

Clinical study of Shenqi Fuzheng decoction directional penetration for the treatment of cancer pain in advanced lung cancer patients

Estudio clínico de penetración direccional de decocción Shenqi Fuzheng para el tratamiento del dolor por cáncer en pacientes con cáncer de pulmón avanzado

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Abstract

Objective: The study aimed at analyzing the effect of Shenqi Fuzheng Decoction directional penetration for treating advanced lung cancer patients with cancer-related pain. **Method:** Eighty-six cases with advanced lung cancer received in Zhoushan Hospital of Traditional Chinese Medicine from June 2022 to June 2023 were divided randomly into a study group ($n = 43$) and control group ($n = 43$). Two groups were treated with the same conservative treatment plan, on the basis of which the control group treated with placebo, and study group received Shenqi Fuzheng Decoction directional penetration treatment. The cancer-related pain intensity, analgesic onset time, the frequency of pain outbreak, and analgesic duration were assessed and recorded. Before and after treatment, the cancer-related fatigue, quality of life, and Karnofsky Performance Status (KPS) score were assessed in two groups. Moreover, the adverse reactions of two groups during treatment were recorded. **Results:** Compared to the control group, the cancer-related pain intensity of the study group was reduced, the analgesic onset time was shortened, the frequency of pain outbreak was reduced, and the analgesic duration was prolonged ($p < 0.05$). After treatment, Piper Fatigue Scale (PFS) scores in the study group were lower than the control group, and the generic quality of life inventory-74 (GQOLI-74) and KPS scores in the study group were higher than the control group ($p < 0.05$). During the treatment period, no significant adverse reactions were observed in both groups ($p > 0.05$). **Conclusion:** Shenqi Fuzheng Decoction directional penetration treatment has a remarkable effect in advanced lung cancer patients with cancer pain, which can relief the pain intensity, prolong the duration of pain relief, reduce the number of pain attacks, relieve patients' cancer-related fatigue, and improve patients' life quality and health status.

Keywords: Shenqi Fuzheng Decoction. Advanced lung cancer. Cancer-related pain. Cancer-related fatigue. Directional penetration.

Resumen

Objetivo: El objetivo del estudio fue analizar el efecto de la penetración direccional de decocción Shenqi Fuzheng para el tratamiento de pacientes con cáncer de pulmón avanzado con dolor relacionado con el cáncer. **Método:** Ochenta y seis casos

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de cáncer de pulmón avanzado recibidos en el Hospital Zhoushan de medicina tradicional China de junio de 2022 a junio de 2023 se dividieron al azar en grupo de estudio ($n = 43$) y grupo control ($n = 43$). Dos grupos fueron tratados con el mismo plan de tratamiento conservador, sobre la base del grupo control tratado con placebo, y el grupo de estudio recibió tratamiento de penetración direccional de decocción Shenqi Fuzheng. Se evaluaron y registraron la intensidad del dolor relacionado con el cáncer, el tiempo de inicio del dolor, la frecuencia del brote del dolor y la duración del dolor. Antes y después del tratamiento se evaluaron el grado de cansancio relacionado con el cáncer, la calidad de vida y el puntaje del estado funcional de Karnofsky (KPS) en dos grupos. Se registraron las reacciones adversas de los dos grupos durante el tratamiento. **Resultados:** En comparación con el grupo control, se redujo la intensidad del dolor relacionado con el cáncer del grupo de estudio, se acortó el tiempo de inicio analgésico, se redujo la frecuencia del brote de dolor y se prolongó la duración analgésica ($p < 0.05$). Después del tratamiento, los resultados de la escala de fatiga de Piper (EFP) en el grupo de estudio fueron más bajos que en el grupo de control, los del inventario genérico de calidad de vida-74 (GQOLI-74) y los del KPS en el grupo de estudio fueron más altos que en el grupo de control ($p < 0.05$). Durante el periodo de tratamiento no se observaron reacciones adversas significativas en ambos grupos ($p > 0.05$). **Conclusión:** el tratamiento de penetración direccional de decocción Shenqi Fuzheng tiene un efecto notable en pacientes con cáncer de pulmón avanzado con dolor de cáncer, que puede aliviar la intensidad del dolor, prolongar la duración del alivio del dolor, reducir el número de ataques de dolor, aliviar la fatiga relacionada con el cáncer y mejorar la calidad de vida y el estado de salud de los pacientes.

