DYNAMICS OF SURVIVAL IN PATIENTS WITH OVARIAN CANCER III-IV DEGREE

Summary. The aim of the study was assessment of survival dynamics of ovarian cancer. The survey was conducted on the basis of OOD (c. Odessa) for 2010 - 2015 were examined 350 patients with ovarian adenocarcinoma of III-IV stage, which was carried with cytoreduction surgery. The average age of patients was 55,3 ± 3,9 years. The sample was dominated by patients with stage IIIC - on average there were 64.9% of the total sample. It is shown that the introduction of integrated circuits based pathogenesis of drug therapy with considering the platinum-resistance can significantly prolong the survival of patients with ovarian cancer. Pathogenetic therapy based on pharmacogenetic peculiarities can significantly improve treatment outcomes (up to 33,1 ± 1,4 months in patients likely to platinum resistance and 36,8 ± 1,9 months in platinum sensitive cases). If probable platynorezystentnosti advisable due to the
Introduction
Ovarian cancer remains the most common cause of death from malignant tumors of the genitals in women [1, 7, 10]. The minute clinical symptoms in the early stages of the disease, a high incidence of metastasis, tumor progression active lead to the late diagnosis of the tumor. The technologies of cytoreduction, chemotherapy and radiotherapy provide only a partial effect on survival. According to statistics at the third stage of the frequency of the 5-year survival does not exceed 34%, while stage IV - 18% only [5, 8, 9].

Unfortunately, about 40% of patients are resistant to primary drugs of platinum, used in current clinical protocols considered as first-line drugs. Depending on the timing of disease progression there were differentiated platinum-sensitive tumors (progressing more than in 6 months after first-line therapy) platinum-resistant (progressing within 6 months after first-line therapy) and platinum-refractory (progressed during first-line chemotherapy with inclusion of platinum drug) [4, 5].

According to current epidemiological studies the average 5-year survival rate for ovarian cancer is 45%. Predictor of prognosis for survival is the age of the patient, the absence of comorbid disease, the presence of the initial stage of the process. Thus, for stages IA and IB inherent in OS at 92%. Unfortunately, only 15% of all cases of ovarian cancer are diagnosed in the early stages.

The aim of the study was the dynamics of survival of ovarian cancer patients

Material and methods
The survey was conducted on the basis of OOD (Odessa, Ukraine) for 2010 - 2015. There were examined 350 patients with ovarian cancer of III-IV stage, which was carried out cytoreduction surgery. Following clinical groups were formed:

The first group (control, n = 50) - patients with ovarian cancer receiving standard first-line chemotherapy (cisplatin - 75-100 mg/m2 intravenously with hydration and diuresis formed every 3 weeks).

The second group (n = 100) - patients with probable platinum refractoriness, they were receiving second line therapy (doxorubicin - 75-100 mg/m2 intravenously every three weeks).

The third group (n = 100) - patients with probable platinum resistance treated on a background of standard first-line therapy with the medication which could correct disregulative disorders (donors of nitric oxide, detoxicant, antyuremic preparations).

Group IV (n = 100) - patients with estimated platinum sensitivity (the standard first-line treatment after prior preventive course: 20 mg dexamethasone for 12 and 6 hours prior to drug administration platinum, cymetidine 300 mg or 50 mg and 50 mg ranitidine, dimedrol in 30-60 minutes).

The survey was conducted of patients accordance with the clinical protocol approved by the Ministry of Health of Ukraine of 17.09.2007 № 554 “On approval of the protocols of care, specialty "oncology" [2, 3].

There were registered indicators of OS (overall survival), DFS (disease free survival), FFTF (freedom from treatment failure), EFS (event free survival), PFS (progression free survival) in accordance with the recommendations of international clinical guidelines [8].

Survival was calculated using Kaplan - Meier using software STATISTICA 13.0 (Dell StatSoft Inc., USA) [6].

Results. Discussion
Established that the age of the patient different groups did not differ, the average age in the group was 55.3 ± 3.9 years. Structure groups stage ovarian cancer also did not differ dominated patients with stage IIIC - 64.9% of the total sample. Clinical disease was stereotyped. Most patients complained of swelling and discomfort in the abdomen, a feeling of pressure in the area of the bladder and rectum, constipation. Every tenth of surveyed women noted vaginal bleeding. Were frequent dyspeptic manifestations, shortness of breath, weakness, fatigue, weight loss, waist and satiation feeling when consumed small amounts of food. In 12.6% of patients were observed edema of the lower extremities, 5.4% - signs of ascites. However, in 17.4% of patients the disease is not accompanied by subjective symptoms and were diagnosed during ultrasonographic screening.

During the ultrasound determined multilocular thick hyperechoic formation larger than 10 cm and enhance blood flow in ovaria. When biochemical screening identifies high numbers of content CA-125 in 44.6% of patients.

During the period of treatment in different clinical groups of patients with advanced complaints of nausea, break of taste, right to food, dizziness, general weakness. In 6.0% of patients assigned to the control group and in 2.0% of patients in group IV marked impairment. For blood count during therapy with platinum drugs were typical signs of mild leucopenia, rarely - anemia. Hypotension was a frequent

Table 1. Survival of patients of different clinical groups.

