

Cognitive Impairment Related to Chemotherapy in 60 Patients with Advanced Gastric Cancer

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How to cite this paper: Cheng, Y.X., Zhang, L.J., Zheng, H., Jiang, X.J. and Yong, H. (2022) Cognitive Impairment Related to Chemotherapy in 60 Patients with Advanced Gastric Cancer. *Open Journal of Internal Medicine*, 12, 129-135.
<https://doi.org/10.4236/ojim.2022.122015>

Received: May 2, 2022

Accepted: June 27, 2022

Published: June 30, 2022

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Abstract

Background: Gastric cancer is one of the most common malignant tumors in the world. In recent years, studies on chemotherapy-induced cognitive impairment have been reported mainly on young women with breast cancer. Only few studies on chemotherapy-related cognitive impairment in patients with gastric cancer. **Objective:** To investigate the effect of chemotherapy on cognitive function in patients with advanced gastric cancer. **Methods:** Sixty patients with stage IV gastric cancer who received fluorouracil based chemotherapy were selected as gastric cancer group, including 25 patients with S-1 (S-1 group) and 35 patients with capecitabine (capecitabine group). 60 healthy controls matched with age and education level were recruited as control group. Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and Auditory Verbal Learning Test (AVLT) were used to test. **Results:** There was no significant difference in MMSE, MoCA and AVLT between healthy control group and gastric cancer group before chemotherapy. MMSE, MoCA, immediate memory and delayed memory decreased in gastric cancer patients after chemotherapy ($t = 2.206$, $t = 2.399$, $t = 2.206$, $t = 2.654$, $P < 0.05$). There was no significant difference in MMSE, MoCA and AVLT between S-1 group and capecitabine group before and after chemotherapy. **Conclusion:** Patients with gastric cancer will have chemotherapy-related cognitive dysfunction after chemotherapy. It is necessary to evaluate and guide or treat patients with cognitive function, so as to improve the quality of life of patients.

Keywords

Gastric Cancer, Chemotherapy, MoCA, MMSE, AVLT

1. Introduction

Gastric cancer is one of the most common malignant tumors in the world. Al-

though its morbidity and mortality have declined in recent years, the incidence rate of gastric cancer remains the fifth in all malignant tumors, with the mortality rate in the third place [1]. In recent years, studies on chemotherapy-induced cognitive impairment (CICI) have been reported. Most of the studies focus on young women with breast cancer [2] [3], and the degree of CICI varies from mild to moderate. At present, there are few studies on chemotherapy-related cognitive impairment in patients with gastric cancer and other solid tumors.

The Mini-Mental State Examination (MMSE) has been the most used screening instrument to detect a decline in cognitive function throughout decades [4]. However, it has shown not to be adequate in detecting MCI and clinical signs of dementia [5]. Montreal Cognitive Assessment (MoCA) was developed by Nasreddine and collaborators (2005) and has been shown as a tracking tool with a high ability to discriminate normal cognitive function and MCI and early onset dementia [6]. The Auditory Verbal Learning Test (AVLT) is the most common test used to identify objective memory impairment in Western countries [7].

In this study, 60 patients with advanced gastric cancer receiving chemotherapy and 60 healthy controls were selected as the research objects to explore the effect of chemotherapy on cognitive function.

2. Materials and Methods

2.1. Participants

60 patients with stage IV gastric cancer who received fluorouracil based chemotherapy were selected as gastric cancer group in The Hefei Affiliated Hospital of Anhui Medical University from January 2013 to September 2021. In addition, 60 healthy controls matched with gastric cancer patients in age, education and physical condition were recruited as control group. This study was approved by the ethics committee of The Hefei Affiliated Hospital of Anhui Medical University and informed consent was obtained.