Palabras clave: Decocción de Shenqi Fuzheng. Cáncer de pulmón avanzado. Dolor relacionado con el cáncer. Fatiga relacionada con el cáncer. Penetración direccional.

Introduction

As a common malignant tumor worldwide, lung cancer is the main cause of cancer death and poses a threat to human life safety¹. For lacking typical symptoms, most lung cancer patients have developed to an advanced stage when they are first diagnosed, thus missing the best opportunity for treatment^{2,3}. Cancer-related pain and fatigue, as the common symptoms in advanced cancer patients, is also an important factor affecting the life quality of patients⁴. Cancer-related pain can influence the sleep and diet of patients, resulting in gradual weakness and weakening the patient's will to live⁵. Cancer-related fatigue can make patients feel weak and lack the energy and physical strength to carry out daily activities⁶. Therefore, it is necessary to take effective treatment measures to relieve cancer-related pain and fatigue.

At present, traditional Chinese medicine has become increasingly prominent for cancer-related pain and fatigue due to its stable curative effect and small side effects. Traditional Chinese medicine believes that the deficiency of vital-qi is the root cause of cancer pain, and it is closely related to the factors of six climatic exopathogens, phlegm and fluid retention, static blood, and damaged by excess of seven emotions⁷. When the vital qi is insufficient or internally weakened, it renders the body vulnerable to invasion by the six climatic exopathogenic factors (the six evils), and also affects the smooth flow of qi and blood. When the vital qi is

insufficient or internally weakened, it renders the body vulnerable to invasion by the six climatic pathogenic factors (the six evils) and also affects the smooth flow of qi and blood. Chronic qi and blood stasis can lead to the generation of cancerous toxins, which develop into cancerous masses. These masses block the meridians and collaterals, leading to qi and blood stagnation and causing pain⁸. Therefore, traditional Chinese medicine believes that invigorating qi and reinforcing the body, promoting blood circulation and regulating qi, resolving blood stasis, and relieving pain are the fundamental treatment methods⁹. Directional penetration therapy belongs to the external treatment of traditional Chinese medicine, which can make the drug directly reach the disease site through the body surface, avoiding the toxic side effects of intestinal administration, and has more advantages in the application of advanced tumor patients^{10,11}.

Shenqi Fuzheng Decoction as commonly used prescription for advanced malignant tumors in Chinese medicine has a remarkable effect on improving the patients' life quality. However, the application of Shenqi Fuzheng Decoction in advanced cancer patients is mostly taken internally, and the therapeutic effect of external use on cancer pain patients has not been reported¹². Therefore, this study applied Shenqi Fuzheng Decoction directional penetration in advanced lung cancer patients and discussed its effects on cancer-related pain and fatigue, to provide evidence for its clinical application.

Research methods

Ethical approval

Before participating in this study, ethical approval was obtained from the hospital review board, and written informed consent was obtained from the patients or their guardians.

Patients

This study included patients with advanced lung cancer who were admitted to Zhoushan Hospital of Traditional Chinese Medicine from June 2022 to June 2023. Inclusion criteria: Age 45–70 years old; all patients follow the guidelines of diagnosis and management of lung cancer; tumor node metastasis (TNM) classification III–IV; patients with an expected survival time of more than 3 months; patients have cancer pain symptoms; patients have no other critical illness; patients consented to a follow-up. Exclusion criteria: patients with other malignant tumors, cardiovascular and cerebrovascular diseases; patients have other non-cancer-related pain; pregnant or lactating women; patients with ulcerated or sensitive skin; patients with mental abnormalities; patients dropped out of the study for multiple reasons. Based on these criteria, 86 cases were chosen as study objects and randomly assigned to two groups, with 43 cases in each group.

