

Effect of Poria polysaccharide oral liquid on cancer-related fatigue in postoperative patients with colorectal cancer

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Abstract

Objective: We aimed to explore the effect of Poria polysaccharide oral liquid (PPOL) on cancer-related fatigue (CRF) in postoperative patients with colorectal cancer. **Methods:** Fifty patients with colorectal cancer who were diagnosed in our hospital from March 2015 to March 2019 were included in this retrospective study. They were all underwent tumor resection. They were randomly divided into control group (n = 25) and observation group (n = 25). Patients in the control group were treated according to the FOLFOX4 chemotherapy regimen, and those in the observation group were treated with FOLFOX4 chemotherapy plus PPOL (10 ml/time, 3 times/day) for 6 weeks. The quality of life index (QL-index) and brief fatigue scale (BFI) were used to investigate the quality of life and fatigue, respectively. The serum levels of inflammatory factors, IL-6 and TNF- α , were measured. **Results:** Compared with the control group, the QL-index score in the observation group was significantly better ($P < 0.05$). Moreover, the BFI in the observation group was significantly lower than that in the control group ($P <$

0.05). Furthermore, the serum levels of IL-6 and TNF- α in the observation group were notably decreased in comparison with the control group ($P < 0.05$). Conclusion: PPOL can effectively improve the fatigue state of postoperative patients with colorectal cancer by reducing the levels of IL-6 and TNF- α and improving the quality of life.

Key words: Poria polysaccharide oral liquid; cancer-related fatigue; colorectal cancer; inflammatory factor

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1 Introduction

Colorectal cancer (CRC) is one of the most common malignant tumors of digestive tract, which refers to the malignant tumor of colorectal mucosa epithelium and glands (Thanikachalam and Khan, 2019). The incidence rate of colorectal cancer in China has been increasing in recent years. In 2018, the incidence and mortality of colorectal cancer in China ranked the 3rd and 5th among all cancers, respectively (Feng et al, 2019). Cancer related fatigue (CRF) is a kind of persistent and subjective fatigue in physiology, emotion or cognition related to cancer or cancer treatment (Ebede et al, 2017). It cannot be relieved after adequate rest, which often occurs in all stages of the tumor, after radiotherapy, chemotherapy, and tumor resection (Mohandas et al, 2017). The treatment of colorectal cancer is currently mainly based on surgery, supplemented by postoperative radiotherapy and chemotherapy. However, most patients will have CRF-related manifestations, such as tired, fatigue, weight loss, and lack of energy. There are also some patients who discontinue treatment because they cannot tolerate the adverse reactions of radiotherapy and chemotherapy, which leads to a decrease in the quality of life and poor prognosis. Therefore, it is particularly important to improve the adverse reactions of patients with colorectal cancer after surgery and during radiotherapy and chemotherapy. Poria cocos is a traditional Chinese medicine. It has been reported that Poria polysaccharide has an antitumor effect by modulating the immune system and apoptosis (Shi et al, 2017). Therefore, the purpose of this study was to explore the effect of Poria polysaccharide oral liquid (PPOL) on CRF in postoperative patients with colorectal cancer.

2 Patients and Methods

2.1 Patients

Fifty patients with colorectal cancer who were diagnosed in our hospital from March 2015 to March 2019 were included in this retrospective study. The patients were selected by random number table method. The study was approved by the committee of Guangdong Provincial People's Hospital (No.GDREC2015128H). They were all

underwent tumor resection in our hospital. Diagnostic criteria for colorectal cancer: pathological examination results as the reference standard. Diagnostic criteria for CRF according to the diagnostic criteria of the 10th International Conference on classification of diseases (ICD-10) (Schneider et al, 1995): (1) Weakness or heavy body; (2) Inability to concentrate; (3) Lack of passion, low mood, lack of energy; (4) Insomnia or lethargy; (5) Feeling that energy is still not restored after sleep; (6) Emotional reactions such as sadness, frustration, or irritability; (7) inability to perform the original daily activities; (8) short-term memory loss; (9) fatigue symptoms lasting for several hours without relief. The patients were included in this study when their fatigue symptoms occurred repeatedly, met 5 (or more than 5) of the above manifestations, and the duration of symptoms was longer than 2 weeks. Exclusion criteria: (1) those with severe cardiovascular, cerebrovascular, liver, or kidney diseases; (2) those with consciousness or mental disorders; (3) those who were allergic to related drugs; (4) those who were unwilling to sign informed consent. They were randomly divided into control group (n = 25) and observation group (n = 25).

