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Study on the treatment of advanced lung adenocarcinoma in the elderly with pemetrexed combined with platinum drugs

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Abstract: To study the treatment of advanced lung adenocarcinoma in the elderly with pemetrexed combined with platinum drugs. 200 elderly patients who had been treated for advanced lung adenocarcinoma in our hospital were enrolled as research objects. They were randomly divided into control group and research group, each containing 100 patients. The control group was given Pemetrexed therapy and routine nursing mode, while the research group was given pemetrexed combined with platinum drugs and evidence-based nursing mode. The therapeutic effect and nursing effect of the two groups were compared. The overall treatment effective rate of the research was 85.00% and that of the control group was 60.00%, indicating the research group had significant advantage over the control group, $p<0.05$. The incidence of adverse reactions including nausea, vomiting, constipation, diarrhea, bone marrow suppression, fatigue and fatigue, and hair loss was significantly lower in the research group (22.00%) than that in the control group (45.00%), $p<0.05$. The quality of life of the research group was higher than that of the control group, $p<0.05$. For the elderly patients with advanced lung adenocarcinoma, the implementation of pemetrexed combined with platinum drug can help patients get better treatment results.

Keywords: Pemetrexed, platinum drugs, combination therapy, elderly patients, advanced lung adenocarcinoma.

INTRODUCTION

Lung cancer is one of the most harmful malignant tumors in the world. In recent years, epidemiological survey results show that the incidence of lung adenocarcinoma has exceeded lung squamous cell carcinoma in both smoking and non-smoking populations of many countries, accounting for almost half of all lung cancers. The incidence of female lung adenocarcinoma in some countries shows an exponential increase, and it is also the most common pathological type of lung cancer in young people (Liu, Hu and Li, 2015; Feng, Xie and Qu, 2019 and Wang, 2019). Lung adenocarcinoma has a high degree of histological heterogeneity in clinical, imaging, molecular biology and pathological aspects, and can be divided into four subtypes: Preinvasive lesion (PL), microinvasive adenocarcinoma (MIA), invasive adenocarcinoma and variant of invasive adenocarcinoma. Atypical adenomatous hyperplasia (AAH) and adenocarcinoma in situ (AIS) are classified as invasive prelesions of lung adenocarcinoma.

Lung adenocarcinoma (fig. 1) comes from the bronchial glands and can occur in all bronchi. Most of lung adenocarcinoma occurs in the bronchioles and more than 3/4 occurs in the periphery (Fang *et al*., 2017). Lung adenocarcinoma has no obvious clinical symptoms in the early stage, which is often found in the chest X-ray or CT examination. Although lung adenocarcinoma generally grows slowly, sometimes hematogenous metastasis occurs early and lymphatic metastasis occurs later. Sometimes cryptic primary lung adenocarcinoma may present as extensive metastasis or pleural involvement with poor prognosis. In this study, the efficacy of pemetrexed combined with platinum drugs in the treatment of advanced lung adenocarcinoma in the elderly was observed and analyzed (Cai *et al*., 2018 and Cui, 2018).

MATERIALS AND METHODS

The 200 elderly patients who had been treated for advanced lung adenocarcinoma in our hospital from August 2015 to May 2019 were enrolled as research objects. Patients meeting inclusion criteria are those aged over 70, with stage IV adenocarcinoma of the lung, meeting the clinical staging criteria for TNM in non-small cell lung cancer the (seventh edition) prescribed by international lung cancer research association (IASLC), without accepting chemotherapy previously, having the basis for objective efficacy evaluation, receiving evaluation according to Response Evaluation Criteria In Solid Tumors RECIST (Response Evaluation Criteria in Solid Tumors) 1.1 and accepting chemotherapy regimen of pemetrexed combined with cisplatin (DDP) or carboplatin (CBP). Patients who were excluded are those with low compliance, serious organic lesions in important organs, and those who cannot tolerate chemotherapy (Huang *et al*., 2018; Jiang *et al*., 2018; Duan *et al*., 2018).

Patients and their families had the right to know and signed the formal informed consent. This study was approved by the hospital ethics association. Patients were

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randomly divided into research group and control group, each containing 100 cases. There were 48 male and 52 female patients in the research group, ranging from 70 to 88 years old, with an average age of (80.38±2.16) years. The control group included 45 male and 55 female patients, ranging in age from 72 to 86 years, with an average age of (81.26±2.49) years. Imaging examination of a patient is shown in fig. 2. There was no significant difference in general data between the two groups ($p>0.05$).

