Efficacy of Aidi Injection Combined with Chemotherapy in the Treatment of Advanced Epithelial Ovarian Cancer

Cong YE1,a, Jun-Rong WANG2,b, Yu-Bo HU2,c,*

1Gynaecology and Obstetrics, China-Japan Union Hospital Jinlin University, 126 Xiantai Street, Changchun 130033, P.R. China
2Anesthesiology Department, China-Japan Union Hospital Jinlin University, 126 Xiantai Street, Changchun 130033, P.R. China

a123953361@qq.com, bjunrongwang1982@outlook.com, c525479868@qq.com
*Corresponding author

Keywords: Advanced epithelial ovarian cancer, Aidi injection; Paclitaxel, Cisplatin.

Abstract. Objective: To study the efficacy, quality of life and side effects of Aidi injection combined with paclitaxel and cisplatin in the treatment of advanced epithelial ovarian cancer. Methods: 68 cases of advanced epithelial ovarian cancer were randomly divided into 2 groups, observation group and the control group, each group contains 34 cases. The patients in the control group were treated with chemotherapy, and the patients in the observation group were treated with Aidi injection combined with chemotherapy. We evaluated the efficacy and toxic and side effects in every 2 treatment cycles. Result: The effective rate of the patients in the observation group had no different with that of the control group (64.7% to67.6%)(P>0.05),the improvement of quality of life in the observation group was better than that of the control group, and the difference was statistically significant (P<0.05),the incidence of leukocyte decline, abdominal pain and nausea in the observation group were significantly lower than those in the control group (P<0.05), and the difference was statistically significant. Conclusion: Aidi injection combined with paclitaxel and cisplatin is safe and effective in the treatment of advanced epithelial ovarian cancer. Compared with chemotherapy alone, it improves the life and does not increase toxicity.

Introduction

The incidence of epithelial ovarian cancer is the first in the ovarian malignant tumors. More than 70% of the patients are in the middle and late stages, and the 5 year survival rate is about 20% to 30%. At present, chemotherapy is the main treatment for advanced epithelial ovarian cancer. It has been reported that chemotherapy combined with traditional Chinese medicine could improve the quality of life in advanced patients and the tolerance of chemotherapy. Aidi injection can induce apoptosis of tumor cells and inhibit the formation of tumor neovascularization, enhance humoral and cellular immunity, and regulate immune function. It has dual functions of killing tumor cells, inhibiting tumor cell growth and metastasis, and improving immunity. We retrospectively analyzed 68 cases of advanced epithelial ovarian cancer from February 2014 to December 2017. We compared the efficacy, quality of life and side effects of Aidi injection combined with chemotherapy and chemotherapy alone in the treatment of advanced epithelial ovarian cancer. The report is as follows:
Materials and Methods

General Information

This study was approved by our hospital ethics committee, and patients signed an informed consent form. 68 patients with advanced epithelial ovarian cancer who were diagnosed in China-Japan Union Hospital of Jilin University from January 2013 to December 2017. Following the strict inclusion and exclusion criteria, they were randomly divided two groups equally, including 34 treated with chemotherapy (Control group) and 34 with Aidi injection and chemotherapy (Observation group). The age of the observation group was 32-69 years old, the median age was (41.32± 9.16) years old, there were 20 cases of stage III, 14 cases of stage IV , confirmed by pathological examination, using FIGO staging. The control group was 30-71 years old, and the median age was (42.46± 8.35) years. there were 21 cases of stage III, 13 cases of stage IV , confirmed by pathological examination, using FIGO staging. There was no statistical difference in age, Karnofsky Performance Status(KPS) scores and stages of the two groups, and was comparable (P>0.05). (Table 1)

Table 1. Comparison of KPS scores in two groups (n).

<table>
<thead>
<tr>
<th>Group</th>
<th>Case number</th>
<th>100</th>
<th>90</th>
<th>80</th>
<th>70</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>34</td>
<td>6</td>
<td>8</td>
<td>9</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Control group</td>
<td>34</td>
<td>7</td>
<td>9</td>
<td>8</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

Criteria of Case Selection

**Inclusion criteria.** The cases were confirmed by pathology, all of them have measurable lesions; the blood routine and liver function is normal , ECG is normal; the expected survival for more than 3 months; the KPS scores is more than 60 points; the important organ like heart,

**Exclusion criteria.** Central nervous system metastasis; the important organ like heart, liver and kidney have serious dysfunction; KPS scores is more than 60 points; patients who refuse chemotherapy