2.2 Treatment

Patients in the control group were treated according to the FOLFOX4 chemotherapy regimen, and those in the observation group were treated with FOLFOX4 chemotherapy plus PPOL (10 ml/time, 3 times/day) for 6 weeks. FOLFOX4 chemotherapy regimen: on the first day, oxaliplatin (85 mg/m²) and calcium folinate (400 mg/m²) were given intravenously for 22 h. On day 1 and day 2, 5-fluorouracil (400 mg/m² and 600 mg/m²) were given intravenously, respectively. At the same time, patients received symptomatic and supportive treatment such as antiemetic and liver protection. Every 2 weeks is an adjuvant chemotherapy cycle.

2.3 Observation indexes

The quality of life index (QL-index) is composed of five aspects, including activity, daily life, health, support and general situation. The total score is between 0-10. The higher the score, the better the quality of life. An increase in the score indicates an improvement in the quality of life.

Brief fatigue scale (BFI) is composed of 9 items. The entry score value range is between 0-10. The comprehensive fatigue level (the first 3 items) was used to assess the current and past 24 h of fatigue level. The comprehensive fatigue impact (the last 6 items) was used to assess the impact of fatigue on the patient's life. The higher the BFI score, the higher the patient's fatigue.

2.4 Detection of inflammatory factors

Before and after treatment, the blood was collected from patients and used to assess the serum levels of IL-6 and TNF- α with the commercial kits (Nanjing Jiancheng Institute

of Biotechnology, Nanjing, China) by ELISA as mentioned in the instrument.

2.5 Statistical analysis

Statistical analysis was made by software SPSS24.0 (International Business Machines, corp., Armonk, NY, USA). The measurement data satisfied the normal distribution after the normality test, and Two independent sample t test was used for comparison between two groups. All measurement data were expressed as means \pm standard deviation (SD). The counting data were analyzed by chi square test. Differences were considered statistically significant when $P < 0.05$.

3 Results

3.1 General clinical characteristics

There were 29 men and 21 women in this study with the average age of (50.68 \pm 6.24) years. There were 14 males and 11 females in the control group, aged (49.76 \pm 6.43) years. There were 15 males and 10 females in the observation group, aged (51.60 \pm 6.02) years. There was no significant difference in general clinical characteristics between the two groups ($P > 0.05$) (Table 1).

Table 1. General clinical characteristics

Items		Control group (n=25)	Observation group (n=25)	χ^2 / t	P values
Gender (male/female)		14/11	15/10	0.08	0.77
Age (years)		49.76 \pm 6.43	51.60 \pm 6.02	1.04	0.30
Weight (kg)		59.09 \pm 3.44	57.97 \pm 3.78	1.09	0.27
Tumor stage	II stage	11	9	0.33	0.56
	III stage	14	16		

3.2 PPOL improved the quantity of life of patients with colorectal cancer

There was no significant difference in QL-index score between the two groups before treatment ($P > 0.05$). After treatment, the QL-index scores in the two groups were both significantly higher than before treatment ($P < 0.05$). Moreover, after treatment, the QL-index score in the observation group was significantly increased than that in the control group ($P < 0.05$) (Table 2).

Table 2. Comparison of QL-index scores between the two groups before and after treatment

Groups	cases	Before treatment	After treatment
Control group	25	2.52 \pm 1.00	3.84 \pm 0.97*
Observation group	25	2.80 \pm 1.08	5.92 \pm 1.25*#

<i>t</i>	-	0.94	6.51
<i>P</i>	-	0.34	< 0.01

* $P < 0.05$ vs. before treatment. # $P < 0.05$ vs. control group before treatment.

3.3 PPOL improved the fatigue state of patients with colorectal cancer

There was no significant difference in BFI score between the two groups before treatment ($P > 0.05$). After treatment, the BFI scores in the two groups were both significantly lower than before treatment ($P < 0.05$). Moreover, after treatment, the BFI in the observation group was significantly lower than that in the control group ($P < 0.05$) (Table 3).

Table 3. Comparison of BFI scores between the two groups before and after treatment

Groups	Cases	Before treatment		After treatment	
		Fatigue level	Fatigue impact	Fatigue level	Fatigue impact
Control group	25	19.68±2.05	38.88±1.94	16.32±2.03*	24.52±2.38*
Observation group	25	20.32±2.15	39.28±2.35	14.72±1.92*#	20.80±2.34*#
<i>t</i>	-	1.07	0.65	2.85	5.56
<i>P</i>	-	0.28	0.51	< 0.01	< 0.01

* $P < 0.05$ vs. before treatment. # $P < 0.05$ vs. control group before treatment.

3.4 PPOL decreased the serum levels of IL-6 and TNF- α of patients with colorectal cancer

There was no significant difference in the serum levels of IL-6 and TNF- α between the two groups before treatment ($P > 0.05$). After treatment, the serum levels of IL-6 and TNF- α in the two groups were both significantly decreased than before treatment ($P < 0.05$). Moreover, after treatment, the serum levels of IL-6 and TNF- α in the observation group were significantly lower than that in the control group ($P < 0.05$) (Table 4).

