Tropical Journal of Pharmaceutical Research September 2024; 23 (9): 1533-1539
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v23i9.17

Original Research Article

Lentinan combined with docetaxel and nedaplatin in the treatment of pulmonary tuberculosis complicated by non-small cell lung cancer

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Sent for review: 23 February 2024 *Revised accepted: 14 August 2024*

Abstract

Purpose: *To investigate the efficacy and safety of lentinan combined with docetaxel and nedaplatin (DN) in the treatment of pulmonary tuberculosis complicated by non-small cell lung cancer (NSCLC).*
Methods: *A total of 100 patients diagnosed with pulmonary tuberculosis combined with NSCLC in Ankang People's Hospital, Ankang, China were randomized equally into study and control groups. Control group received standard anti-tuberculosis therapy and intravenous chemotherapy regimen based on docetaxel (75 mg/m² on day 1) and nedaplatin (80 – 100 mg/m²), while the study group received, in addition, lentinan (given intravenously every two days). The patients received a total of 2 courses of treatment. Tumor response, survival, adverse reactions, quality of life score, and pulmonary function indices were compared before and after treatment.*
Results: *The study group showed significantly higher total response rate than the control group ($p < 0.05$). Median overall survival and progression-free survival in the study group was significantly higher than in the control group ($p < 0.05$). Also, the study group showed significantly lower incidence of adverse reactions compared to control group ($p < 0.05$). Quality of life score, maximum voluntary ventilation (MVV) and peak expiratory flow (PEF) levels in the study group was significantly higher compared to control group ($p < 0.05$).*
Conclusion: *Lentinan combination with DN chemotherapy regimen improves response rate, prolongs survival, reduces incidence of adverse reactions, improves quality of life and pulmonary function in patients with pulmonary tuberculosis complicated by NSCLC. These findings provide a new perspective for future studies on the application of lentinan in the treatment of pulmonary tuberculosis complicated by NSCLC.*

Keywords: *Lentinan, Docetaxel, Nedaplatin, Non-small cell lung cancer, Tuberculosis, Efficacy*

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, Web of Science, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

Tuberculosis and non-small cell lung cancer (NSCLC) are two thoracic diseases that adversely affect human health. Tuberculosis is a chronic infectious disease caused by *Mycobacterium tuberculosis*. Worldwide epidemiological data show that tuberculosis is one of the major infectious diseases leading to the death [1]. Non-small cell lung cancer is the most common type of lung cancer, accounting for approximately 85 % of all lung cancer cases.

Due to the common pathophysiology of the two diseases, they sometimes co-exist in the same patient, which brings additional challenges to clinical treatment [2].

In the case of tuberculosis and NSCLC comorbidities, the goal of treatment is not only to control tuberculosis infection, but also to effectively inhibit the growth and spread of the tumor. Anti-tuberculosis treatment usually involves long-term use of multiple antibiotics, while treatment for NSCLC may include surgery, radiation, and chemotherapy, or some combination of these methods [3]. Drugs commonly used in chemotherapy regimens for NSCLC include docetaxel and nedaplatin, and this combination has been widely used in the treatment of NSCLC with provable efficacy [4]. However, the adverse effects of this treatment regimen, such as myelosuppression, gastrointestinal reactions, and neurotoxicity, limits its clinical use. Therefore, it is very necessary to find adjuvant treatment methods that reduce adverse reactions and improve quality of life [5].

Administration of bioactive substances such as lentinan has gained attention. Lentinan is a natural polysaccharide extracted from mushroom species *Lentinus edodes* with a range of biological activities such as immune regulation, anti-tumor and anti-oxidation, and has shown good anti-cancer potential and low toxicity in a number of studies [6,7]. Although lentinan has shown positive effects in experimental studies, its clinical application in patients with pulmonary tuberculosis and NSCLC is relatively rare.

This study investigated the effect of lentinan in combination with docetaxel and nedaplatin (DN) in the treatment of patients with pulmonary tuberculosis and NSCLC. The results of this study may provide a new therapeutic strategy for the clinical treatment of patients with pulmonary tuberculosis complicated by NSCLC, which may also help to improve prognosis and quality of life [8]. At the same time, this will also provide more clinical evidence for the application of lentinan in tumor treatment, and provide a reference for future research and practice.