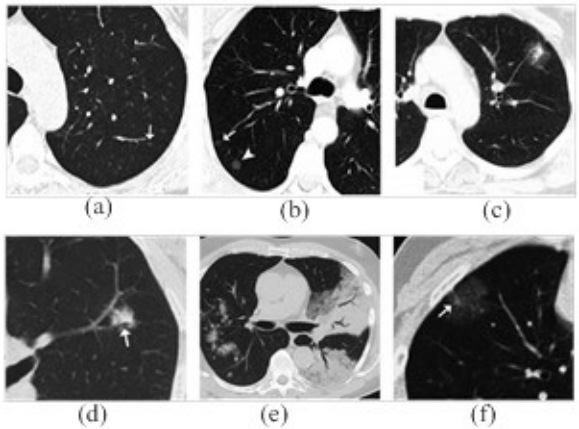

Fig. 1: Lung adenocarcinoma [(a): pre-invasive lesions by CT scan; (b): multiple frosted glass nodules of AIS/AAH by CT scan; (c): some solid nodules of infiltrating adenocarcinoma by CT scan; (d): mucinous original adenocarcinoma by CT scan; (e): infiltrating mucinous adenocarcinoma by CT scan; (f): infiltrating non-mucinous adenocarcinoma by CT scan]

The research group was treated with pemetrexed combined with platinum drugs, and the control group was treated with pemetrexed only. The patients began taking folic acid tablets 7 days before chemotherapy with pemetrexed, with dose of 400 g per day until the end of chemotherapy. Meanwhile, intramuscular injections of vitamin B12 were conducted once every three weeks, with dose of 1000μg per each time. On the day before, the day after and the day after chemotherapy, the patient was instructed to take dexamethasone twice a day, 4 mg each time, to prevent and control rash and allergy problems. Intravenous drip of pemetrexed (500mg/m2) and cisplatin (70 mg/m2) was performed on the first day, every three weeks as a course. Pemetrex is an antifolate with pyrropyrimidine as its core. It inhibits cell replication and tumor growth by disrupting folate-dependent normal cellular metabolism. The molecular formula is $C_{20}H_{19}N_5Na_2O_6•7H_2O$, and the main component is pemetrexed disodium. Pharmacological analysis shows that after systemic administration of pemetrexed (AUC38．3—316．8μg•hr/mL), neutrophils fall to their lowest point for about 8-9.6 days, and after the lowest point, neutrophils return to baseline for 4.2-7.5 days. Cisplatin is a platinum-containing anticancer drug, namely cis-dichlorodiamine platinum (II), which is brown-yellow powder. It is a non-specific drug of cell cycle and has therapeutic effect on sarcoma, malignant epithelial tumor, lymphoma and germ cell tumor (Fu *et al*., 2017; Liu, 2019). The molecular formula of cisplatin is Cl2H4N2Pt, which is prepared by complexing potassium tetrachloroplatinate with ammonium chloride and ammonia (Minamin *et al*., 2017; Ren and Yu, 2018).

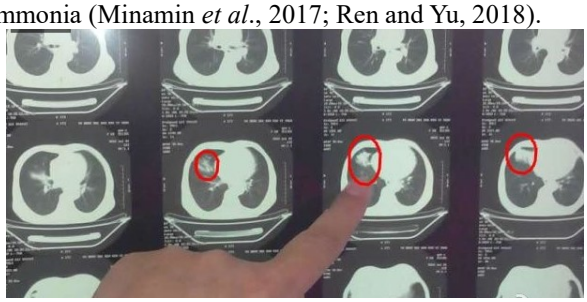

Fig. 2: Imaging examination

Nursing method

The patients in the control group were applied with general routine nursing mode, and the research group was given evidence-based nursing mode on this basis of routine nursing mode. First, an evidence-based team including experienced oncology nurses and clinicians should be established. By analyzing the medical records of the patients, the nursing staff can grasp the ill status of the patients, strengthen the communication with the patients and their families, and obtain the basic information, conditions, symptoms and psychological state and other information. Secondly, the evidence-based problems should be clarified, and the data of patients, the clinical experience of physicians and nursing staff, and the possible symptoms during treatment should be summarized and analyzed as the basis. Third, implement evidence-based nursing. Nursing staff should search evidence-based problems with the help of computer and network system, and put forward evidence-based nursing program based on the knowledge network, WanFang database and foreign medical papers database. Fourth, Conduct psychological guidance to improve the psychological state of patients, and at the same time, carry out health education to enhance the treatment of patients' faith. According to the abnormal symptoms during the treatment, nursing staff should evaluate the effect of nursing program and operation method, and adjust the nursing program according to the results. In addition, nursing staff should implement preventive care, link the patient's condition to the course of treatment, and administer medication and care for possible adverse reactions. Fifth, nursing staff should timely analyze and summarize nursing programs, nursing procedures, operating methods, nursing effects, etc., so as to provide valuable guidance for nursing work (Gong, 2019; Jiang *et al*., 2018).

