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The Observation of Clinical Efficacy and Safety of De-Platinum-Based Pleural Perfusion in the Treatment of Malignant Pleural Effusion and Its Correlation with the Expression of VEGF in Pleural Fluid

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Abstract

Background: Malignant pleural effusion (MPE) is the most common complication of advanced NSCLC. Infusion chemotherapy is currently one of the most common intracavitary treatments for MPE. Unfortunately, there is no definitive consensus on which intracavitary infusion drug has the best effect on the treatment. The use of de-platinum-based thoracic perfusion therapy can offer several advantages, such as reducing drug toxicity and contributing to an improvement in patients' physical condition. Therefore, this study was to investigate the clinical efficacy and safety of de-platinum-based pleural perfusion bevacizumab combined with Brucea Javanica Oil Emulsion Injection (BJOEI) in the treatment of malignant pleural effusion in advanced lung adenocarcinoma. **Methods:** A total of 60 patients diagnosed with lung adenocarcinoma and malignant pleural effusion were selected from Binzhou People's Hospital, Shandong Provincial Cancer Hospital, and Binzhou Central Hospital between June 2022 and May 2024, with 30 cases treated in each group. The study was divided into two groups: the treatment group received bevacizumab injection perfusion in combination with intravenous infusion of Brucea Javanica Oil Emulsion Injection (BJOEI), while the control group received bevacizumab

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injection combined with cisplatin perfusion. To analyze the data and evaluate their efficacy and adverse reactions, such as disease control rate (DCR), overall response rate (ORR), Karnofsky Performance Status (KPS), vascular endothelial growth factor (VEGF), and so forth. **Results:** Following the treatment, the quality of life scores in both groups exhibited an increase compared to pretreatment levels. Moreover, the enhancement observed in the treatment group was deemed statistically significant ($P = 0.007$). Following treatment, The expression of VEGF in the pleural effusion of both groups of patients was significantly decreased, and the disparity within the same group was found to be statistically significant ($P < 0.001$). The expression level of VEGF in the pleural effusion of the treatment group was significantly lower than that of the control group, and the difference was statistically significant ($P < 0.001$). In the treatment group, the objective response rate (ORR) was 73.3% (22/30), and the disease control rate (DCR) was 93.3% (28/30). In the control group, the ORR was 66.7% (20/30), and the DCR was 90.0% (27/30). There was no statistically significant difference between the two groups ($\chi^2 = 0.317$, $P = 0.573$; $\chi^2 = 0.218$, $P = 0.640$). A stratified analysis of factors influencing the ORR revealed that the ORR in both groups exhibited statistical significance when the previous KPS score was below 70 ($\chi^2 = 5.850$, $P = 0.016$). The main adverse reactions in both groups included nausea, vomiting, gastrointestinal reactions, fatigue, and hematological toxicity. Among them, there was a statistically significant difference in the occurrence of gastrointestinal reactions and fatigue between the two groups ($\chi^2 = 8.148$, $P = 0.004$; $\chi^2 = 6.696$, $P = 0.010$). **Conclusion:** Bevacizumab, when combined with Brucea Javanica Oil Emulsion Injection (BJOEI), demonstrates noteworthy efficacy in treating malignant pleural effusion. This combination therapy reduces VEGF expression, in which the reduction supports the efficacy of thoracic perfusion and is associated with minimal adverse reactions, contributing to an improvement in patients' physical condition and overall clinical tolerability, especially for the poor physique, especially in the elderly and KPS score is less than 70. Therefore, it can be considered a recommended approach for managing malignant pleural effusion, offering significant clinical value.

Keywords

Bevacizumab, Brucea Javanica Oil Emulsion Injection, Advanced Lung Adenocarcinoma, Malignant Pleural Effusion

1. Introduction

In recent years, lung cancer has become the highest incidence and mortality of all malignant tumors in the world; at the same time, NSCLC has become the most common histopathological subtype of lung cancer [1]-[3]. Relevant data shows that three-quarters of patients are already in the middle or advanced stages of diagnosis, missing the opportunity for radical surgical resection. Meanwhile, malignant pleural effusion (MPE) is the most common complication of advanced NSCLC.