2.2. Inclusion Criteria

1) Patients with definite diagnosis of stage IV adenocarcinoma gastric cancer (with cytological or pathological evidence); 2) Patients was treated with fluorouracil based chemotherapy (capecitabine or S-1); 3) Mini Mental State Examination (MMSE) score ≥ 24 , Montreal Cognitive Assessment (MoCA) score ≥ 26 ; 4) General cognitive function was normal. Activities of daily living were basically normal. Right handedness (vision or corrected vision was normal, bin-aural hearing was ok, and can cooperate to complete the examination). ECOG score was less than or equal to 2; 5) No hearing, vision, language and other functional barriers.

2.3. Exclusion Criteria

1) Patients with advanced cachexia; 2) Accompanied with dementia and mental symptoms; 3) Accompanied with other physical and mental disorders that

can lead to cognitive impairment; 4) History of alcohol/drug dependence or taking related drugs to improve cognition; 5) Complicated with severe heart, liver, kidney, brain and hematopoietic system diseases.

2.4. Assessment Methods

MMSE and MoCA were used to assess the cognitive function of the patients, and AVLT was used to assess the ability of immediate memory and delayed memory. The patients were tested before chemotherapy and at least after 4 times standard dose chemotherapy (within 1 - 2 weeks). The test environment is quiet without external interference, the testers are trained intensively and the test methods are unified.

2.5. Statistical Methods

All data were analyzed by SPSS 19.0 software, and all continuous data were analyzed by means \pm SD. According to the data type, independent sample t test was used to compare the continuous data between gastric cancer group and healthy group, and chi-square analysis was adopted for ordinal data. Paired t-sample test was used to compare the continuous data of gastric cancer patients before and after chemotherapy. If p value is less than 0.05, there is statistical difference.

3. Results

3.1. Comparison of Basic Data between Gastric Cancer Group and Control Group

We analyzed the difference of general data between the two groups, the result show that there were no significant differences in gender, age, years of education, between gastric cancer group and healthy controls. The MMSE score and MoCA score were also found no significant differences (See **Table 1**).

3.2. Comparison of Cognitive Function of Gastric Cancer Patients before and after Chemotherapy

As shown in **Table 2**, the MMSE score and MoCA score of gastric cancer patients after chemotherapy were significantly lower than those before chemotherapy ($P < 0.05$). The scores of short-term memory (AVLT-I) and AVLT delayed recall (AVLT-II) were significantly lower than those before chemotherapy ($P < 0.05$).

3.3. The Effect of Different Chemotherapy Schemes on Cognitive Function

According to the different fluorouracil drugs used in chemotherapy regimens of gastric cancer patients, the patients were divided into two groups: S-1 group (25 cases) and capecitabine group (35 cases). There were no significant differences in MMSE score, MOCA score, instant memory score and delayed memory score between the S-1 group and the capecitabine group before and after chemotherapy (**Table 3**).

Table 1. Comparison of basic data between gastric cancer group and healthy controls.

Patient characteristics	Gastric cancer group	Healthy controls	χ^2/t	P value
Sex (Female, %)	60	55	0.307	0.580
Age	65.67 ± 2.87	64.63 ± 3.19	1.863	0.065
Educational years	5.85 ± 1.80	5.78 ± 1.79	0.204	0.839
MMSE score	25.75 ± 1.20	26.07 ± 1.36	1.349	0.180
MoCA score	26.93 ± 0.66	27.15 ± 0.69	1.764	0.080

Table 2. Comparison of cognitive function of gastric cancer group before and after chemotherapy.

Patient characteristics	Before chemotherapy	After chemotherapy	t	P value
MMSE score	25.75 ± 1.20	25.62 ± 1.21	2.206	0.031
MoCA score	26.93 ± 0.66	26.80 ± 0.71	2.399	0.020
AVLT-I	2.90 ± 0.82	2.77 ± 0.83	2.206	0.031
AVLT-II	1.77 ± 0.67	1.63 ± 0.71	2.654	0.010

Table 3. Comparison of cognitive function before and after different chemotherapy regimens.

