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Study on Clinical Nursing of Nano Albumin Paclitaxel in The Treatment of Advanced Lung Cancer

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Abstract: This study aims to observe the clinical efficacy, safety and nursing experience of nano albumin paclitaxel in the treatment of advanced lung cancer. At this moment, 100 patients with advanced lung cancer admitted from January 2019 to December 2019 were selected and given nano albumin paclitaxel 100 mg / m^2 single drug regimen or combined regimen to observe adverse reactions and evaluate the efficacy. With the experimental results show nano albumin paclitaxel-based treatment scheme has a certain effect on the treatment of advanced lung cancer regardless of the pathological type and the number of treatment lines. Patients after line therapy were well tolerated. The application of nano albumin paclitaxel in the treatment of advanced malignant tumors should pay attention to observe the changes of the disease and give proper nursing measures, and the patients can tolerate adverse reactions.

Keywords: nano albumin paclitaxel; lung cancer; nursing

1. The introduction

As it were, lung cancer is a major cause of cancer death worldwide (Torre et al., 2015; Molina et al., 2008; Morgensztern et al.,2010; Howlader et al.,2010) Paclitaxel is a broad - spectrum anti - tumor drug used in the treatment of lung cancer, breast cancer and other solid tumors. Generally speaking, 130 nm nano albumin paclitaxel (nab-Pacilitaxel, Abraxane) is a new type of paclitaxel preparation that does not require castor oil as a cosolvent, so it can reduce the common toxic reactions of traditional paclitaxel, and its special structure can pass endogenous albumin the pathway allows more paclitaxel to enter the tumor tissue to play an anti-tumor effect (Edelman, 2006; Green et al.,2006). Phase III clinical studies show that its clinical efficacy is significantly better than traditional paclitaxel preparations(Socinski et al.,2012)which was respectively approved by the US Food and Drug Administration (FDA) in 2012 and approved by Europe for the treatment of NSCLC in 2015. At the same time, there are related studies(Yoshida et al., 2016)reported that nano albuminsingle drug has a certain clinical effect even for small cell lung cancer after multi-line treatment. This study analyzed 100 clinical cases of advanced lung cancer regardless of the pathological type using nano albumin paclitaxel-based treatment regimens, and explored the efficacy and adverse reactions of nano albumin in treatment.

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2. Information and methods

2.1 Case selection and general information

This time the clinical data of 100 patients with advanced lung cancer admitted from January 2019 to December 2019 were selected. The inclusion criteria were stage III / IV lung cancer confirmed by histopathology as advanced or inoperable. As we are mentioned, of the 100 patients, 78 were male and 22 were female. Age around 25 to 78 years old. With the diagnosis was based on the 1982 Eastern Cooperative Oncology Group (ECOG) scoring criteria.

2.2 Method

2.2.1 Treatment plan

In this study, nano albumin paclitaxel (abraxane, American New Base Pharmaceutical Co., Ltd.) 100 mg / m^2 was used in all patients. With no anti-allergic pretreatment was given before medication. Each intravenous infusion was 45 minutes. During chemotherapy, adverse reactions were observed and recorded. The specific treatment plan is as follows: ① nano albuminpaclitaxel monotherapy in 80 cases; ② nano albuminpaclitaxel dual-therapy regimen in 20 cases; combined cisplatin 5 cases, combined carboplatin 3 cases, combined TS-1 2 cases, combined with Irinotecan 2 cases;

③Among 100 cases, nanoalbumin paclitaxel combined with anti-angiogenesis targeted therapy in 22 cases; 14 cases combined with recombinant human endostatin and 8 cases combined with bevacizumab. None of the patients used prophylactic granulocyte colony-stimulating factor drugs (G-CSF), but G-CSF was used when hematological toxicity was above 3 degrees. Treatment until disease progression and the patient refuses or cannot tolerate chemotherapy.