The clinical manifestations of MPE include shortness of breath, chest tightness, chest pain, etc. Infusion chemotherapy is currently one of the most common intracavitary treatments for MPE [4]-[6]. In clinical practice, there are various types of intracavitary infusion drugs available, such as sclerosants, cell biological response regulators, anti-tumor angiogenesis drugs, and traditional Chinese medicine preparations. Unfortunately, there is no definitive consensus on which intracavitary infusion drug has the best effect for the treatment of certain conditions. According to the relevant research reports [7]-[9], the combination of anti-angiogenic drugs and platinum-based intracavitary perfusion demonstrates a certain synergistic effect, leading to improved clinical efficacy. While Bevacizumab combined with cisplatin thoracic perfusion has shown promise in reducing MPE, it is important to note that cisplatin can cause significant local irritation and gastrointestinal reactions. Additionally, cisplatin may have limited efficacy in treating patients with lung malignancies accompanied by malignant pleural effusion. Therefore, it is essential to consider these factors when selecting treatment options for patients with such conditions. Also, high-dose cisplatin therapy can lead to various adverse effects, including ototoxicity (damage to the ear), bone marrow suppression (resulting in decreased blood cell production), and hepatorenal toxicity (affecting the liver and kidneys). These side effects can significantly impact the tolerance and quality of life of patients undergoing treatment with high-dose cisplatin. Therefore, careful monitoring and management of these potential toxicities are crucial in the clinical setting to optimize patient outcomes and safety [10]-[12].

In the current era of de-chemotherapy and the recognized challenges associated with traditional chemotherapy, the using of de-platinum-based thoracic perfusion therapy can offer several advantages. This approach can significantly reduce drug toxicity and side effects, such as nausea and vomiting, commonly associated with systemic chemotherapy. This targeted approach may offer a promising alternative for patients who may benefit from localized therapy while avoiding some of the drawbacks of traditional cisplatin chemotherapy.

In recent years, with the rapid development of molecular biomedicine, vascular endothelial growth factor has been more and more widely detected, which has further clarified the mechanism of the formation of MPE. Relevant researches show [13]-[15] that the content of VEGF is significantly increased in MPE, and the VEGF family is mainly divided into five glycoprotein ligands, A, B, C, D and E, and two placental growth factors, PLGF-1 and PLGF-2, which are expressed to a certain extent with the generation and development of malignant tumors; it can improve the permeability of blood vessels, accelerate the formation of tumor new vessels, and increase the formation of pleural effusion to a certain extent. Theoretically, giving drugs to inhibit VEGF during thoracic perfusion can reduce the VEGF level and have a certain effect on controlling MPE.

Relevant research report [16]-[18], the main components of Brucea Javanica Oil Emulsion are oleic acid and linoleic acid, which have effects on the anti-tumor and immune enhancement. It can control the growth of tumor cells, induce apoptosis

of tumor cells, and regulate tumor angiogenesis, which can reduce the VEGF level. Based on the less research on the application of combination therapy in thoracic treatment, there is a lack of data on efficacy and safety evaluation. Therefore, this study investigated the clinical efficacy and safety of the combination of Brucea Javanica oil emulsion and Bevacizumab thoracic perfusion therapy, and further analyzed the clinical value of the de-platinum-based thoracic perfusion therapy for malignant pleural effusion. The report is as follows.

2. Materials and Methods

2.1. Patients Selection

A total of 60 patients with lung adenocarcinoma and malignant pleural effusion were collected from June 2022 to May 2024 from Binzhou People's Hospital, Shandong Provincial Cancer Hospital, and Binzhou Central Hospital, who confirmed moderate or above pleural effusion by Ultrasound in all cases. The collection of patients from multiple hospitals may help to provide a diverse sample for the study and potentially improve the generalizability of the findings.

2.2. Inclusion Criteria

1) The lung adenocarcinoma patients who were diagnosed by cellular or histopathological examination, and who have pleural effusion with the result of ultrasound, were performed to extract pleural effusion for examination, and the results were MPE;

2) Moderate or above fluid accumulation, estimated survival time ≥ 6 months, KPS score ≥ 50 points;

3) The patients have not received radiotherapy, chemotherapy, and intracavity infusion therapy within the past 30 days;

4) The electrocardiogram, blood cells, and coagulation function are normal;

5) The EGFR and ALK of genetics can be detected by tissues or blood in patients with lung adenocarcinoma;

6) The research methods, diagnostic and treatment processes must be explained to the participants, and they must sign the informed consent form.

