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Original Research Article

Application of combined erlotinib and bronchoscopic interventional therapy in the treatment of bronchial lung cancer

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Abstract

Purpose: *To evaluate the efficacy of combined drug therapy and bronchoscopy intervention in the treatment of bronchial lung cancer.*
Methods: *A total of 80 patients with bronchial lung cancer admitted in The Third People's Hospital of Xindu District, Chengdu, China were enrolled and assigned in control and study groups (n = 40), and received bronchoscopy intervention alone and combined bronchoscopy intervention/erlotinib therapy, respectively, over a period of 4 weeks. Erlotinib therapy was given by oral administration of 150 mg once daily. Efficacy, levels of serum tumor marker, matrix metalloproteinase (MMP) content, and incidence of adverse reactions in the two groups of patients were evaluated.*
Results: *The overall response rate (ORR) in the study group was significantly higher than that of the control group (27.5 vs 55.0 %, p < 0.05). Carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), and neuron-specific enolase (NSE) decreased significantly after treatment, when compared to the control group (p < 0.05). Furthermore, after treatment, matrix metalloproteinase-2 (MMP-2) and matrix metalloproteinase-9 (MMP-9) levels in the study group were lower than in the control group (p < 0.05). The incidence of adverse reactions was 12.5 and 17.5 % in the control and study groups, respective (p > 0.05).*
Conclusion: *The combination of erlotinib therapy and bronchoscopy intervention significantly improves therapeutic efficacy, as well as serum tumor marker and MMP levels in bronchial lung cancer patients. Furthermore, it is safe as it does not significantly increase the risk of adverse reactions. However, further and broader clinical trials are recommended prior to its application in clinical practice.*

Keywords: *Bronchial lung cancer, Bronchoscopy intervention, Erlotinib, Median survival time, Serum tumor markers*

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INTRODUCTION

Bronchogenic carcinoma is a malignant tumor that threatens human health, and its incidence is rising globally, making it one of the most important causes of death worldwide [1]. With the continuous advancement in medical technology, treatment methods have become increasingly diverse and integrated. Currently, bronchoscopic intervention therapy and drug therapy have

become the main approach for the treatment of bronchogenic carcinoma [2,3].

Bronchoscopic intervention therapy is a minimally invasive surgery that involves placing interventional devices into the trachea and bronchi of the patient using a bronchoscope to perform operations such as excision, burning, or freezing of the tumor [4]. Drug therapy uses anticancer drugs or chemotherapy regimens to kill or inhibit the growth and proliferation of cancer cells [5]. With the advancement in tumor molecular biology techniques, an increasing number of targeted therapies aimed at gene mutations are being employed in the precision treatment of lung cancer. Among these, EGFR gene mutations are the most common. In comparison to traditional chemotherapy, epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) have shown significant efficacy in the treatment of lung cancer patients with EGFR-sensitive mutations, making them the preferred treatment option for such patients. Combined drug therapy and bronchoscopic intervention therapy have complementary and synergistic effects. This strategy prolongs the patient's survival time [6]. Although combined drug therapy and bronchoscopic intervention therapy has achieved some results in the treatment of bronchogenic carcinoma, their therapeutic effect and safety still need further investigation and research.

Therefore, this study aims to investigate the application of combined drug therapy and bronchoscopic intervention therapy in the treatment of bronchogenic carcinoma, in order to provide further reference and guidance for clinical treatment.

METHODS

Patients

The present study enrolled 80 patients with bronchial lung cancer admitted in The Third People's Hospital of Xindu District, Chengdu, China. Basic information about the patients, including gender, age, smoking history, tumor size, degree of differentiation, and pathological type were collected. The patients were randomly divided into control and study groups, with 40 patients in each group.

Inclusion criteria

① Patients aged 18 years or older; ② Patients confirmed to have bronchial lung cancer by histopathology; ③ Patients with a survival time greater than 6 months; ④ Patients with a clear smoking history or long-term exposure to smoke; ⑤ Patients who can undergo the required treatments and surgical procedures for this study; ⑥ Patients who volunteered to participate in this study and sign the relevant consent form.