Therapeutic methods

The control group was given placebo treatment: 50 mg lemon yellow was dissolved in 1000 mL 5% sodium chloride injection, and then evenly mixed, an appropriate amount of liquid was dipped in sterile cotton and gently applied to the cancer pain site, once every 6 h, continuous treatment for 14 days.

The study group was received Shenqi Fuzheng Decoction directional penetration treatment: Shenqi Fuzheng Decoction is composed of Dang-shen, Huang-qi, Bai-shu, Dang-gui, Dan-shen, Ji-xue-teng, Sang-zhi, Chi-shao, and Yan- hu-suo. After the above medicines were soaked for 30 min, they were boiled with a military fire and then boiled over gently. The medicinal liquid was collected and then added nitrogen ketone into the medicinal liquid to make a mixture. Then 10 mL of the medicinal liquid was injected into a special cotton pad. After the liquid permeated, the cotton pad was placed on the electrode plate, the electrode was pressed close

to the patient's skin pain point, and the parameters of the traditional Chinese medicine directional penetration instrument were set, 30 min/time, 1–2 times/day, and the treatment was continuous for 14 days.

Outcome measures

After treatment for 7 days, the pain intensity of the patients was evaluated by verbal rating scale, which divided the pain intensity into for grades. The analgesic onset time, analgesic duration, and the number of pain outbreaks were recorded in both groups. Before and after treatment, the Piper Fatigue Scales (PFS) were used to evaluate the fatigue degree of patients from four dimensions: behavior dimension, emotion dimension, perception dimension, and cognition dimension. Each dimension was scored from 0 to 10 points and the higher the score, the more severe degree of cancer-related fatigue. The life quality was evaluated by generic quality of life inventory-74 (GQOLI-74) scale, which including four aspects of physical function, social function, mental health, and health status, with a total score of 100 points. A higher score indicates a better quality of life for patients. The health status of two groups was evaluated by Karnofsky Performance Status (KPS) with a total score of 100 points, and a higher score indicates better health status of patients. The adverse reactions during treatment in two groups were observed.

Statistical methods

The data were analyzed by SPSS 24.0 statistic software. Patient's age, body mass index, analgesic onset time, frequency of pain outbreak, analgesic duration, GQOLI-74, KPS, and PFS scores were represented as mean $\pm$ standard deviation and t-test was used to compare between groups. Classification data and grade data were reported by frequency and percent, and analyzed by Chi-squared test and Wilcoxon rank sum test. $p < 0.05$ was considered significant.

Results

Baseline characteristics

No visible differences were observed in terms of sex, age, body mass index, TNM classifications, and squamous carcinoma between two groups ($p > 0.05$) (Table 1).

Table 1. Baseline characteristics in two groups

Variable	Study group (n = 43)	Control group (n = 43)	t/ χ^2 -values	p
Sex (male/female)	26/17	28/15	0.199	0.655
Age (years)	61.46 $\pm$ 6.38	62.03 $\pm$ 6.79	0.401	0.689
Body mass index (kg/m ²)	22.23 $\pm$ 2.08	21.86 $\pm$ 1.64	0.916	0.362
TNM classifications				
III	19 (44.19)	21 (48.84)	0.187	0.665
IV	24 (55.81)	22 (51.16)		
Pathological types				
Squamous carcinoma	16 (37.21)	15 (34.88)	0.724	0.733
Adenocarcinoma	22 (51.16)	25 (58.14)		
Adenosquamous carcinoma	5 (11.63)	3 (6.98)		

Table 2. Comparison of pain intensity between two groups

Groups	Painless	Mild pain	Moderate pain	Severe pain
Study group (n = 43)	7 (16.28)	19 (44.19)	14 (32.56)	3 (6.98)
Control group (n = 43)	1 (2.32)	13 (30.23)	21 (48.84)	8 (18.60)
Z		2.935		
p		0.003		

The pain intensity

After treatment, the pain intensity in the study group was apparently relieved than control group ($p < 0.05$) (Table 2).