2.3. Exclusion Criteria

1) Patients who have received systemic chemotherapy within the past month;

2) Mixed with other interventional therapy;

3) Patients have combined with consciousness and mental disorders and poor compliance;

4) The contraindication of thoracentesis or a history of allergies to the investigational drug;

5) The pregnant and lactating period of women;

6) Patients have autoimmune diseases or other diseases that can affect immune function.

The Ethics Committee of **Binzhou People's Hospital** approved the study.

2.4. Treatment Methods

After hydropleural positioning, pleural puncture and drainage were performed according to the principle of aseptic operation, and the catheter entered the chest 8 - 12 cm, connected to the drainage bag, and fully drained. When ultrasound confirmed that the fluid was basically drained, the administration of a combination of ondansetron and dexamethasone 30 minutes before a procedure is a standard practice to prevent vomiting and nausea in patients.

In the control group: Bevacizumab (Qilu Pharmaceutical Co., Ltd., S20190040) 200 mg Q2w chest perfusion + cisplatin (Qilu Pharmaceutical Co., LTD., H20023461) 60 mg d1, 8; In the treatment group: Bevacizumab (Qilu Pharmaceutical Co., LTD., S20190040) 200 mg Q2w chest perfusion + (Brucea Javanica Oil Emulsion 30 ml intravenous infusion, once per day).

After completing the drug perfusion, the chest drain was promptly closed, and it remained closed for a period of 48 hours. This duration allowed for optimal contact between the medication and the pleura, facilitating the desired therapeutic effect. To enhance the distribution and absorption of the drug within the pleural space, the patient was instructed to change positions every 2 hours during the drug retention period. These position changes likely helped ensure uniform exposure of the pleura to the medication and promoted its effective action.

In cases where pleural effusion persists despite initial treatment, repeat thoracic perfusion therapy may be warranted. The procedure described earlier, involving chest drain placement, drug perfusion, and patient positioning, can be repeated to address ongoing effusion and promote effective drug delivery to the pleura.

A maximum of four treatment cycles may be considered for thoracic perfusion therapy to manage pleural effusion. Throughout the treatment process, if the patient experiences nausea and vomiting, proton pump inhibitors (PPIs) or other medications for acid suppression and antiemetic drugs can be administered to alleviate these symptoms.

Additionally, providing nutritional support to the patient is important to maintain their overall well-being and aid in recovery. After two cycles of continuous administration, the efficacy of the treatment can be assessed to determine the response to thoracic perfusion therapy for pleural effusion. Both groups of patients, those receiving the treatment and the control group, should continue to receive their prescribed chemotherapy and targeted medications. It is important to ensure that there is a gap of more than one month between the administration of chemotherapy and the intrathoracic drug injection to avoid potential interactions or adverse effects.

2.5. Observation Indicators

Changes in the volume of pleural effusion will be reviewed every 2 cycles by using the ultrasound or chest CT. At the same time. Measurement of VEGF: Pleural effusion was extracted before and after the course of treatment, and VEGF was

measured by ELISA. Also, the improvement in physical condition was evaluated using the Karnofsky (KPS) Performance Scale before and after treatment.

2.6. Efficacy Evaluation

The evaluation of MPE was based on thoracic CT or ultrasound. The efficacy assessment was based on the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. As defined previously, the disease control rate (DCR) was calculated as the percentage of patients with CR plus PR plus stable disease (SD) among all patients. Objective Response Rate (ORR) was calculated as the percentage of patients with CR plus PR among all patients.

2.7. Evaluation of Toxic Side Effects

The occurrence and severity of gastrointestinal reactions such as nausea and vomiting, fatigue, chest tightness, chest pain, and leukocyte reduction were recorded in both groups. The degree and severity of the toxicity reactions were evaluated by the NCI CTC AE3.0 grading criteria, and the severity included 0-IV degree.

2.8. Statistical Analysis

All the statistical analyses were performed using the statistical software SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Measurement data were expressed as mean ± SD, and differences between the groups were assessed using t-test. Enumeration data were expressed as rate (%) and analyzed using the X^2 test or Fisher's exact test. Variables with p-values of < 0.05 were considered statistically significant.