2.2.2 Nursing program

Psychological care and health education, medication care, leukopenia care, digestive system reaction, neurotoxicity care and cardiovascular system care are provided to patients.

2.3 Evaluation of efficacy, adverse reactions and follow-up

Before treatment, all patients underwent baseline imaging examination and baseline measurement of all measurable lesions. The imaging assessment was performed after every 2 cycles of treatment. According to the evaluation standard of solid tumor efficacy (RECIST): complete response（CR）; partial response（PR）; progressive disease（PD）; stable disease（SD)。Objective response rate（ORR）=CR+PR，disease control rate（DCR）=CR+PR+SD；progression-free survival（PFS）. To be brief, defined as the time interval from the start of treatment to the first occurrence of PD or death from any cause. Adverse reactions were judged according to the NCI-CTC Common Terminology Standards for Adverse Reaction Events of the National Cancer Institute, and the standards were graded from 0 to 4. With 100 patients were not lost to follow-up, and the follow-up rate was 100%.

2.4 Statistical methods

On the whole, SPSS 20.0 was used for statistical analysis. The clinical efficacy and adverse reactions are calculated directly from the original data. The clinical characteristics and treatment efficacy were compared using χ2 test or Fisher's exact test, $P<0.05$ was considered statistically significant.

3. Results and discussion

3.1 Characterization of nano albuminpaclitaxel

Figure 1 is a transmission electron microscope observation result of nano albuminpaclitaxel provided by the United States New Base Pharmaceutical Co., Ltd., showing that the appearance of the nanoparticles is round and uniform. The average particle size detected by the laser particle size analyzer is 182.6 nm.

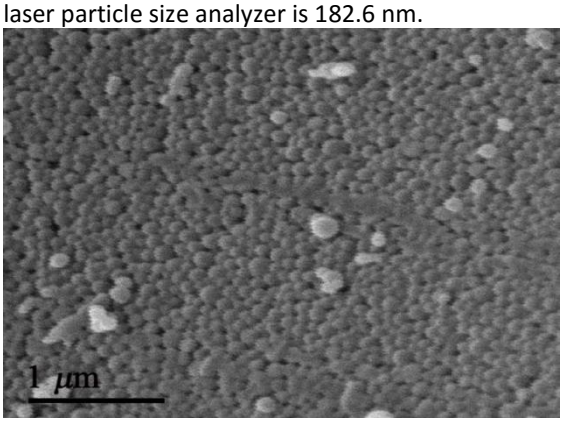

Figure 1. **Transmission electron micrograph of paclitaxel nanoparticles**

3.2 Clinical efficacy

While the 100 patients completed 184 cycles of chemotherapy. The clinical treatment results showed that there were no CR patients, 20 PR patients, 48 SD patients, and 32 PD patients. The ORR was 20% and the DCR was 68%. Nowadays, there are 100 patients underwent subgroup analysis according to different pathological types. Among 50 adenocarcinomas, 10 were PR, 24 were SD, 16 were PD, ORR was 10%, and DCR was 71%; Among 30 cases of squamous cell carcinoma, 8 cases were PR, 16 cases were SD, 6 cases were PD, ORR was 27.5%, DCR was 81.2%; 20 cases of small cell lung cancer were 2 cases PR, 8 cases SD, 10 cases PD, ORR was 11% the DCR is 52%.

Subgroup analysis was conducted according to different treatment options. With 12 cases of PR, 40 cases of SD, 26 cases of PD, ORR of 15.4%, and DCR of 67.6% in the chemotherapy group; 8 cases of PR, 8 cases of SD, and 6 cases of PD in the chemotherapy combined targeted therapy , ORR is 35.4%, DCR is 74.2%, among the patients receiving chemotherapy combined with recombinant human endostatin, there were 8 cases of adenocarcinoma (6 cases of SD, 2 cases of PD), 4 cases of squamous cell carcinoma (2 cases of PR, 2 cases of SD) and 2 cases of small cell lung cancer (PD) the 8 patients who received chemotherapy and bevacizumab were all adenocarcinoma (6 PRs and 2 PDs). The ORR of the first-line treatment with paclitaxel containing nano albumin was 52.4%, also the DCR was 61.5%; while the ORR of the second-line and above was 15.1%, the DCR was 69.7%.