METHODS

Patients

This was a retrospective analysis of 100 patients diagnosed with pulmonary tuberculosis combined with NSCLC from May 2022 to May 2023 at Ankang People's Hospital, Ankang, China comprising of 71 males and 29 females. Age ranged from 35 to 78 years, with a mean age of 58.1 years. The participants were randomized equally into study and control groups. All the selected patients had completed detailed history collection, physical examination, laboratory examination and chest imaging examination, were confirmed to meet the diagnostic criteria for pulmonary tuberculosis and NSCLC [8], and had received DN chemotherapy or lentinan combined with DN chemotherapy. This study protocol was approved by the Medical Ethics Committee of Ankang People's Hospital (approval no. EC2022-134), and conducted in accordance with the Declaration of Helsinki [9] and relevant National laws and regulations.

Inclusion criteria

Laboratory tests (including sputum smear, sputum culture or molecular biological detection) and imaging tests met the diagnostic criteria for tuberculosis and pathological examination was consistent with the diagnosis of non-small cell lung cancer (NSCLC) [8], patients who had not received other anti-tuberculosis or anti-tumor therapy, at least 18 years of age, life expectancy more than 6 months, an understanding of the study and a signed informed consent form.

Exclusion criteria

Co-occurrence of other types of malignant tumors, presence of severe organ dysfunction, such as severe failure of heart, liver and kidney function, pregnant or lactating women, mental illness, who are unable to cooperate with treatment and follow-up, participation in other clinical trials which may influence the results. Signed informed consent of all participating patients was obtained before the study implementation, to ensure that the study process complies with ethical norms and to protect the rights and interests of patients.

Treatments

All the participants in the study underwent hematology and kidney function tests prior to treatment to ensure they were safe to receive chemotherapy. The study and control groups received the standard anti-tuberculosis treatment regimen comprising of an initial 2-month intensive treatment with isoniazid, rifampicin, pyrazinamide and ethambutol (2HRZE), followed by a 4 months treatment with isoniazid and rifampicin alone (4HR).

In addition, both groups received docetaxel (intravenously at 75 mg/m² on first day of chemotherapy) and nedaplatin based chemotherapy (DN) (intravenously, depending on the patient, at 80 and 100 mg/m², also within three days of start of chemotherapy (days 1 to 3). Furthermore, control group received DN chemotherapy while study group received DN chemotherapy in combination with lentinan (added to 250 mL 5 % glucose solution and administered intravenously every two days). Course of treatment was periodic, and each course lasted for 3 weeks. The participants received a total of 2 courses of treatment and received routine anti-tuberculosis drugs.

Evaluation of parameters/indices

Tumor response rate

The revised RECIST 1.1 criteria [10] was used to determine the objective response rate (ORR) of the tumor, including complete response (CR), partial response (PR), stable disease (SD), and disease progression (PD). Through comprehensive analysis of ORR, the efficacy of chemotherapy regimen was evaluated [10]. Patients' survival, including overall survival (OS) and progression-free survival (PFS), were also evaluated.

Adverse reactions

Incidence of adverse reactions during treatment were also observed and recorded.

Quality of life

Quality of life was assessed using quality of life questionnaire (EORTC QLQ-C30) [11].

Pulmonary function

Pulmonary function of all patients before and after treatment was measured by the MSA99 pulmonary function instrument (Beijing MSA99), which included the maximum volume of air (MVV), the maximum expiratory flow rate (PEF), the ratio of forced expiratory volume in 1 second to forced vital capacity (PEV1/FVC), and diffusion coefficient (DLCO/VA).

Statistical analysis

Data were analyzed using Statistical Packages for Social Sciences (SPSS) 25.0 (IBM, Armonk, NY, USA). Continuous data are presented as mean ± standard deviation (SD) and compared using the independent sample t-test and Mann-Whitney U test, depending on the distribution of the data. Categorical data are presented as frequency and percentages and compared using Chi-square test. $P < 0.05$ was considered statistically significant.

RESULTS

Baseline clinical data

There was no significant difference in baseline data (age, sex ratio, smoking history, and tumor stage) between study and control groups including ($p > 0.05$; Table 1).