Observational indexes

Solid tumor evaluation criteria released by WHO (world health organization) were adopted to evaluate the efficacy,

Table 1: Comparison of the overall treatment effective rate between two groups [n (%)]

Group	Complete response	Partial response	No change	Progression	Overall treatment effective rate
Research group (n=100)	50	35	10	5	85(85.00)
Control group (n=100)	40	20	30	10	60(60.00)
X^2					16.58
p					<0.05

Table 2: Comparison of quality of life between the two groups ($\bar{x}$ ±s)

Group	Number of case	Physiological function	Emotional function	Social function	General health state	Mental function	Energy
Research group	100	79.80±3.25	78.96±3.20	82.35±2.18	60.78±3.22	75.63±4.02	65.79±2.04
Control group	100	72.20±2.46	66.88±2.58	73.20±2.59	49.06±3.01	65.80±2.06	55.49±3.28
t		6.70	20.19	6.79	8.53	11.22	13.27
p		<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Table 3: Comparison of incidence of adverse reactions between the two groups [n(%)]

Group	Diarrhea	Constipation	Nausea and vomiting	Fatigue	Hair loss	Incidence of adverse reactions
Research group (n=100)	3	6	5	5	3	22(22.00)
Control group (n=100)	6	4	15	11	9	45(45.00)
X^2						20.18
p						<0.05

including complete response (CR), partial response (PR), no change (NC) and progression (PD). At the same time, sf-36 scale was used to evaluate the quality of life of the two groups of patients. The incidence of adverse reactions was calculated.

STATISTICAL ANALYSIS

Statistical analysis software SPSS21.0 was used to process data. The measurement data were expressed by mean ± average ($\bar{x}$ ± s), with t test conducted for intergroup comparison. Enumeration data were expressed by natural (n) and percentage (%), with X2 used for intergroup comparison. The intergroup difference is of statistical value when $p<0.05$.

RESULTS

Comparison of the overall treatment effective rate between two groups

As shown in table 1, compared with the control group, the overall treatment effective rate of the patients in the research group was significantly higher, $p<0.05$.

Comparison of quality of life between the two groups

According to the statistics in table 2, the quality of life of the patients in the research group and the control group was observed after the implementation of different nursing modes. The results showed that the research group was significantly superior to the control group, $p<0.05$.

Comparison of incidence of adverse reactions between the two groups

As shown in table 3, the rate of adverse reactions in the research group was significantly lower than that in the control group, $p<0.05$.

DISCUSSION

Advanced lung adenocarcinoma is a non-small cell tumor, which has become the difficulty and focus of clinical and research because of its low sensitivity to conventional radiotherapy and chemotherapy and the onset at early age. Pemetrexed is a multi-target anti-folic acid drug, which can inhibit the activity of folate-dependent enzymes such as glycylamide nucleotide methyltransferase, dihydrofolate reductase and thymidine synthase, reduce the synthesis of thymine and purine nucleosides, hinder the synthesis of DNA and RNA in tumor cells, so as to exert anti-tumor effect. Pemetrexer has low toxicity, high efficiency and extensive anti-tumor effect, and has been approved by the FDA as the second-line treatment of advanced NSCLC in 2004 [9-10]. Platinum is a non-specific drug that regulates cell cycle and has certain cytotoxicity. It can damage the membrane structure of cancer cells and inhibit the DNA replication of cancer cells. Platinum has a strong broad-spectrum anti-cancer effect, which is normally administrated together with pemetrexed or docetaxel to achieve a better effect. In addition, hematological toxicity and non-hematological toxicity (such as nephrotoxicity, ototoxicity and

neurotoxicity) of cisplatin are significant. For elderly patients, creatinine clearance rate and decreased renal excretion capacity may increase the potential toxicity, and the presence of complications and progressive withdrawal of physical status may also affect the drug safety of a considerable number of patients.

Evidence-based nursing is a concept, practice and decision-making method, which is of great significance to the progress of global medical and health care and the professional development of nursing. Especially in the era of translational medicine, Evidence-based nursing is the most advanced and effective nursing method applied in clinical practice, which not only ensures the nursing effect, but also has important value for the research, management and teaching of nursing. The results of this study showed that the patients in the research group treated with pemetrexed combined with platinum drugs had higher overall treatment effective rate and lower adverse reaction rate, which is consistent with the results of other studies.

CONCLUSION

In conclusion, elderly patients with advanced lung adenocarcinoma can achieve good efficacy and has higher tolerance to pemetrexed combined with platinum chemotherapy regimen. However, this paper is a retrospective study with few enrolled patients, so the sample size needs to be further expanded for verification. Moreover, compared with developed countries, China's evidence-based nursing research and practice, especially the application of malignant tumor nursing, is still in the primary stage, so its development has a broad space. Evidence-based nursing in elderly patients with advanced lung adenocarcinoma has been rarely studied, and clinical application also lacks the necessary data support. Therefore, the nursing operation needs constant development and improvement.

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