3. Result

3.1. Patient Population

According to the above criteria, a total of 60 patients were admitted from June 2022 to May 2024 and randomly divided into a treatment group and a control group. There were 30 cases in the treatment group (treated with Bevacizumab Injection combined with Brucea Javanese Oil Emulsion Injection for drug infusion), including 16 male cases and 14 female cases; KPS score: 66.00 ± 10.03. There were 30 cases in the control group (Bevacizumab injection combined with cisplatin infusion therapy), including 17 male cases and 13 female cases; KPS score: 66.33 ± 9.64. The comparison between the two groups of patients showed no statistically significant difference ($P > 0.05$), indicating comparability. See **Table 1** for details.

3.2. Comparison of KPS Scores

KPS scores increased in both the treatment and control groups following treatment. In the treatment group, which received Bevacizumab combined with Brucea Javanica Oil Emulsion (BJOEI), the increase in KPS scores was statistically significant ($P = 0.007$). In the control group, which received Bevacizumab with cisplatin,

KPS scores also improved, but the change was not statistically significant (P = 0.061). When comparing the final KPS scores between the two groups after treatment, there was no statistically significant difference (P = 0.238). See Table 2 for details.

Table 1. Clinical data of 60 patients with stage IV lung adenocarcinoma [n (%)].

Variable	Treatment group (n = 30)	Control group (n = 30)	χ^2	P
Age	65.03 ± 6.79	65.47 ± 7.00	t = −0.243	0.809
Gender			0.067	0.795
Male	16 (53.3)	17 (56.7)		
Female	14 (46.7)	13 (43.3)		
History of smoking			0.601	0.438
Yes	13 (43.3)	16 (53.3)		
No	17 (56.7)	14 (46.7)		
KPS scores	66.00 ± 10.03	66.33 ± 9.64	t = −0.131	0.896
Pleural effusion Colour			0.606	0.436
Red	15 (50.0)	12 (40.0)		
No-red	15 (50.0)	18 (60.0)		
History of previous chemotherapy			0.073	0.787
No	19 (63.3)	20 (66.7)		
Yes	11 (36.7)	10 (33.3)		
Previous treatment history of the effusion			0.089	0.766
No	23 (76.7)	22 (73.3)		
Yes	7 (23.3)	8 (26.7)		

Table 2. Comparison of KPS scores (x ± s).

Group	n	Before	After	t	P
Treatment group	30	66.00 ± 10.03	73.67 ± 11.29	−2.780	0.007
Control group	30	66.33 ± 9.64	70.67 ± 7.85	−1.909	0.061
t		−0.131	1.195		
P		0.896	0.238		

3.3. Comparison of VEGF Levels of Pleural Effusion before and after Treatment in Both Groups

Before treatment, the VEGF level was not statistically significant in both groups ($P = 0.459$). After treatment, the VEGF level in both groups was lower, and the treatment group was significantly lower than the control group. The difference in VEGF reduction between the two groups was statistically significant ($P < 0.001$), suggesting a stronger effect of the BJOEI combination on lowering VEGF levels. See Table 3 for details.

Table 3. Comparison of VEGF levels before and after the two groups (x ± s).

Group	VEGF (ng/L)		t	*P*
	Before	After		
Treatment group	616.23 ± 39.62	385.01 ± 31.32	151.12	$P < 0.001$
Control group	608.14 ± 44.31	473.97 ± 34.55	69.40	$P < 0.001$
t	0.746	−10.45		
P	0.459	$P < 0.001$		

3.4. Comparison of Recent Efficacy in the Two Groups

The recent efficacy of the patients was evaluated according to the control of the pleural effusion. The DCR in the treatment group was 93.3%, which is better than the 90.0% in the control group. However, when comparing the two groups, the difference was not statistically significant ($P > 0.05$). See Table 4 for details.

Table 4. Comparison of recent efficacy between the two groups [example (%)].

Group	Numbers	Efficacy				ORR	DCR
		CR	PR	SD	PD		
Treatment group	30	1	21	6	2	22 (73.3%)	28 (93.3%)
Control group	30	0	20	7	3	20 (66.7%)	27 (90.0%)
χ^2						0.317	0.218
P						0.573	0.640

3.5. Analysis of the Stratified Factors Affecting the ORR

In order to further explore the influence of different factors on the efficacy, the following factors can be analyzed such as whether there was previous systemic chemotherapy, whether the KPS score is less than 70, whether it was more than 65 years of age, whether the effusion is the initial treatment, whether the effusion is bloody, whether the effusion is full drainage, and so on. The results showed that the KPS score was below 70 points, and the difference in ORR between the two patient groups was statistically significant ($P = 0.016$). See Table 5 for details.