<table>
<thead>
<tr>
<th>Index</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS, months</td>
<td>28.3±1.4</td>
<td>25.2±0.8</td>
<td>33.1±1.4</td>
<td>36.8±1.9</td>
</tr>
<tr>
<td>DFS, months</td>
<td>14.1±0.4</td>
<td>12.6±0.4</td>
<td>17.2±1.6</td>
<td>29.8±1.4</td>
</tr>
<tr>
<td>FFTF, months</td>
<td>14.4±0.3</td>
<td>12.7±0.2</td>
<td>17.0±1.6</td>
<td>29.7±1.5</td>
</tr>
<tr>
<td>EFS, months</td>
<td>14.5±0.3</td>
<td>12.4±0.3</td>
<td>16.8±0.9</td>
<td>29.5±1.1</td>
</tr>
<tr>
<td>PFS, months</td>
<td>13.9±0.3</td>
<td>11.6±0.2</td>
<td>16.9±0.8</td>
<td>28.9±0.4</td>
</tr>
</tbody>
</table>

Note. * - differences in other clinical groups is statistically significant (p<0.05).
During treatment, the patients in I and IV groups also complained of cough, rash, erythematous and extravasation at the site of injection.

As for the second group of patients, the therapy with doxorubicin for their determined subfebrile symptoms, palpitations, thrombocytopenia and leukopenia, nausea, vomiting, stomatitis symptoms, diarrhea. Early treatment patients group II marked discoloration of urine reddish appearance. A common phenomenon is alopecia, dark soles and palms, sometimes - palmar erythema, change in shape of the nail, itching and rash. Some patients determined a phenomenon photophobia and increased lacrimation. The smallest number of subjective complaints during treatment was observed in patients III and IV groups receiving pathogenesis due to complex metabolic support.

In assessing the dynamics of survival (Table 1) revealed that in group III and IV patients had longer survival periods, with the value of log-rank test \( p = 0.02 \) answered.

As seen from the above data, the introduction of pathogenesis based integrated circuits drug therapy in view of the degree platynorezystentnosti can significantly podovshyty term survival of patients with ovarian cancer. In particular, the overall survival rate in the third group increased to 33.1 ± 1.4 months, and in IV - to 36.8 ± 1.9 months. This corresponds ranges 5.0-71.1 and 3.0-73.3 months, respectively.

As shown in the following figure 1 is the most critical reduction in the number of patients who survived begins 2 years after beginning treatment with modified scheme (a) and in a year - with the use of standard regimens (b) that do not adjust existing violations reox homeostasis and nitrergic autoregulation mechanisms.

**Conclusions and prospects for further development**

1. In our opinion, the use of pathogenesis-based therapy, taking into account pharmacogenetic features can significantly improve treatment outcomes. If probable platinum resistance advisable due to the standard first-line therapy than medications correcting disregulation disorders should be applied (donors of nitric oxide, detoxicant, antiuremic preparations.

2. With predictable platinum sensitivity standard first-line treatment can be supplemented by the medications increasing tolerability of therapy (300 mg cymetidine, ranitidine, or 50 mg and 50 mg dimedrol) but the use of the medications for correction of disregulatory disorders is inappropriate.

The prospect of further research is linked to finding highly informative markers of platinum resistance.

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**References**


9. Why have ovarian cancer mortality rates
Рибін А.І., Свінціцький В.С.
ДИНАМІКА ВИЖИВАННЯ ХВОРІХ НА РАК ЯЄЧНИКІВ ІІІ-IV СТУПЕНІ

Резюме. Метою дослідження була динаміка виживання хворих на рак яєчників. Дослідження проведене на базі ООД (м. Одеса) протягом 2010 - 2015 рр. Було обстежено 350 пацієнток з аденокарциномою яєчників ІІІ-IV стадії, яким було виконано циторедуктивні операції. Середній вік хворих склав 55,3±3,9 років. У вибірці переважали хворі з ІІІС стадією - у середньому їх було 64,9% у загальній вибірці. Показано, що впровадження патогенетично обґрунтованих схем комплексної медикаментозної терапії з урахуванням ступеня платинорезистентності дозволяє суттєво подовжити термін виживання пацієнтів з раком яєчника. Застосування патогенетично обґрунтованої терапії, що враховує фармакогенетичні особливості, дозволяє суттєво покращити результати лікування (до 33,1±1,4 місяців у пацієнтів з ймовірною платинорезистентністю та до 36,8±1,9 місяців у платиночувствитіх випадках). При ймовірній платинорезистентності доцільно на фоні стандартної терапії першої лінії застосовувати медикаментозну корекцію дизрегуляційних порушень (донатори оксиду азота, детоксиканти, антиурикемічні засоби). При прогнозованій платиночувствительності стандартна терапія першої лінії може бути доповнена засобами, які покращують переносимість терапії, але використання медикаментозної корекції дезрегуляційних порушень є недоцільним.

Ключові слова: рак яєчників, виживання, лікування.

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