Table 4. Comparison of inflammatory factors between the two groups before and after treatment

Groups	Cases	IL-6 (pg/ml)		TNF- α (pg/ml)	
		Before treatment	After treatment	Before treatment	After treatment
Control group	25	35.16±3.38	28.87±2.87*	36.88±3.83	31.39±3.06*
Observation group	25	34.97±5.25	25.89±3.14*#	38.03±5.54	25.33±4.27*#
<i>t</i>	-	0.15	3.50	0.84	5.76

<i>P</i>	-	0.88	0.01	0.42	< 0.001
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**P* < 0.05 vs. before treatment. #*P* < 0.05 vs. control group before treatment.

4 Discussion

At present, colorectal cancer is one of the common malignant tumors in the digestive tract. The incidence ratio of male to female is about 3:2 (Wu et al, 2020). Early colorectal cancer is asymptomatic, and its onset is insidious. Surgery is currently the main treatment for colorectal cancer, and the main reason for treatment failure is postoperative recurrence and metastasis. Chronic inflammation microenvironment is one of the conditions for tumor occurrence and development (Nisticò and Ciliberto, 2020). Inflammatory factors, such as TNF- α and IL-6, are the important inflammatory basis for the pathogenesis of colorectal cancer, which can initiate chronic inflammation of the body, and is closely related to the development and prognosis of colorectal cancer (Wang, 2012; Song and Sun, 2006; Yang and Tian, 2006). While inflammatory factors play the inflammatory killing effect, they can also promote the growth and migration of tumor cells and the formation of tumor blood vessels, and have a certain relationship with the immune escape of tumor cells (Liu et al, 2015; Toyoshima et al, 2019; Dunican et al, 2000).

CRF is a common symptom of patients with cancer and is closely related to the body's inflammatory response (Li et al, 2019; Li et al, 2016). CRF runs through before and after cancer treatment. The direct impact of cancer is the primary cause of CRF. Surgical trauma and radiotherapy and chemotherapy will cause the aggravation of CRF, which is a major problem in current cancer treatment.

It has been demonstrated that traditional Chinese traditional medicine has a good effect on alleviating the adverse effects of resection, radiotherapy and chemotherapy (Zhang et al, 2017; Tian and Hu, 2014). Traditional Chinese medicine believes that CRF belongs to the category of "asthenia", the main cause of which is cancer toxin damaging healthy qi and weakness of viscera. If combined with surgery, radiotherapy and chemotherapy, the loss of vital energy is even more serious. According to the treatment principles of "treating deficiency with tonification", the core of the treatment is to strengthen the body and tonify the deficiency and restore the function of viscera. The main effect of Poria polysaccharide oral liquid is to strengthen spleen, replenish qi and enhance immunity. Its main ingredient is poria polysaccharide, which is mainly used for adjuvant treatment of patients with cancer after radiotherapy and chemotherapy. It has been reported that Poria polysaccharides can inhibit the release of IL-1, IL-6, TNF- α and other inflammatory factors to reduce inflammation, and have many functions such as immune regulation, anti-inflammatory, and anti-tumor (Cheng et al, 2020).

In this retrospective study, compared with the control group, the BFI and QL-index scores of patients in the observation group after taking Poria polysaccharide oral liquid for 6 weeks were significantly better than those of the control group, indicating that Poria polysaccharide oral liquid can effectively improve the fatigue state and quality of life of patients with colorectal cancer. The levels of serum inflammatory factors, IL-6 and TNF- α , in the observation group are significantly decreased than those in the control group, suggesting that Poria polysaccharide oral liquid reduces the levels of serum inflammatory factors and reduces inflammation in the body. This may be one of its mechanisms for relieving CRF-related symptoms, and it is also conducive to reducing postoperative complications.

The limitation of this study is that the number of included cases is small. In addition, due to the short follow-up time, the long-term survival data were not collected and analyzed. In the future, we can further expand the sample size and extend the research time. The mechanism of PPOL in improving fatigue was studied to provide more sufficient basis for its clinical application. Although PPOL can improve tumor related fatigue, the cost of treatment will be relatively increased. Therefore, the effect of long-term use of PPOL on the economic pressure and psychological pressure of patients is worth further study.

5 Conclusion

In conclusion, the adjuvant treatment of PPOL for patients with CRC after resection can reduce postoperative inflammation and adverse reactions during chemotherapy, effectively improve the patient's fatigue state and quality of life. As a kind of Chinese patent medicine, PPOL has high patient compliance and is convenient to take. It is a safe and effective clinical adjuvant treatment plan to improve cancer-related fatigue.

6 Acknowledgments

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7 Conflict of interest

The authors declare that they have no conflict of interests.

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