Table 5. Analysis of the stratification factors of ORR [example (%)].

Factors	Treatment group	Control group	χ^2	*P*-value
Age > 65			0.303	0.582
Effective	10 (76.9)	9 (60.0)		
Uneffective	3 (23.1)	6 (40.0)		
Blood pleural effusion			0.024	0.877
Effective	11 (73.3)	10 (83.3)		
Uneffective	4 (26.7)	2 (16.7)		
KPS score < 70			5.850	0.016
Effective	11 (84.6)	5 (38.5)		
Uneffective	2 (15.4)	8 (61.5)		
The effusion had no previous treatment			0.180	0.672
Effective	17 (73.9)	15 (68.2)		
Uneffective	6 (26.1)	7 (31.8)		
Received previous chemotherapy			0.208	0.648
Effective	13 (68.4)	15 (75.0)		
Uneffective	6 (31.6)	5 (25.0)		
Full of drainage			0.163	0.686
Effective	15 (62.5)	17 (68.0)		
Uneffective	9 (37.5)	8 (32.0)		

Table 6. Comparison of adverse drug reactions in the two groups of patients with malignant pleural effusions [(n)%].

Adverse reactions	Grade I-II		χ^2	*P*-value	Grade III-IV		χ^2	*P*-value
	Treatment group	Control group			Treatment group	Control group		
Gastrointestinal	8 (26.7)	19 (63.3)	8.148	0.004	5 (16.7)	7 (23.3)	0.417	0.519
Fatigue	11 (36.7)	21 (70.0)	6.696	0.010	3 (10.0)	6 (20.0)	0.523	0.470
Granulocytopenia	14 (46.7)	16 (53.3)	0.267	0.606	9 (30.0)	11 (36.7)	0.300	0.584
Chest tightness and chest pain	3 (10.0)	5 (16.7)	0.144	0.704	0 (0.0)	0 (0.0)	-	-
Anemia	10 (33.3)	12 (40.0)	0.287	0.592	9 (30.0)	10 (33.3)	0.077	0.781
Hemorrhage	0 (0.0)	0 (0.0)	-	-	0 (0.0)	0 (0.0)	-	-
Hypertension	2 (6.7)	3 (10.6)	0.000	1.000	0 (0.0)	0 (0.0)	-	-

3.6. Comparison of Adverse Reactions after Thoracic Drug Injection in the Two Groups

After treatment, the two groups had gastrointestinal reactions such as nausea and vomiting, fatigue, chest tightness, chest pain, and leukocyte reduction, among which gastrointestinal reactions and fatigue were significantly different between the two groups ($P < 0.05$). See Table 6 for details.

4. Discussion

In our study, from the aspect of effectiveness, the Objective Response Rate (ORR) of the treatment group was 73.3% (22/30), and the Disease Control Rate (DCR) was 93.3% (28/30). In the control group, the Objective Response Rate (ORR) was 66.7% (20/30), and the Disease Control Rate (DCR) was 90.0% (27/30). There was no significant difference between the two groups. ($\chi^2 = 0.317$, $P = 0.573$; $\chi^2 = 0.218$, $P = 0.640$). An analysis of various factors affecting the ORR included evaluating whether there was previous systemic chemotherapy, whether the KPS score was less than 70, whether the patient was over 65 years of age, whether the effusion was the initial treatment, whether the effusion was bloody, whether there was full drainage of the effusion and other relevant factors. The results indicated that when the KPS score was below 70 points, there was a statistically significant difference in the ORR between the two groups ($\chi^2 = 5.850$, $P = 0.016$). Despite there being no significant difference between the two groups in terms of age (older than 65 years) with a χ^2 value of 0.303 and P-value of 0.582, the ORR was significantly higher in the treatment group compared to the control group. Therefore, when the Karnofsky Performance Status (KPS) score is less than 70, it indicates that patients with poor physical condition, especially in the elderly group, may be more suitable candidates for the strategy of de-cisplatin-based thoracic perfusion chemotherapy.

After treatment, the two groups had gastrointestinal reactions such as nausea and vomiting, fatigue, chest tightness, chest pain, and leukocyte reduction, among which gastrointestinal reactions and fatigue were significantly different between the two groups ($\chi^2 = 8.148$, $P = 0.004$; $\chi^2 = 6.696$, $P = 0.010$).