Exclusion criteria

① Patients under 18 years of age; ② Patients with severe organ dysfunction, such as heart, lung, liver, or kidney failure; ③ Patients with other lung diseases or other malignant tumors; ④ Patients who have received radiotherapy or chemotherapy previously; ⑤ Patients who would not fully cooperate during this study due to various reasons.

Treatments

Control group

The treatment involved bronchial artery chemoembolization intervention. This was accomplished using Seldinger puncture technique, with catheter insertion through the femoral artery on one side, guided by a digital subtraction angiography (DSA) machine, and super-selective targeting of the tumor-feeding arteries. Treatment for the primary lung lesions included the use of hydroxycarbamide (Guizhou Hanfang Pharmaceutical Co. Ltd; China National Medical Products Administration approval no. H52020626; Guiyang, Guizhou, China), carboplatin (Chengdu Standard Biotech Co. Ltd; CAS no. 41575-94-4; Chengdu, Sichuan, China), docetaxel (Zhejiang Haijiang Pharmaceutical Co. Ltd; China National Medical Products Administration approval no. H20093092; Taizhou, Zhejiang, China), or gemcitabine (Lilly France S.A.S.; China National Medical Products Administration approval no. H20020180; Hauts-de-Seine, France). These drugs were dissolved in either 5 % glucose solution or 0.9 % sodium chloride solution and then slowly infused into the target arteries using an infusion pump.

Study group

The treatment combined selective bronchial artery chemoembolization and epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) drug, erlotinib (Nanjing Yoke Pharmaceutical Co. Ltd; China National Medical Products Administration approval no. H20213492; Nanjing, Jiangsu, China). During bronchial artery chemoembolization intervention, each treatment cycle typically spanned 4 weeks, and patients orally receive 150 mg of erlotinib once daily.

Evaluation of parameters/indices

Efficacy

RECIST1.1 criteria were used to evaluate the treatment effect of patients [17], including *complete response* (CR, disappearance of all target lesions, with no symptoms or signs); *partial response* (PR, a decrease in the size of the lesion by more than 30 %, or significant improvement in symptoms and signs); *stable disease* (SD, little change in the size of the lesion, or no significant improvement or worsening of symptoms and signs); *disease progression* (PD, increase in the size of the lesion by more than 20 %, or the appearance of new lesions, or worsening of symptoms and signs). ORR was used to determine the therapeutic effect as in Eq 1.

ORR = (CR + PR)/no. of treated patients …… (1)

Serum tumor marker levels

Before and after treatment, 5 ml of fasting elbow venous blood was collected from the patients, and centrifuged to obtain serum. Enzyme-linked immunosorbent assay (ELISA) was used to determine the levels of carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), and neuron-specific enolase (NSE) in the patients.

Matrix metalloproteinase (MMP) content

Prior to and after treatment, 5 ml of fasting elbow venous blood was collected from the patients, and centrifuged to obtain serum. The levels of matrix metalloproteinase-2 (MMP-2) and matrix metalloproteinase-9 (MMP-9) in the patients were evaluated by ELISA.

Incidence of adverse reactions

The adverse reactions assessed in the study include bleeding, infection, pneumothorax, nausea and vomiting, gastrointestinal reactions, etc. The incidence of adverse reactions in each group was recorded by the hospital's relevant medical staff.

Statistical analysis

The graphing software used was GraphPad Prism 8, while SPSS 21.0 was used for data analysis. Continuous variables were assessed using t-tests or analysis of variance (ANOVA), and chi-square tests were employed for categorical variables. A significance threshold of $p < 0.05$ was applied for statistical significance.

RESULTS

Baseline characteristics of the patients

The baseline characteristics of the two groups of patients were similar ($p > 0.05$; Table 1).