Analgesic onset time, analgesic duration, and frequency of pain outbreak

The analgesic onset time and the frequency of pain outbreak in the study group were distinctly reduced, and the analgesic duration was prolonged compared with the control group ($p < 0.05$) (Table 3).

Cancer-related fatigue

After treatment, the scores of behavior fatigue, emotion fatigue, perception fatigue, and cognition fatigue in the study group were lower than the control group ($p < 0.05$) (Table 4).

The life quality and health status

After treatment, the GQOLI-74 and KPS scores of the study group were increased observably compared to the control group ($p < 0.05$) (Table 5).

Adverse reactions

During treatment, no severe adverse reactions occurred in both groups, one case had dizziness, one case had gastrointestinal discomfort in the study group with a total incidence of 4.65% (2/43); two cases had gastrointestinal discomfort and one case had constipation in control group with a total incidence of 6.98% (3/43) ($p > 0.05$).

Discussions

Lung cancer is a malignant disease threatening human life and health, its morbidity and mortality increase year by year, and the incidence group tends to be younger¹³. Advanced lung cancer patients are intolerant to surgery, radiotherapy, chemotherapy, and other treatments due to decreased physical tolerance, and they also suffer from cancer pain while undergoing treatment pain¹⁴. Cancer pain can lead to depression, anxiety, depression, and other conditions, affect their sleep and mental state, and greatly reduce the life quality of patients. Therefore, taking valid treatment measures to relieve cancer pain for advanced lung cancer patients is very important for the improvement of patients' life quality. Western medicine mainly uses non-hormone analgesics and opioids to treat cancer pain. Although this type medicines can relieve cancer pain to a certain extent, long-term use of them will lead to intolerance of patients, drug dependence, or accumulation of toxins in the body, which will damage the function of other healthy parts^{15,16}. At present, traditional Chinese medicine has gradually shown its superiority in cancer pain due to its high safety, high patient tolerance, low price, and no dependence¹⁷.

Table 3. Comparison of analgesic onset time, analgesic duration, and frequency of pain outbreak between two groups

Groups	Analgesic onset time (min)	Frequency of pain outbreak (times/day)	Analgesic duration (h)
Study group (n = 43)	57.69 ± 7.75	2.38 ± 0.55	12.62 ± 2.46
Control group (n = 43)	65.27 ± 8.06	3.45 ± 0.64	10.74 ± 2.67
t	4.428	8.315	3.396
p	0.000	0.000	0.001

Table 4. Comparison of cancer-related fatigue between two groups

Groups	Behavior fatigue		Emotion fatigue		Perception fatigue		Cognition fatigue	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Study group (n = 43)	6.86 ± 1.48	4.08 ± 1.05 ^a	6.74 ± 1.47	4.14 ± 1.07 ^a	6.87 ± 1.74	4.29 ± 0.86 ^a	4.57 ± 1.14	2.72 ± 0.45 ^a
Control group (n = 43)	6.43 ± 1.54	5.04 ± 1.26 ^a	6.82 ± 1.44	5.26 ± 1.06 ^a	6.59 ± 1.68	5.28 ± 1.13 ^a	4.39 ± 1.08	3.78 ± 0.64 ^a
t	1.320	3.838	0.255	4.876	0.759	4.572	0.752	8.884
p	0.190	0.000	0.799	0.000	0.450	0.000	0.454	0.000

^ap < 0.05 versus before treatment.**Table 5. Comparison of GQOLI-74 and KPS scores between two groups**

Groups	GQOLI-74		KPS	
	Before treatment	After treatment	Before treatment	After treatment
Study group (n = 43)	56.86 ± 8.38	70.08 ± 6.75 ^a	50.18 ± 6.37	72.57 ± 7.86 ^a
Control group (n = 43)	58.43 ± 7.54	65.44 ± 7.26 ^a	49.86 ± 5.46	64.42 ± 6.75 ^a
t	0.913	3.069	0.250	5.158
p	0.364	0.003	0.803	0.000

^ap < 0.05 versus before treatment.