3.3 Adverse reactions

At this meantime, 75% of patients completed more than 2 cycles of treatment, with no patients discontinued treatment due to adverse reactions,

either no treatment-related deaths occurred. With the common adverse reactions of the nano albumin paclitaxel-based treatment regimen are hematological toxicity, mainly leukopenia (45%), neutropenia (38%) and anemia (43%), but most of the adverse reactions are in grade 1 to grade 2, 4 cases had grade 3 leukopenia and 2 cases had grade 3 neutropenia. Non-hematological toxicity mainly manifests as peripheral nerve numbness (35%), fatigue (47%), lipsotrichia (62%), and gastrointestinal reaction (51%), etc., all of which are grade 1 to grade 2. For specific results, see Figure 2-3. As has been noted, 100 patients were treated with nano albumin-containing paclitaxel. The overall treatment was well tolerated and adverse reactions were controllable. There were no allergic reactions and hypersensitivity reactions during use.

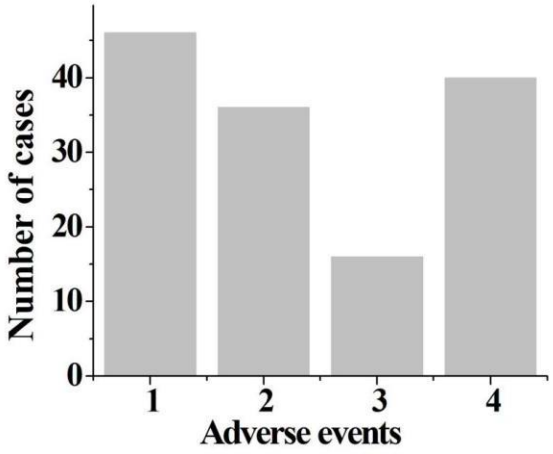

Figure 2. **Hematologic adverse events in the treatment of advanced lung cancer with a nanoalbumin-binding paclitaxel regimen（1. Leukopenia；2. Neutropenia；3. Thrombocytopenia；4. Anemia.）**

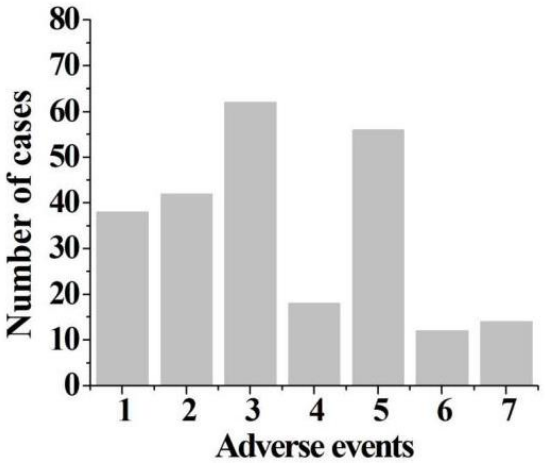

Figure 3. **Non-hematologic adverse events in the treatment of advanced lung cancer with nanoalbumin-binding paclitaxel regimen（1. Peripheral neurotoxicity;2. Fatigue; 3. Alopecia;4. Arthralgia/Myalgia;5. Digestive tract reactions；6. Mucositis;7.ALT/AST elevation.）**