Treatment

The patients in the control group were treated with chemotherapy, the treatment prescription were as follows, take 135 mg/m² of paclitaxel and 25mg/m² of cisplatin per time with intravenous injecting , once a week and lasted for 4 weeks. Before paclitaxel chemotherapy, dexamethasone and cimetidine are pretreatment. Before conventional chemotherapy, patients were given 5- serotonin receptor 3 antagonist antiemetic symptomatic treatment. Patients with leukocyte and neutrophils dropping after chemotherapy were treated with granulocyte colony stimulating factor . The observation group were treated with chemotherapy and Aidi injection therapy, Patients with intravenous infusion of Aidi injection in 50mg for each time, 1 times a day, lasted for 8 days.
Standard of Curative Effect and Evaluation Method

Before and after 1 week’s treatment, the size of the tumor was measured by Doppler ultrasound and CT examination, and the curative effect was evaluated according to the solid tumor evaluation standard formulated by WHO. Complete remission: the tumor completely disappeared; partial remission: tumor shrinkage degree > 50%; improvement: the tumor has narrowed, but the degree is less than or equal to 50%; no change: no change in tumor size; disease progression: progress in tumor. Efficiency = (complete remission number + partial remission number) / total number x 100%

The Karnofskys performance scoring (KPS) is used to evaluate patients 3 months after treatment. Improvement: KPS increased is more than 10 points; stability: KPS is range within 10 points; deterioration: KPS decreased more than 10 points after treatment.

The incidence of side-effects during the treatment of two groups of patients were observed such as leukocyte descent, abdominal pain and nausea.

Statistical Methods

All data using SPSS 21.0 statistical software for processing, measurement data using mean and standard deviation (X±S) to represent. And paired t test for data comparation between two groups, P <0.05 considered statistically significant.

Result

Comparison of Effect after Treatment in Two Groups of Advanced Epithelial Ovarian Cancer Patients

The effective rate of the patients in the observation group had no different with that of the control group (64.7% to67.6%) (x²=1.839. 324, P > 0.05).(Table 2)

<table>
<thead>
<tr>
<th>Group</th>
<th>Case number</th>
<th>Complete remission</th>
<th>Partial remission</th>
<th>Improvement &amp; No change</th>
<th>Disease progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>34</td>
<td>4(11.8)</td>
<td>18(52.9)</td>
<td>6(17.6)</td>
<td>6(17.6)</td>
</tr>
<tr>
<td>Control group</td>
<td>34</td>
<td>5(14.7)</td>
<td>16(47.1)</td>
<td>6(17.6)</td>
<td>7(20.6)</td>
</tr>
</tbody>
</table>

Comparison of the Improvement of Quality of Life in Two Groups of Patients with Advanced Epithelial Ovarian Cancer after Treatment

After treatment, the improvement of quality of life in the observation group was better than that of the control group, and the difference was statistically significant.(Z = 9.67, P < 0.05), (Table 3)
Table 3. Comparison of the improvement of quality of life in two groups of patients with advanced epithelial ovarian cancer after treatment [Case NO. (%)].

<table>
<thead>
<tr>
<th>Group</th>
<th>Case number</th>
<th>Improvement</th>
<th>Stability</th>
<th>Deterioration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>34</td>
<td>21(61.8)</td>
<td>9(26.5)</td>
<td>4(11.8)</td>
</tr>
<tr>
<td>Control group</td>
<td>34</td>
<td>12(35.2)</td>
<td>14(41.2)</td>
<td>8(23.5)</td>
</tr>
</tbody>
</table>

Comparison of Side-effects of two Groups of Patients with Advanced Epithelial Ovarian Cancer after Treatment

After treatment, the incidence of leukocyte decline, abdominal pain and nausea in the observation group were significantly lower than those in the control group (P < 0.05), and the difference was statistically significant (Table 4).

Table 4. Comparison of side effects of two groups of patients with advanced epithelial ovarian cancer after treatment [Case NO. (%)].

<table>
<thead>
<tr>
<th>Group</th>
<th>Case number</th>
<th>leukocyte decline</th>
<th>abdominal pain</th>
<th>nausea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>34</td>
<td>10(29.4)</td>
<td>11(32.4)</td>
<td>9(26.5)</td>
</tr>
<tr>
<td>Control group</td>
<td>34</td>
<td>23(67.6)</td>
<td>18(52.9)</td>
<td>16(47.1)</td>
</tr>
</tbody>
</table>

\[X^2 \] 4.764  4.294  3.905
\[P \] 0.032  0.037  0.044

Discussion

Ovarian tumor is the most fatal gynecologic malignant tumor at present. In recent years, the incidence of ovarian cancer has been increasing year by year. Among them, epithelial ovarian cancer is the most common ovarian tumor. Epithelial ovarian cancer can occur at any age, but most often occur in middle-aged and old women, and young children and puberty rarely occur. Goodman et al. [2] showed that the overall incidence of ovarian cancer increases with age, reaching a peak at about 75 years old and decline after 80 years of age. In Chinese, epithelial ovarian cancer is usually found in 50-60 year old women.