In the view of traditional Chinese medicine, the cancer pain is relative to the deficiency of vital qi, the invasion of pathogenic factors, and the stasis of qi and blood in the organs and bones, which can lead to the blockage of qi and blood in the channels and collaterals, and the stasis causes pain¹⁸. Therefore, the treatment should be based on strengthening the body and removing evil, nourishing qi and activating blood circulation, removing blood stasis, and relieving pain. Shenqi Fuzheng Decoction is a prescription composed of Dang-shen, Huang-qi, Bai-shu, Dang-gui, Dan-shen, and other medicinal herbs. Among them, Dang-shen can tonify middle and replenish qi, Huang-qi can replenish qi and consolidating exterior, Dan-shen can invigorate blood circulation and regulate

menstruation, remove blood stasis and relieve pain, Dang-gui can tonify blood and invigorate menstruation, move qi and relieve pain, Bai-shu can invigorate the spleen and benefit qi, Chi-shao can remove blood stasis and relieve pain, Ji-xue-teng and Sang-zhi can remove blood stasis and clear collaterals, and Yan-hu-suo can invigorate blood and relieve pain. The combination of the above herbs can invigorate qi and reinforce the body, promote blood circulation and regulate qi, resolve blood stasis, and relieve pain. Therefore, this study tried to apply Shenqi Fuzheng Decoction to advanced lung cancer patients and explore its therapeutic effect on cancer pain. In addition, considering the gastrointestinal weakness of patients with advanced

tumors, this study attempted to use percutaneous directional penetration therapy.

The results in this study displayed the pain intensity in the study group was relieved apparently, the analgesic onset time and the frequency of pain outbreak were distinctly reduced, and the analgesic duration was prolonged compared with the control group, suggesting that Shenqi Fuzheng Decoction directional penetration therapy can effectively mitigate the cancer pain of patients. This result also confirmed that the analgesic onset time of directional penetration therapy is shorter and the effect is more durable and stable. This may be because percutaneous directional penetration absorbs medicine through the skin and mucosal surface, allowing the drug to reach the disease. Luo et al. confirmed that transdermal administration of traditional Chinese medicine has obvious advantages in pain relief¹⁹. The results showed that the scores of behavior fatigue, emotion fatigue, perception fatigue, and cognition fatigue of the study group were decreased compared with the control group after treatment, revealing that Shenqi Fuzheng Decoction can improve markedly cancer-related fatigue of patients with advanced lung cancer. In Zhu's study²⁰, a tumor-bearing mouse fatigue model was established to confirm the anti-fatigue effect of Shenqi Fuzheng injection; the results indicated that Shenqi Fuzheng injection might be as a potential therapy for cancer-related fatigue. The results showed that GQOLI-74 and KPS scores in the study group were higher than control group after treatment, illustrating that Shenqi Fuzheng Decoction directional penetration treatment can improve the life quality and health status of patients, which may be related to the alleviation of cancer pain and cancer fatigue in patients. No obvious adverse reactions were found during treatment, suggesting that Shenqi Fuzheng Decoction directional penetration has no obvious safety risks in advanced lung cancer patients, clarifying the feasibility of its application.

Conclusion

Shenqi Fuzheng Decoction directional penetration has a remarkable therapeutic effect on advanced lung cancer patients, which can quickly relieve the cancer pain, prolong the efficacy time, reduce the frequency of outbreak pain, alleviate cancer fatigue, and improve the life quality of patients.

Despite its findings, this study is not without flaws. This study is a single-center analysis, not a large sample study. In the future, multi-center and large

sample size prospective researches are still necessary to verify and promote the results of this study, so as to provide a more powerful basis for the treatment of advanced lung cancer patients with cancer pain, further improve the life quality of patients.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. Ethical approval was given by the Zhoushan Hospital of Traditional Chinese Medicine and written informed consent was obtained from all patients.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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