Therapeutic efficacy

As Table 2 shows, the ORR of control group was 11 (27.5%), which consisted of 2 cases of CR and 9 cases of PR, while the ORR of the study group was 22 (55.0%), including 5 cases of CR and 17 cases of PR. Thus, efficacy was greater in the study group than in control group ($p < 0.05$).

Table 1: Baseline characteristics of patients

Variable	Control group (n=40)	Study group (n=40)	t/x²	*P*-value
Gender			0.204	0.651
Male	22	24		
Female	18	16		
Mean age (years)	61.5±5.6	62.1±4.9	0.510	0.611
Smoking history			0.250	0.616
Yes	28	30		
No	12	10		
Mean tumor size (cm)	2.8±0.4	2.9±0.3	1.264	0.209
Differentiation			0.392	0.531
High	5	6		
Middle	28	29		
Low	7	5		
Pathological type			0.312	0.576
Squamous cell carcinoma	16	15		
Adenocarcinoma	11	10		
Large cell carcinoma	7	9		
Small cell carcinoma	6	6		

Table 2: Comparison of therapeutic efficacy between the two groups of patients (n = 40)

Group (n)	CR	PR	SD	PD	ORR (%)
Control group (n= 40)	2	9	21	8	11 (27.5%)
Study group (n= 40)	5	17	15	3	22 (55.0%)
χ^2	-	-	-	-	6.241
P-value	-	-	-	-	0.012

CR=complete response; PR=partial response; SD=stable disease; PD=disease progression

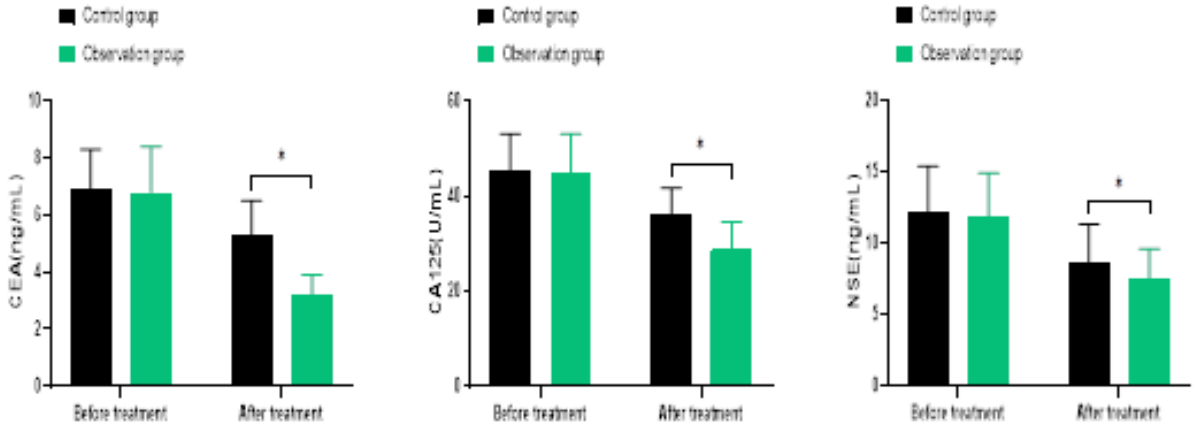

Figure 1: Comparison of serum tumor marker levels between the two groups of patients. *P < 0.05

