tumors grew rapidly; mice began to die on day 13 in all three groups. On day 3 post-inoculation, when the first batch of mice was sacrificed, no tumors were apparent. On day 9, the tumor weight was markedly lower in the TCM group than in the control or the chemotherapy group (P< 0.01 or P< 0.05). On day 13, there were no differences in tumor weights among the three groups (P> 0.05).
Data for the dynamic changes of RBC immune function in mice are shown in Table 4. With the development of tumor, the rate of RBC-C₃bRR decreased and that of RBC-ICR increased. On post-inoculation days 3 and 9, the RBC-C₃bRR of the TCM group was higher and the RBC-ICR was lower than that of the chemotherapy and control groups (P < 0.01); however, on day 13 there were no differences between the RBC-C₃bRR and RBC-ICR for the three groups (P > 0.05). At no time did the chemotherapy and control group show differences in RBC-C₃bRR and RBC-ICR.

### DISCUSSION

Malignancy is closely correlated with RBC immunity. At present, RBC immune activity is often assessed by means of determination of RBC immune adhesion and the execution of RBC immune adhesion via the C₃b receptor.

Assuming that patients with advanced gastric carcinoma are always in a state of deficiency of healthy qi and stagnation of exogenous factor, YWK granules would then function to support healthy qi, dissipating blood stasis and clearing away toxic materials. The prescription of YWK granules combined with Rhizoma atractylodis and Radixs scutellariae, both of which can strengthen body resistance, Lignum sappan, which can activate blood circulation to dissipate blood stasis in the stomach and spleen, and Rhizoma paridis, which can clear away heat and toxic material. Our clinical and experimental study of this prescription showed that, in both patients with gastric cancer and mice bearing tumors, the RBC-C₃bRR and RRTR were low and the RBC-ICR was high before treatment. The experiment on mice further demonstrated that as the tumors grew, the red blood cell immunity gradually declined. On the ninth day of bearing tumor, the tumor weight in the YWK treatment group was lower than that of the other groups; correspondingly, the RBC immunity was higher than that of the other two groups. On the thirteenth day of bearing tumor, there was no obvious difference of tumor weight, and no difference of RBC immunity existed among the three groups.

Clinical data had shown that the short-term effectiveness of YWK combined with chemotherapy was superior to that of chemotherapy alone and that the post-treatment RBC immunity was higher than that of the pre-treatment samples from the patients who were treated with the combination of YWK granules and chemotherapy. According to the amount concept, the fewer the tumor cells the better the effect of the chemotherapy regimen, and of the immune therapy that is administered in conjunction or afterwards; moreover, when the number of tumor cells is below 10⁶, the immune system may be able to eliminate it. Therefore, we believe that the anti-cancer mechanism of YWK granules involves its improvement of immune activity, especially of the RBC immune activity, and this can make the treatment level effective in cases with 10⁴ and 10⁵ tumor cells or even higher. This is also the theoretical basis that supports effectiveness of YWK granules combined with chemotherapy is better than that of chemotherapy alone. Of course, whether YWK granules can directly kill tumor cells as chemotherapy awaits further study. As to the cause underlying the observation that the inhibitory rate in the chemotherapy group was lower than that in the YWK group, we speculate that 5-FU was not sensitive to Fc cells and it inhibited the immune function of the organism.

The anti-cancer effect of RBC immunity is due to its ability to not only clear the immune complex in circulation but also to control and regulate other immune cells, which is supported by the observed correlation between the RBC and T-lymphocyte subset.

### REFERENCES

1. Siegel I, Lin TL, Gleicher N. The red-cell immune system. Lancet 1981; 2: 556-559 [PMID: 6116004]
2. Guo F, Yu Zi Q, Zhao Zhong P. Primary studies on red cell immunity. Zhonghua Yi Xue ZaZhi 1982; 62: 715
3. Shau H, Gupta RK, Golub SH. Identification of a natural killer enhancing factor (NKEF) from human erythroid cells. Cell Immunol 1993; 147: 1-11 [PMID: 8462106 DOI: 10.1006/cimm.1993.1043]
4. Sun Y. Some important questions in internal treatment to tumor at present. Pro Onc J 1990; 5: 129-134
