Discussion on the efficacy of two different chemotherapy regimens to NSCLC and their influence & therapeutic mechanism to tumor markers

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ABSTRACT

Objective: To discuss the clinical efficacy of gemcitabine+vinorelbine and paclitaxel+cis-platinum two kinds of chemotherapy regimens in the treatment of advanced non-small cell lung cancer (NSCLC), and their influence and therapeutic mechanism to tumor markers. Method: Selected 102 cases of patients with NSCLC, who were randomly divided into study group and control group (n=51), and were given gemcitabine+vinorelbine and paclitaxel+cis-platinum treatment respectively. Compared the recent clinical effective rate and time to progression of both groups; expression of excision repair cross complementing1 (ERCC1) and tumor marker-CA125, CEA and NSE level changes. Results: Clinical effective rate in study group was 70.59%, which was obviously higher than that (58.82%) in control group (P<0.05); clinical TTP in study group was (6.4±1.6) months, which was obviously higher than that (3.8±1.2) months in control group (P<0.05); the overall score in study group was (89.2±2.3) points, which was obviously higher than that (71.5±2.6) points in control group (P<0.05); CA125, CEA and NSE levels in study group after 2-cycles treatment were obviously lower than before treatment and the levels after treatment in control group (P<0.05); ERCC1 positive expression rate was 43.14%, which was obviously lower than that (54.90%) in control group (P<0.05). Conclusion: Clinical effective rate and benefit rate of gemcitabine+vinorelbine treatment was high, no-time to progression was long, postoperative life quality was good, efficacy was superior to paclitaxel+cis-platinum treatment, and its therapeutic mechanism might be related with gemcitabine inhibition to ERCC1 expression.

1. Introduction

Non-small cell lung cancer, NSCLC was a kind of common malignant tumor, accounted for more than 80% of lung cancer, patients often have entered into middle and advanced stage when diagnosed and have lost the best opportunity to radical treatment[1]. Accordingly, the first-line therapy for advanced NSCLC was combined chemotherapy based on platinum drugs[2]. Although platinum chemotherapy regimens had certain curative effects, but the long-term use of platinum drugs chemotherapy could cause drug-resistance increases, lowered the effect of chemotherapy; therefore, how to choose chemotherapy drugs with high efficiency and low toxicity became a focus in the study of NSCLC treatment[3]. In this study, we have done a preliminary discussion on the curative effect and therapeutic mechanism of gemcitabine combined with vinorelbine in the treatment of advanced NSCLC patients, aiming to provide reference for the selection of advanced NSCLC chemotherapy regimens, reports were as follows.

2. Materials and methods

2.1. Clinical information

Selected 102 cases of patients with NSCLC in our hospital from January 2013 and January 2015, diagnosed by cytology and pathology examination for advanced NSCLC. All cases
fitted follow-up, it was expected that lifetime was more than 3 months. Karnofsky grades>60 points, and excluded chemotherapy taboo through peripheral hemogram, liver, renal function, electrocardiogram etc. routine examination. Cases were randomly divided into study group and control group (n=51). Study group: male-27 cases, female-24 cases; age (45-72) years old; squamous carcinoma-28 cases, adenocarcinoma-23 cases, TNM staging B-30 cases, C-11 cases. Control group: male-28 cases, female-24 cases; age (46-73) years old; squamous carcinoma-27 cases, adenocarcinoma-24 cases, TNM staging B-31 cases, C-20 cases. Both groups had no significant difference in baseline information on various aspects (P>0.05), had comparability.

2.2. Treatment method

Both groups were given intravenous drip 40 mg of diphenhydramine and 8 mg of ondansetron before chemotherapy, control group were given paclitaxel+cis-platinum treatment, 175 mg/m² of paclitaxel dissolved in 250 mL of normal saline, intravenous drip, 21 d as a treatment cycle. From the first day to third day, 30 min after paclitaxel intravenous drip, then intravenous drip of 75 mg/m² of cis-platinum, 2 h, 21 d as a treatment cycle. Orally took 50 mg of diphenhydramine and intravenous injection of 400 mg of cimetidine 30-60 min before given medicine; taking 20 mg of dexamethasone to prevent drug (paclitaxel) allergy 6 h and 12 h before given medicine. Study group were given gemcitabine+vinorelbine treatment. On the 1st day and 8th day, intravenous drip of 1 000 mg/m² of gemcitabine, intravenous drip for 30 min, 21 d as a treatment cycle, intravenous injection of 25 mg/m², continuous treatment of 2 cycles for both groups.