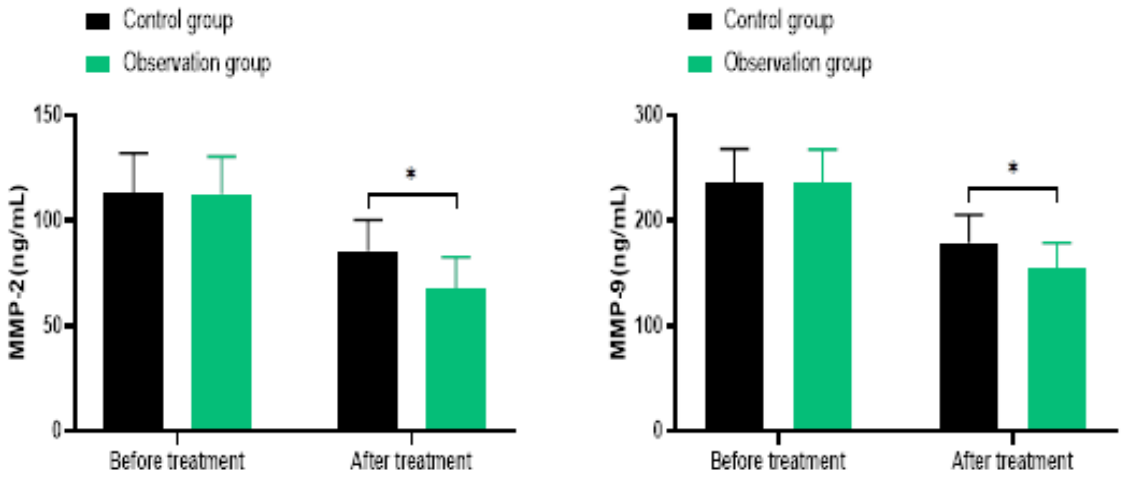

Figure 2: Comparison of matrix metalloproteinase (MMP) levels in the two patient groups. *P < 0.05

Serum tumor marker levels

The serum tumor marker levels are shown in Figure 1. Before treatment, the levels of CEA, CA125, and NSE were comparable between the two groups (p > 0.05). However, following treatment, the study group exhibited significantly lower levels of these markers compared to the control group (p < 0.05).

Matrix metalloproteinase (MMP) levels

As shown in Figure 2, t The differences in MMP-2 and MMP-9 levels between the two groups before treatment were insignificant (p > 0.05). Nevertheless, the study group demonstrated significantly lower post-treatment MMP-2 and MMP-9 levels than the control group (p < 0.05).

Incidence of adverse reactions

The incidence of adverse reactions in the control group was 12.5%, while in the study group, it reached 17.5%, and the discrepancies were insignificant (p>0.05), as shown in Table 3.

Table 3: Comparison of adverse reactions between the two groups of patients

Adverse reaction	Control group (n=40)	Study group (n=40)	χ^2	*P*-value
Bleeding	2	2	-	-
Infection	1	0	-	-
Pneumothorax	2	1	-	-
Feel sick and vomiting	0	2	-	-
Gastrointestinal reaction	0	2	-	-
Total incidence (%)	5 (12.5%)	7 (17.5%)	0.392	0.531

DISCUSSION

Bronchogenic carcinoma is a malignant tumor that originates from the epithelial cells of the bronchi in the lungs, and is a type of upper respiratory tract disease [8]. It is usually caused by genetic mutations in lung tissue cells resulting from multiple factors, which can lead to abnormal cell proliferation and differentiation, ultimately forming tumors [9]. It is also a common cancer that typically causes respiratory symptoms such as coughing, shortness of breath, and chest pain, and is usually classified into two types: small cell lung carcinoma and non-small cell lung carcinoma, which differ in diagnosis and treatment [10].

Although bronchogenic carcinoma is a dangerous disease, early diagnosis and treatment can significantly improve patient survival rates. Currently, clinical treatment for bronchogenic carcinoma is usually based on the patient's cancer stage and condition, and treatment methods mainly include surgery, radiation therapy, chemotherapy, and targeted therapy [11]. Bronchoscopic intervention is an interventional bronchoscopic technique that primarily aims to treat respiratory tract diseases or collect relevant biological specimens for diagnosis, using instruments such as bronchoscopes [12]. In bronchogenic carcinoma treatment, bronchoscopic intervention usually refers to interventional treatment guided by bronchoscopy, which typically includes lesion resection, biopsy guidance, photodynamic guidance, as well as bronchoalveolar lavage (BAL) and bronchial vein infusion (BVI) under endoscopy [13]. Overall, bronchoscopic intervention provides a minimally invasive and low-risk treatment option for early-stage bronchogenic carcinoma patients, and can also serve as an adjuvant to other treatment methods, thereby improving treatment outcomes.