In terms of hematological toxicity, it can be observed that the incidence of adverse reactions in patients ≥ 5 years old is higher than in patients under 65 years old, especially the incidence of anemia is significantly different. Grouped according to the number of treatment lines, there was no statistical difference in the incidence of hematological toxicity among patients with different treatment lines. At the same time, we can also observe the incidence of hematological toxicity in patients with ECOG performance status (PS) score ≥ points is significantly higher than that in patients with less than 2 points, also there is a statistical difference (leukopenia: 67.5% vs 37.5% , P <0.05); Neutropenia: 61.2% vs 22.4%, P <0.05; anemia: 64.2% vs 27.1%, P <0.05). Although the incidence of hematological toxicity in the combination therapy group was also higher than in the monotherapy group, it was not statistically significant. In terms of non-hematological toxicity, whatever there is significant difference in the incidence of adverse reactions regardless of the age is ≥ 5 years or different treatment lines. The incidence of gastrointestinal reactions in the combined drug treatment group was significantly higher than in the albumin paclitaxel monotherapy group (91.2% vs 48.1%, P <0.05); patients with ECOGPS score ≥ the exact score were fatigued (63.5% vs 32.6%, P <0.05) 0.05) and the incidence of gastrointestinal reactions was significantly higher than patients with a score of 0-1 (81.3% vs 47.2%, P <0.05), with the difference statistically significant.

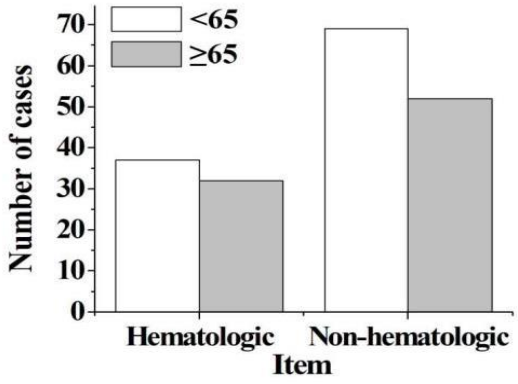

Figure 4. **Comparison of incidence of adverse reactions by age group**

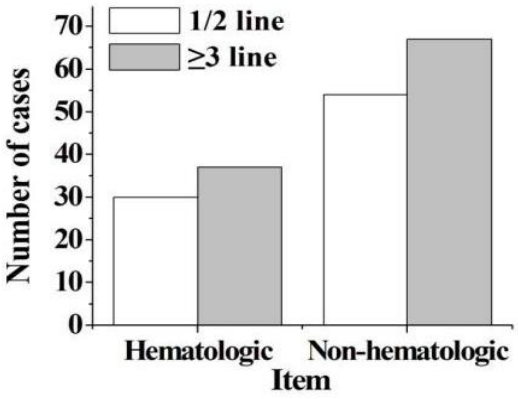

Figure 5. **Comparison of incidence of adverse reactions by treatment group**

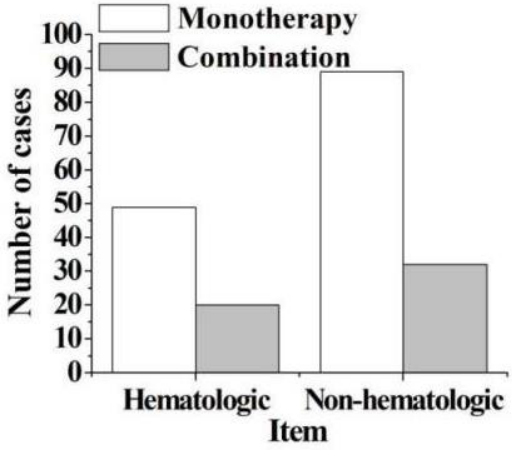

Figure 6. **Comparison of incidence of adverse reactions by treatment group**

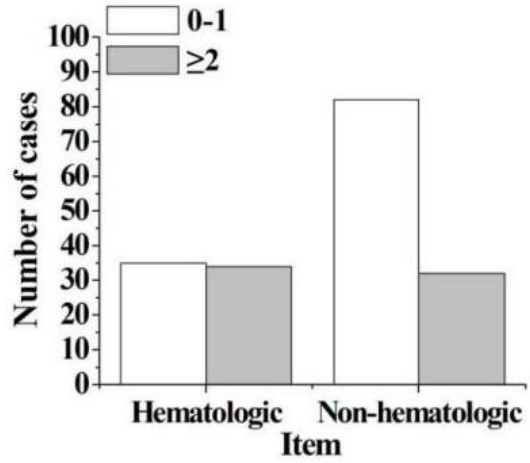

Figure 7. **Comparison of incidence of adverse reactions by ECOG PS score group**