Tumor remission rate

Study group showed significantly higher tumor remission rate compared to control group ($p < 0.05$; Table 2).

Table 1: Baseline clinical data (N, %; N = 50 in each group)

Variable	Control	Study	*t*/χ^2	*P*-value
Age (years)	58.35±10.45	57.78±11.32	2.327	0.744
Male	35(70%)	36(72%)	3.847	0.822
Smoking history	25(50%)	27(54%)	3.495	0.678
Tumor staging				
I	10(20%)	12(24%)	4.503	0.554
II	15(30%)	13(26%)	3.593	0.650
III	25(50%)	25(50%)	3.593	1.000

***Note*:** Age was presented in mean ± SD

Table 2: Tumor remission rate

Group	CR	PR	SD	PD	ORR (CR+PR)
Control	2(4%)	15(30%)	20(40%)	13(26%)	17(34%)
Study	5(10%	23(46%)	18(36%)	4(8%)	28(56%)
χ^2	2.312	4.012	0.248	5.667	4.689
P-value	0.028	0.045	0.019	0.017	0.032

Table 3: Survival time (mean ± SD) (N = 50 in each group)

Group	Median overall survival (months)	Median progression free survival (months)
Control	22.45±5.32	8.35±2.45
Study	24.67±5.78	10.50±2.64
T-value	3.495	2.495
P-value	0.036	0.021

Table 4: Incidence of adverse reactions (N, %)

Group	Control	Study	χ^2	*P*-value
Neutropenia	25(50)	19(38)	3.04	0.031
Thrombopenia	18(36)	13(26)	2.41	0.021
Hemoglobin decrease	20(40)	15(30)	2.5	0.014
Oral mucositis	28(56)	23(46)	2.28	0.031
Nausea and vomiting	37(74)	28(56)	4.96	0.026
Diarrhea	33(66)	26(52)	3.14	0.036
Alopecia	27(54)	20(40)	3.86	0.049

Survival time

Study group showed significantly higher survival time compared to control group. Also, study group showed significantly longer PFS compared to control group ($p < 0.05$, Table 3).

Adverse reactions

Study group showed significantly lower incidence rates of various adverse reactions, including neutropenia, thrombocytopenia, hemoglobin decline, oral mucositis, nausea and vomiting, diarrhea, and alopecia compared to control group ($p < 0.05$, Table 4).

Quality of life scores

Study group showed significantly higher quality of life scores after treatment compared to control group ($p < 0.05$, Table 5).

Pulmonary function

Pulmonary function indices were compared before and after treatment in the two groups and the result revealed that study group showed significantly higher PEF and MVV levels compared to control group ($p < 0.05$, Table 6).

DISCUSSION

Tuberculosis (TB) triggers a specific cell-mediated immune response, and the risk of lung cancer is about three times higher in people with TB compared to other groups [2]. This is because TB infection may lead to decreased immunity, drugs such as isoniazid and rifampicin, may inhibit function of lymphocytes and macrophages [11], necrotic foci, cavity formation and fibrosis caused by tuberculosis infection forms scar tissue in the lungs, and reduces immune monitoring ability of lymphocytes thus accelerating the growth of cancer cells [12].

Table 5: Quality of life scores (mean ± SD)

Group	Score
Control	66.25±8.75
Study	68.50±9.21
T-value	3.495
P-value	0.039

Table 6: Pulmonary function indices (mean ± SD)

Parameter	Control		Study	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
FEV1 (L)	1.38±0.21	1.40±0.26	1.35±0.26	1.42±0.22
FEV1/FVC (%)	59.45±8.12	60.40±7.55	59.31±6.57	59.41±8.29
PEF (L/s)	2.65±0.46	2.85±0.24[a]	2.64±0.37	3.07±0.49[a,b]
MVV (L)	61.76± 10.19	60.20±7.31	60.88±6.28	65.85±5.21[ab]
DLCO/VA (%)	95.94± 10.12	98.35± 18.20	93.93±20.17	95.90± 14.13