However, some studies [14] have found that the efficacy of bronchoscopic intervention alone is not adequate for late-stage bronchogenic carcinoma patients, and thus recommend combining bronchoscopic intervention with other treatment methods. Based on these research viewpoints, this study attempted to combine bronchoscopic intervention with antitumor drugs for the treatment of bronchogenic carcinoma patients, and compared the differences in effectiveness between the single bronchoscopic intervention treatment and the combined drug treatment plan, in order to summarize the advantages of drug combination therapy.

Selective arterial infusion intervention chemotherapy is a treatment method that delivers chemotherapy drugs directly to tumor tissues, bypassing the dilution and first-pass clearance effects of the venous system, thereby enhancing the drug's effectiveness against tumor cells. This approach also offers the advantages of reducing systemic drug exposure, minimizing adverse effects on various organs, and improving patient drug tolerance [15]. Nevertheless, standalone arterial infusion intervention chemotherapy has not significantly improved long-term survival rates in patients. In recent years, with advancements in the field of medicine, small-molecule tyrosine kinase inhibitors (TKIs) have gained widespread attention. In patients with adenocarcinoma and EGFR mutations, TKIs have demonstrated significant benefits in terms of patient survival.

Erlotinib is a novel small-molecule EGFR-TKI that competitively inhibits the activity of EGFR-TKI by binding to the intracellular portion of EGFR. It reduces EGFR's autophosphorylation, leading to increased expression of the cell cycle inhibitory protein p27, causing cancer cells to arrest in the G1 phase and inducing apoptosis [16]. This mechanism ultimately halts tumor cell growth and promotes apoptosis, thereby extending patient survival. Through these innovative treatment approaches, tumors can be more effectively managed, alleviating patient symptoms, with the hope of further improving patient survival rates.

The results of this study show that the study group of patients treated with a combination drug therapy had significant advantages compared to the control group of patients treated with a single bronchoscopic intervention. The efficacy of treatment in the study group was significantly

higher than that of the control group; the levels of CEA, CA125, and NSE indicators in the study group after treatment were significantly lower than those in the control group; and the levels of MMP-2 and MMP-9 indicators in the study group after treatment were also significantly lower than those in the control group. These results are similar to those of previous related studies [17], which all indicate that a combination of drug therapy and bronchoscopic intervention plays a synergistic role in the treatment of bronchial lung cancer, thereby further improving efficacy in patients. The incidence of adverse reactions in the control group was 12.5%, while that in the study group was 17.5%. The incidence of adverse reactions between the two groups was not significantly different. Although the adverse reactions in the study group were slightly more severe, they were significantly alleviated after timely and effective treatment and did not affect efficacy. Based on previous research [18] and personal experience, it may be postulated that the combination drug therapy improves treatment efficacy via different pathways and targets. For example, chemotherapy drugs can interfere with the synthesis and division of cancer cell DNA, affecting its growth and reproduction. Immune therapy drugs can activate the body's immune system, enhancing anti-tumor immunity. Targeted therapy drugs can also interfere with specific targets on cancer cells, inhibiting their growth and reproduction.

Limitations of this study

Firstly, the sample size of this study is small, which may affect the reliability of the results. Secondly, the duration of this study is short and thus, there is insufficient long-term follow-up data, making it impossible to evaluate the recurrence and survival status after treatment. Finally, this study did not involve specific drug and intervention treatment selection and plans, which will require further in-depth research and exploration in the future.

CONCLUSION

Combining erlotinib with bronchoscopic intervention has a significant therapeutic effect in the management of bronchogenic carcinoma, and significantly improves patient outcomes, as well as reduce the levels of serum tumor markers and matrix metalloproteinases (MMP). Moreover, the combination strategy does not significantly increase the risk of related adverse reactions in patients, and thus is safe. However, expanded clinical trials over a longer duration as well as follow-up studies are required to validate the foregoing findings.

DECLARATIONS

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Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. All authors equally contributed to the study conception, design, and operations. All authors read and approved the final manuscript draft for publication.

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