The pathogenesis of epithelial ovarian carcinoma is related to the activation of the proto oncogene and the inactivation of the tumor suppressor gene. The occurrence of most epithelial ovarian cancer may be related to long-term ovulation stimulation. In the long term repeated ovulation, active cell proliferation is needed, while cell proliferation is also accompanied by spontaneous mutation in DNA synthesis. Schildkraut et al. suggest that spontaneous mutations in the p53 gene seem to play an important role in the process of ovarian epithelial cancer. 5%-10% of epithelial ovarian cancer may be related to genetic factors. The risk of ovarian cancer with the BRCA gene mutation at birth is higher than that of the general population and
time onset is earlier than the general case[3]. Mammas et al. [4] believes that the incidence of a few cases may be due to the accumulation of genetic mutations leading to malignant transformation of tumors, that is, the development of benign tumors into borderline tumors, and then the development of invasive ovarian cancer.

The epithelial cells of the ovary differentiate into various other cells, and the histological classification of ovarian epithelial cancer is complex. Because the ovary is located in the deep features of ovarian tissue, most ovarian cancer has been found when advanced, coupled with the shedding of tumor cells caused widespread intraabdominal metastasis, epithelial ovarian cancer is often shown as whole abdominal lesions, the treatment result is poor, with high mortality. The early diagnosis of ovarian cancer has become a hot and difficult point in the research [5-7]. At present, the tumor markers for the diagnosis of epithelial ovarian cancer include CA125, CEA, CA19-9 and so on, but these markers are not specific. Eighty percent of the patients with epithelial ovarian cancer have higher CA125 level. Therefore, serum CA125 combined with transvaginal color Doppler examination is considered as a common index in screening and diagnosing of ovarian cancer. However, data indicate that about 50% of the patients with stage I ovarian cancer have false negative results, that is, CA125 detection is within the normal range. Similarly, the increase of CA125 can also happen in some benign gynecologic diseases, such as endometriosis, pelvic inflammatory disease and so on. The search for tumor markers with high specificity and sensitivity has become a hot research field [8].

The current treatment of ovarian epithelial carcinoma is mainly by surgical resection combined with chemotherapy and radiotherapy. Surgery is the most effective treatment for epithelial ovarian cancer. Through surgical treatment, large lump tumor can be cut or basically cleared, which will create favorable conditions for later chemotherapy and radiotherapy. Therefore, the thoroughness of the first operation is related to the prognosis of the patients.

The first line of chemotherapy for epithelial ovarian cancer is combined of paclitaxel and platinum. Chemotherapy is often accompanied by different degrees of chemotherapy side effects. The most common side effects of paclitaxel combined with platinum are gastrointestinal reaction, bone marrow suppression, ear neurotoxicity and nephrotoxicity. In the course of chemotherapy, the digestive reaction and bone marrow suppression are still very common, which seriously affect the quality of life of the patients. Serious toxic and side effects affect the efficacy of chemotherapy. How to prevent and control the side effects of chemotherapy and improve the quality of life of patients is the hot direction of the study for ovarian cancer[9].

Aidi injection is a pure natural Chinese medicine preparation synthesized by modern pharmaceutical technology. It is composed of acanthopanax, cantharidis, astragalus and ginseng. It has the effect of nourishing qi and supporting the positive, eliminating stasis and dissipating the knot. It is suitable for lung cancer, primary liver cancer, rectal cancer, malignant lymphadenocarcinoma, gynecologic malignant tumor and other kinds of tumors. Modern pharmacological studies have shown that the cantharidis in Aidi injection has anti-tumor effect and can enhance the immune ability of the body, but it has great toxicity. Ginseng, astragalus, and acanthopanax also have some antitumor effect, but it is more important to improve the immunity of the body itself [10-12]. In addition, the protective effects of these three drugs on the kidney can also weaken the renal toxicity of cantharidis, and increase the antitumor effect of cantharidis. The role of Aidi injection in clinical adjuvant chemotherapy can directly kill tumor cells and enhance the efficacy of chemotherapy through enhancing the body’s immunity.
same time, the drug can also reduce the toxic and side effects of chemotherapy and improve the quality of life of the patients.

In short, Aidi injection combined with chemotherapy has synergistic effects in the treatment of advanced epithelial ovarian cancer. It can increase anticancer effect, improve the life quality of the patients, decrease the toxicity, so it can be used as first-line treatment of advanced epithelial ovarian cancer, and it is worthy of further clinical use.

References