2.3. Observational index

2.3.1. Evaluation of therapeutic efficiency

Evaluated the efficacy of the treatment after 2 cycles of treatment, evaluation criterion referred to solid tumor efficacy evaluation criterion (RECIST), lesions disappeared for more than 4 weeks meant complete remission, length diameter of baseline lesions became smaller, >30% meant partial remission. Clinical effectivrate=complete remission+partial remission. Followed up for 1 year, compared the no-time to progression, TTP and living quality of patients of both groups. Life quality score adopting Lung cancer patients quality of life scale-FACT-L, the higher that score was, the better the living quality was.

2.3.2. Tumor marker levels

Adopting full-automatic chemiluminescence immune analysis meter to determine the level changes of tumor marker-Cancer Antigen125 (CA125), carcino-embryonicantigen (CEA) and neuron-specific enolase (NSE).

2.3.3. Excision repair cross–completion

Excision repair cross–completion 1 (ERCC1) expression adopting SP method to carry out immunohistochemistry determination. When the tumor cell nucleus with-out staining, which meant ERCC1 had no expression (negative). When the tumor cell nucleus turned yellow, which meant ERCC1 expression (positive).

2.4. Statistical treatment

Adopting SPSS17.0 for statistic analysis, measurement data using Mean±Standard Deviation (Mean±SD) to show, adopting t test; Enumeration data using ratio or constituent ratio to show, adopting χ² test, P<0.05 meant difference was statistically significant.

3. Results

3.1. Clinical efficacy comparisons

Short-term efficacy comparisons of both groups: clinical effective rate in study group was 70.59%, which was obviously higher than that (58.82%) in control group (χ²=9.40, P=0.38<0.05). Long-term efficacy comparisons of both groups: Clinical TTP was (6.4±1.6) months, which was obviously higher than that (3.8±1.2) months in control group (t=7.13, P=0.40<0.05).

3.2. FACT-L scoring comparisons of both groups after treatment

Clinical prognosis comparisons of both groups: FACT-L functional status, physiological status, emotional status and social status scoring in study group was obviously higher than that in control group (P<0.05); the overall score in control group and study group arrived to (71.5±2.6) points and (89.2±2.3) points respectively, the overall score in study group was obviously higher than that in control group (P<0.05). See Table 1.

Table 1

<table>
<thead>
<tr>
<th>Status</th>
<th>Functional</th>
<th>Physiological</th>
<th>Emotional</th>
<th>Social</th>
<th>Overall Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Group</td>
<td>16.1±2.4</td>
<td>18.3±2.2</td>
<td>17.0±1.9</td>
<td>19.4±2.3</td>
<td>71.5±2.6</td>
</tr>
<tr>
<td>Study Group</td>
<td>20.3±2.5*</td>
<td>25.5±2.0*</td>
<td>22.0±1.8*</td>
<td>23.8±2.2*</td>
<td>89.2±2.3*</td>
</tr>
</tbody>
</table>

Notes: compared with control group,*P<0.05.

3.3. Tumor marker levels comparisons before and after treatment of both groups

Tumor marker CA125, CEA and NSE levels of both groups before
treatment had no statistical significance \((P>0.05)\); CA125, CEA and NSE levels of both groups were obviously lower than before treatment after 2 cycles of treatment \((P<0.05)\); CA125, CEA and NSE levels after treatment in study group were obviously lower than that in control group \((P<0.05)\). See Table 2.

### Table 2
Analysis of microcirculation parameters of patients among three groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>CA125 (U/mL)</th>
<th>CEA (μg/mL)</th>
<th>NSE (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>Treatment</td>
<td>Treatment</td>
</tr>
<tr>
<td>Control Group</td>
<td>268.7±8.2</td>
<td>137.2±7.7</td>
<td>127.4±6.9</td>
</tr>
<tr>
<td>((n=51))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Group</td>
<td>270.3±8.4</td>
<td>84.9±6.4*</td>
<td>126.1±8.0</td>
</tr>
<tr>
<td>((n=51))</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 3.4. ERCC1 positive expression rate and its relationship with TTP

ERCC1 positive expression rate in control group was 54.90% after 2 cycles treatment, while ERCC1 positive expression rate in study group was 43.14%, ERCC1 positive expression rate in study group was obviously lower than that in control group \((\chi^2=7.23, P=0.40<0.05)\), the relationship between ERCC1 positive expression rate and TTP was as following Figure 1: TTP lengthened along with the rising of ERCC1 positive expression rate.