As we know, cisplatin is one of the earlier tumor chemotherapeutic drugs used, but the local stimulation of cisplatin is obvious, and adverse reactions such as gastrointestinal reactions of cisplatin are more and more common. At the same time, the use of large doses of drugs will cause ototoxicity, myelosuppression, and other problems, which can affect the tolerance of patients. From here, we see that de-platinum-based pleural perfusion has significantly fewer adverse effects and higher drug safety. Analysis of different factors affecting the ORR in this study also demonstrated that the advantage people of de-platinum-based drugs combined with thoracic perfusion may be poor physique, especially in the elderly. I believe that it may become a new strategy.

Bevacizumab is a recombinant humanized monoclonal antibody that selectively binds to VEGF and interferes with its receptor interactions, thereby inhibiting

differentiation, migration, and proliferation of vascular endothelial cells [19] [20]. Bevacizumab also promotes apoptosis of endothelial cells. The antagonism of VEGF reduces vascular permeability within tumors and, consequently the interstitial pressure. This property of Bevacizumab is believed to enhance the efficacy of concurrent cytotoxic chemotherapy by improving drug delivery to the neoplastic cells. Potential interference with normal angiogenesis and, therefore, tissue integrity explains the most serious toxicities of Bevacizumab, which include hemorrhage and astrointestinal perforation. Clinical studies reported [21]-[23] that thoracic infusion of the antiangiogenic drug bevacizumab can enhance the efficacy of treatment for pleural effusion. Although we can often use chemotoxic drugs combined with Bevacizumab, which the combination of the two drugs has clinically synergistic effects, the clinical adverse effects on patients can be increased. Therefore, better treatment methods need to be found for further studies to observe the clinical efficacy and safety of MPE.

We can see that in the Chinese experts' consensus on the treatment of antitumor angiogenic drugs in advanced NSCLC, it is recommended to combine local application of bevacizumab with systemic treatment for the treatment of malignant pleural effusion [24]. Brucea Javanica Oil Emulsion Injection (BJOEI) is a new type of anti-cancer drug consisting of active ingredients extracted from the mature fruits of the sorrelaceae plant, mainly containing oleic acid and linoleic acid. BJOEI is a non-specific anti-cancer drug that targets the cell cycle. It can inhibit DNA synthesis by inhibiting G0, G1, S, G2 and M phases of tumor cells, and it can also enhance the immune function and hematopoietic function of the human body. When combined with chemotherapy, BJOEI can enhance efficacy. Some studies have shown that BJOEI can suppress tumor angiogenesis and induce apoptosis of tumor cells. In combination with Bevacizumab, it is synergistic.

In this study, before the treatment, there was no statistically significant difference in VEGF levels between the two groups ($P > 0.05$). However, following the treatment, the treatment group exhibited significantly lower VEGF levels (385.01 ± 31.32) compared to the control group (473.97 ± 34.55), and this difference was found to be statistically significant ($P < 0.001$). I believe that this data, to some extent, indicates the synergistic antiangiogenic effect of combining Bevacizumab with BJOEI, and the reduction in VEGF levels further supports the efficacy of thoracic perfusion therapy. The study revealed that following treatment, the Karnofsky Performance Status (KPS) score of the treatment group was significantly higher than that of the control group, with a statistically significant difference observed between the treatment group and the control group ($P = 0.007$). The expression levels of VEGF in pleural effusion were lower in both groups, with the treatment group showing a significantly lower level of VEGF compared to the control group. This difference was statistically significant ($P < 0.001$).

5. Conclusions

In summary, this study verified that BJOEI in combination with Bevacizumab

could enhance the therapeutic effect of MPE, effectively improve patients' quality of life, and reduce the toxic and side effects of chemotherapy drugs, especially for the poor physique, especially in the elderly and KPS score is less than 70. At the same time, the reduction in VEGF levels supports the efficacy of thoracic perfusion therapy.

So, de-platinum-based drugs combined with thoracic perfusion are worth further clinical promotion. Of course, due to the relatively small sample size selected in this study, without consideration of systemic medication, there are certain limitations. If there are more accurate scientific research conclusions, a larger sample should be selected for scientific research.

Ethics Statement

The study involving human participants was reviewed and approved by Binzhou People's Hospital.

Authors' Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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