3.3 Nursing effect

On this step, before using the drug, we should detail the advantages of nano albumin paclitaxel and the usage of the drug, precautions, costs, adverse reactions and preventive measures to help patients build confidence in defeating the disease. After effective psychological care and health education, patients can all cooperate with treatment. In this group, leukocytopenia of 1 to 3 degrees occurred. With the changes in blood were closely observed during nursing. The principle of strict aseptic operation was used. Then the ultraviolet disinfection of the wards guided patients to pay attention to personal hygiene. Do not go to public places and reduce frequent visits. Use Yinertong preventive gargle to prevent oral ulcers, enter high protein, enrich vitamin food, and subcutaneously inject subcutaneous injection of recombinant granulocyte colony-stimulating factor as required by the doctor if necessary. After treatment, white blood cells rose to normal and no infection occurred. It should not be too large when instructing patients to move, which prevent falls and bruises. Brush your teeth with a soft-bristled toothbrush, do not use excessive force when defecating, and do not dig your nose with your fingers. According to the doctor's instructions, subcutaneous injection of Ji Jufen, Tebio, etc., after treatment, platelets rose to normal. All cases in this group suffered from decreased appetite, nausea, and vomiting. Do a good job in nursing, so that patients understand the adverse reactions of drugs, be aware of them, guide patients to light diet, eat less and eat more meals, prohibit spicy greasy, create in the dining environment, drink plenty of water and give antiemetics as directed by your doctor.

3.4 Discussion

To put it briefly, lung cancer is a histologically diverse disease, currently divided into non-small cell lung cancer (NSCLC) and small cell lung cancer. As has been noted, 130 nm nano albuminpaclitaxel (Abraxane, Celgene Corporation) is a new type of paclitaxel preparation without co-solvent. Phase III studies show that ORR can be significantly improved especially compared with traditional paclitaxel preparations; regardless of histopathological type or age. One of the treatment options(Socinski et al.,2012). A study from Japan also showed that for refractory or relapsed small cell lung cancer that failed second-line treatment, with the ORR of albumin paclitaxel alone was 33%(Yoshida et al., 2016). To get back to the point, some retrospective analyses at home or abroad show that nano albumin paclitaxel can achieve 20% -30% of NSCLCORR, which is significantly higher than the accepted standard second-line treatment drug docetaxel(Xing et al., 2013; Li et al.,2016; Jin et

al.,2016), even for patients with multi-line treatment 18.75% efficacy(Chen et al., 2012; Socinski et al.,2013; Heist et al.,2015).