![Figure 1. ERCC1 positive expression rate and its relationship with TTP](image)

### 4. Discussion

Non-small cell lung cancer (NSCLC) accounted for about 70%–90% of the total number of lung cancer, including adenocarcinoma, squamous carcinoma and large cell lung cancer etc[4-5]. Accordingly, the first choice treatment for patients with lung cancer was still surgery, but about 70% of patients often have entered into advanced stage when diagnosed and have lost the surgery opportunity[6]. Most researches showed that platinum combined with paclitaxel etc. the third generation of chemotherapy drugs duplex chemotherapy regimens were standard solution in the treatment of advanced NSCLC. Platinum drugs could through the combination with the DNA of tumor cells to form into Platinum-DNA adduct, which led to DNA intrastrand cross-linking or intrastrand cross-linking, caused DNA replication obstacle, and then killed tumor cells[7]. Paclitaxel mainly through promoting cancer cell microtubule polymerization and stability to prevent cancer cell proliferation, meanwhile paclitaxel could also induce cancer cells apoptosis and adjust function of human body[8]. In this study, through paclitaxel+cis-platinum chemotherapy regimens in the treatment of advanced NSCLC, we found that clinical effective rate arrived to 58.82%, tumor marker CA125, CEA and NSE levels were obviously lower than before treatment, which indicated that paclitaxel+cis-platinum chemotherapy regimens had the exact curative effect in the treatment of patients with advanced NSCLC, and which was in accordance with the research results of Zhang Nini et al[9]. However, most researches showed that long-term use of platinum chemotherapy could increase drug resistance, which was also the reason of the curative effect of clinical platinum drugs reduced after a period of use[10].

Gemcitabine was nucleoside drugs, through killing and wounding s-stage tumor cells to block proliferative cells developing from G1 phase to S phase[11]. Gemcitabine could increase the sensibility of tumor cells to other drugs, meanwhile could also inhibit the efficacy of DNA synthesis; vinorelbine could combined with microtubulin, which made microtubule dyspoiesis during cells mitosis process, therefore, two drug combination could work together from many links, many channels, had good curative effect, and not easy to cause drug-resistance[12]. In this study, adopting gemcitabine+vinorelbine chemotherapy regimens to treat advanced NSCLC, and the results showed that the clinical effective rate arrived to 70.59%, which was obviously higher than that in control group; while tumor marker CA125, CEA and NSE levels were obviously lower than before treatment, which was obviously lower than that in control group, in addition, FACT-L scoring in study group after treatment was obviously lower than that in control group, all these indicated that gemcitabine+vinorelbine chemotherapy regimens had exact curative effect to advanced NSCLC, and was superior to paclitaxel+cis-platinum chemotherapy regimens.

Modern medical research proved that nucleotide excision repair (NER) system could repair DNA damage caused by platinum agents and ERCC1 played a key role in NER approach[13]. ERCC1 located on chromosome 19, was the important member of the nucleotide excision repair (NER) family, encoding 297 of amino acid protein, combined with DNA repairing azymia complementary genes to form into heterodimer, which proceeded excision to functioning at 5 ends of DNA singly-linked damage; in addition, ERCC1 over expression could make the damaged DNA stagnated in G/
M-stage cells repair rapidly, which led to its drug resistance to cis-platinum, and the high-low levels of its activity could reflect the level of the whole NER repair activity\[14\]. NER system could repair DNA damage caused by platinum drugs, and its repair ability was a "double-edged sword"-low-level repair ability could lead to occurrence and postoperative recurrence of lung cancer, but was sensitive to chemotherapy based on platinum drugs, not easy to produce drug-resistance; while high-level repair ability could reduce postoperative recurrence, but was easy to produce drug-resistance. This research showed that gemcitabine+vinorelbine chemotherapy regimens: ERCC1 positive expression rate was obviously lower than paclitaxel+cis-platinum chemotherapy regimens, which indicated that gemcitabine+vinorelbine chemotherapy regimens was superior to paclitaxel+cis-platinum chemotherapy regimens, maybe related to the low expression of ERCC1. In conclusion, we thought that as to gemcitabine+vinorelbine chemotherapy regimens in the treatment of NSCLC, the clinical effective rate, benefit rate was high, no-time to progression was long, postoperative living quality was good, curative effect was superior to paclitaxel+cis-platinum chemotherapy regimens, its curative effect mechanism might be related to gemcitabine inhibiting the ERCC1 Expression.

References