	Before chemotherapy				After chemotherapy			
	S-1 group	Capecitabine group	t	P value	S-1 group	Capecitabine group	t	P value
MMSE score	25.64 ± 1.29	25.83 ± 1.15	0.596	0.554	25.44 ± 1.44	25.74 ± 1.01	0.902	0.372
MOCA score	27.00 ± 0.65	26.89 ± 0.68	0.658	0.513	26.76 ± 0.78	26.83 ± 0.67	0.367	0.715
Instant memory score	2.92 ± 0.76	2.89 ± 0.87	0.159	0.874	2.84 ± 0.75	2.71 ± 0.89	0.574	0.568
Delayed memory score	1.60 ± 0.58	1.89 ± 0.72	1.644	0.106	1.48 ± 0.59	1.74 ± 0.78	1.421	0.161

4. Discussion

With the continuous improvement of survival and life quality of tumor patients in recent years, the impact of tumor treatment on cognitive function of patients has been paid more and more attention. It has been found that the cognitive impairment of patients receiving chemotherapy is significantly higher than that before treatment, but the research is mainly focused on breast cancer [2] [3]. Our results showed that the cognitive function of patients with gastric cancer also decreased after chemotherapy.

At present, there are few studies on the effect of chemotherapy on the cognitive function of patients with gastrointestinal cancer, and there is still no consensus on whether chemotherapy will affect the cognitive function of patients with gastrointestinal cancer. On the one hand, Vardy [8] and Shaffer [9] show that chemotherapy has no effect on the cognitive function of patients with colorectal cancer. On the other hand, Cruzado [10] and Fardell [11] show that chemotherapy can cause chemotherapy-related cognitive impairment in patients

with gastrointestinal cancer, mainly the decline of memory, including immediate memory and delayed memory. Our result shows that MMSE score, MoCA score, instant memory score and delayed memory score of gastric cancer patients after chemotherapy were lower than before chemotherapy. This suggested that chemotherapy would affect the cognitive function of gastric cancer patients.

Our study further studied the effects of different fluorouracil drugs on cognitive function of patients with gastric cancer. It was found that MMSE score, MoCA score, instant memory and delayed memory scores of patients with gastric cancer after receiving chemotherapy regimen containing S-1 or capecitabine were lower than those before treatment. However, there was no significant difference between the two groups. Both S-1 and capecitabine are the third generation of oral fluorouracil drugs. The efficacy and safety of S-1 and capecitabine in the treatment of gastric cancer are basically the same [12]. Therefore, it is reasonable to believe that the effects of S-1 and capecitabine on cognitive function of gastric cancer patients are basically the same. However, due to the small sample size of this study, the results still need to be further confirmed by large sample studies.

The mechanism of cognitive dysfunction induced by chemotherapy remains unclear. At present, it is considered that the main reasons for the influence of chemotherapy on cognitive function include [13] [14] [15]: 1) Chemotherapy can affect the level of estrogen and testosterone, and weaken its protective effect on nerve cells; 2) Chemotherapy can reduce the antioxidant capacity of cells and increase DNA damage; 3) Chemotherapy can lead to immune imbalance and release inflammatory cytokines. When these cytokines penetrate the blood-brain barrier, they will lead to cognitive decline, including thinking, executive function, spatial ability and reaction speed; 4) Chemotherapy can damage small blood vessels of central nervous system and reduce blood flow. Fluorouracil may also affect the cognitive function of gastric cancer patients in the above ways, but these specific mechanisms still need to be further confirmed in gastric cancer patients.

In conclusion, this study suggests that patients with gastric cancer will have chemotherapy-related cognitive dysfunction after chemotherapy. Therefore, it is necessary to evaluate or treat patients with cognitive function after chemotherapy in order to improve the quality of life of patients. In addition, large sample studies are needed to confirm the research results.

Funding

This work is funded by Natural Science Foundation Project of Bengbu Medical College (Project Name: Study on chemotherapy-related cognitive impairment of gastric cancer with fluorouracil as the main drug).

Conflicts of Interest

All authors declared that they have no conflict of interest.

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