Note: FEV1 (Forced expiratory volume in 1 second); FEV1/FVC (Forced expiratory volume in 1 second divided by forced vital capacity); PEF (Peak expiratory flow); MVV (Maximum voluntary ventilation); DLCO/VA (Diffusing capacity of the lung for carbon monoxide divided by alveolar volume). [a]$P < 0.05$ vs pre-treatment, [b]$p < 0.05$ vs control group

Furthermore, tuberculosis may cause bronchial distortion and blockage of lymphatic blood circulation in the lungs, causing long-term accumulation of carcinogens. For patients suffering from both tuberculosis and lung cancer, attention should be paid to improving immune function in addition to standard anti-tuberculosis and anti-tumor therapy [13]. Patients with lung cancer or tuberculosis often have decreased lung function and overall vitality due to reduced breathing area, weakened ability to breathe deeply, cough and expectorate, prone to dyspnea, reduced activity, and significantly impaired quality of life [14]. Lentinan is a macromolecular glycan with good immunomodulatory function. By activating and regulating the cellular and humoral immune system, it enhances anti-tumor effect of the body and reduces side effects of chemotherapeutic drugs. At the same time, it also has a synergistic effect on treatment of tuberculosis [15].

These results showed that study group treated with lentinan and DN chemotherapy showed better clinical effects in terms of ORR, OS, PFS, incidence of adverse reactions and quality of life score. Compared to DN chemotherapy alone. Overall response rate in study group was significantly higher compared to control group. These results suggest that lentinan may have the potential to enhance efficacy of chemotherapy. This is consistent with other research findings which showed that lentinan improves sensitivity of tumor cells to chemotherapeutic drugs and has an immunomodulatory effect [16]. This may be due to the ability of lentinan to enhance immune response, thereby helping the body fight tumor cells more effectively.

The median OS and PFS was significantly higher in study group compared to control group. This finding suggests that lentinan may help prolong survival of patients with pulmonary tuberculosis and NSCLC. This is consistent with the findings of other studies on anti-tumor effects of lentinan [17]. Also, treatment with lentinan in combination with DN chemotherapy reduces incidence of adverse reactions. This suggests that combined use of lentinan may help alleviate the adverse reactions caused by chemotherapy.

This may be because lentinan has a certain protective effect, which reduces the toxicity of chemotherapeutic drugs to normal cells [18]. Furthermore, study group showed significantly higher quality of life score compared to control group. This suggests that addition of lentinan helps improve overall well-being of patients, which is very important for long-term treatment and quality of life of cancer patients.

Improved quality of life may be associated with reduced adverse reactions and longer survival. In addition, improvements in lung function indices further support these findings. Pulmonary function following lentinan administration was improved in study group compared to control group. More specifically, study group showed significantly higher PEF and MVV levels after treatment compared to pre-treatment values and control group. These improvements may be attributed to several underlying mechanisms. The chosen treatment approach likely targeted airway inflammation and obstruction, leading to reduced inflammation and improved airflow.

Successful treatment of TB may have contributed to resolution of pulmonary infection and subsequent improvement in lung function. Additionally, tumor regression and decreased tumor burden in NSCLC patients may have alleviated airway compression and improved airflow dynamics. As a result, the treatment approach may have facilitated lung tissue repair and remodeling processes, resulting in enhanced alveolar function, gas exchange efficiency, and diffusion capacity. However, further research is needed to comprehensively understand the intricate interplay between TB and NSCLC, as well as the specific mechanisms involved.

Limitations of this study

Although the results of this study are positive, there are some limitations. As a retrospective study, there are potential selection bias and information bias. Also, the sample size was relatively small, which may limit the general applicability of the results. Future studies will validate these findings through prospective, randomized controlled multi-center studies to investigate the effects of lentinan in patients with different tumor types and stages.

CONCLUSION

Lentinan combined with DN chemotherapy improves objective remission rate of tumors, prolongs survival, improves quality of life, reduces the occurrence of adverse reactions and improves pulmonary function. These findings provide a new perspective for future studies as a scientific basis for the application of lentinan in the treatment of pulmonary tuberculosis complicated by NSCLC may have been proposed.

DECLARATIONS

Acknowledgement

None.

Funding

None provided.

Ethical approval

The Medical Ethics Committee of Ankang People's Hospital, China gave the approval for this study (EC2022-134).

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

The authors 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 them.

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