On the whole this study further explored the efficacy and safety of nanoalbumin paclitaxel-based regimens in the treatment of advanced lung cancer, and conducted relevant analysis based on clinical characteristics to explore the characteristics of the beneficiary population. With the results of this study show that in the treatment of advanced lung cancer, the nano albumin paclitaxel-based treatment scheme can achieve a total ORR of 20% and a DCR of 68% regardless of the pathological type and number of treatment lines. At this meantime, among the different pathological types of lung cancer, ORR and DCR are the highest in squamous cell carcinoma, also the lowest in small cell lung cancer, 26.7% vs 10% (P = 0.61), 80% vs 50% (P = 0.255), but not yet statistical differences. Given this point this study once again proved that the application of nanoalbumin paclitaxel-based treatment programs for patients with lung squamous cell carcinoma can achieve better ORR and DCR, and still have some clinical activity for small cell lung cancer. This study also showed that combined with anti-angiogenesis therapy based on nano albumin paclitaxel single drug or combination of two drugs can achieve better ORR (36.4% vs 15.4%) than chemotherapy alone (P = 0.267). With the anti-angiogenesis therapy used in this research includes bevacizumab and recombinant human endostatin. The ORR of chemotherapy combined with anti-angiogenesis therapy group is higher than chemotherapy alone group, also ORR and the above foreign research results meet similarities(Socinski et al.,2010； Rizvi et al.,2008；Chen et al.,2015； Skwarczynski et al.,2006； Marupudi et al.,2007), it also suggests that our combination of chemotherapy with nano albumin paclitaxel and anti-angiogenesis therapy is also an ideal choice for the treatment of advanced lung cancer. According to the results of this study, we finally found as the number of treatment lines increased, the ORR then gradually decreased (P = 0.122). For patients on the fourth line or above, the ORR was only 7.7%; still DCR could always be maintained at 60% -80%. Even for the fourth-line or above treatment, DCR can still reach 69.2%, and there is no significant difference in the treatment of DCR with different line numbers (P = 0.84), in this case, for advanced lung cancer patients with multi-line treatment, we can always consider the application of nano albumin paclitaxel. In this paper, there were no grade 4 toxic reactions in the treatment-related adverse reactions, also no allergic reactions and hypersensitivity reactions occurred in the above-mentioned patients. No treatment-related toxic reactions caused treatment delay, interruption or death. Only the most common adverse reactions include leukopenia, neutropenia, anemia or lipsotrichia, fatigue, gastrointestinal reactions, and peripheral nerve numbness. Adverse reactions above grade 3 include leukopenia, neutropenia, and fatigue. For elderly patients (≥5 years old), the incidence of only anemia is high and statistically different, which is relatively safe; while the incidence of hematological toxicity, fatigue or gastrointestinal reactions in patients with ECOGPS score ≥ some points is relatively significant, so special attention should be paid to the clinical application, with the dosage can be adjusted appropriately according to individual circumstances. In this study, the incidence of peripheral nerve numbness was 38%, which was also significantly lower than traditional paclitaxel preparations, however no grade 3/4 adverse reactions occurred, once again showing the advantages of nanoalbumin paclitaxel. Related research at home or abroad explored the optimal dosage and administration method of nano albumin paclitaxel. With the results showed that the administration method on days 1 and 8 (21d is a chemotherapy cycle) was 200 mg / m^2 every 3 weeks one time administration method has better efficacy and tolerability, also significantly reduces the occurrence of peripheral neuropathy, muscle or joint pain, even contains better clinical benefit-risk ratio(Desai et al.,2006; Gradishar et al.,2005; Huh et al.,2005; Seow et al.,2007; Zhang et al.,2010; Temming et al.,2006)

At any rate, the results of this study once again confirmed this method of administration not only can achieve satisfactory ORR or DCR, but also rarely have grade 3 / grade 4 adverse reactions and have good safety.

4. Conclusion

In a word, this study shows nano albumin-based paclitaxel-based regimen is safe for advanced lung cancer regardless of age and initial or re-treatment; among different pathological types of lung cancer, ORR and DCR of squamous cell carcinoma are the most advantageous, but for small cells Lung cancer is equally effective, even in patients with second-line or above treatment, DCR can still approach 70%. For the purpose nano albumin paclitaxel-based chemotherapy can achieve better ORR if combined with anti-angiogenesis therapy. With the above results have certain reference value for clinical work. According to the different psychological characteristics of patients, relevant psychological care and health education are given,

strictly according to the application procedures and methods of nano albumin paclitaxel, the drugs are stored, formulated, and infused, and the adverse reactions are observed in time, and proper nursing measures are strictly followed in accordance with the nursing procedures, achieved the desired effect.

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