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EXPERIENCE WITH THE USE OF HIPEC IN ADVANCED SEROUS OVARIAN CANCER AFTER COMPLETE AND OPTIMAL CYTOREDUCTION

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***Background*: Ovarian cancer (OC) is one of the most demanding unresolved issues in oncogynecology. In Ukraine, there are over 3000 new cases of the disease annually. 24.6% of patients die within the first year after diagnosis. It indicates the relevance of developing new and optimizing existing OC treatment programs. *Aim:* To analyze the short-term results of hyperthermic intraperitoneal chemotherapy (HIPEC) in patients with primary (non-recurrent) advanced serous OC, in comparison with the group of patients after standard cytoreductive surgery (CRS) of high and medium complexity, according to the following indicators: the effect on metabolism, postoperative complications, length of stay in intensive care unit and hospital, timing of adjuvant chemotherapy initiation. *Materials and Methods:* Cases of 35 patients with advanced serous OC who underwent the treatment at the Oncogynecology Department of the National Cancer Institute from December 2018 to April 2020 were analyzed. For the assessment of surgical procedures volumes, a surgical complexity scoring system was used. HIPEC was performed in 20 patients (57.1%), while 15 patients (42.9%) underwent standard CRS. *Results:* At the beginning and end of the HIPEC procedure, a shift in acid-base state and the development of hyperthermia were evident. At the end of the 1st day of the postoperative period, statistically significant changes ($p < 0.05$) were revealed in pH, base excess, body temperature, alanine transaminase and aspartate transaminase levels in patients from HIPEC group indicating the development of metabolic acidosis and toxic liver damage. The negative effects of HIPEC developed at the end of the procedure may persist at the end of the first postoperative day. While metabolic acidosis diminishes, the signs of hepatotoxicity persist. Toxic liver damage is the most frequent complication of the postoperative period detected more often ($p < 0.05$) after HIPEC in comparison with standard CRS. Standard adjuvant chemotherapy began on average in 31.9 ± 4.4 days in HIPEC group and 18.6 ± 1.6 days in CRS group ($p < 0.05$). *Conclusions:* The data obtained indicate that HIPEC negatively affects metabolism and aggravates the severity of disorders that develop during the CRS phase. The use of HIPEC postpones the initiation of adjuvant chemotherapy, which is probably associated with a longer period of restoration of the functions of organs and systems of patients (in particular, liver function). The feasibility of HIPEC in advanced serous OC treatment requires further research.**

***Key Words:* serous ovarian cancer, surgical treatment, cytoreduction, hyperthermic intraperitoneal chemotherapy.**

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Ovarian cancer (OC) is one of the most demanding unresolved problems in oncogynecology. Every year over 3 thousand new OC cases are detected in Ukraine. According to the updated data of the National Cancer Registry 3,539 new cases of OC were registered in 2018 [1]. The incidence rate of OC in Ukraine has been stable for the last 3 years and in 2019 totaled 18.4 per 100,000 of the female population. A similar trend is observed in mortality rates. In 2019, OC death rate in Ukraine was 9.4 per 100 000 of the female population. During the first year after diagnosis, 24.6% of newly diagnosed patients die [1].

All the above indicates the relevance of developing new and optimizing existing treatment programs for OC. Nowadays, the international medical community is actively discussing the feasibility of using hyperthermic intraperitoneal chemotherapy (HIPEC) in patients with advanced OC. The European Recommendations (2019) consider the existing evidence base of eight randomized trials (№ 02124421, № 01628380, № 00426257, № 02328716, № 01091636, № 01539785 – HORSE, № 01767675, № 01376752 — CHIPOR) being insufficient for the use of HIPEC as an adjuvant to cytoreductive surgery (CRS) in patients with advanced OC (recommendation 17.3, IV/A) [2].

For example, in GOG study, 172 patients with stage III of the disease were randomized into three weeks of intravenous administration of cisplatin/paclitaxel or intravenous administration of paclitaxel followed by intraperitoneal administration of cisplatin/paclitaxel, which demonstrated a remarkable improvement in overall survival (OS) [3], persisting even after 10 years [4]. However, the toxicity of intraperitoneal chemotherapy (grade 3–4 leukopenia, complications from the gastrointestinal tract, kidneys, infection and pain syndrome) was noted much more often, and the quality of life of such patients decreased even comparing to earlier studies [5, 6].

The phase III randomized controlled trial of GOG 252 in patients with stage II–IV epithelial OC (EOC) also compared intraperitoneal *vs* intravenous chemotherapy and did not confirm the improvement in progression-free survival (PFS) with intra-abdominal

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Abbreviations used: ABGs – arterial blood gases; APCT – adjuvant polychemotherapy; BE – base excess; CRS – cytoreductive surgery; EOC – epithelial ovarian cancer; HIPEC – hyperthermic intraperitoneal chemotherapy; IDS – interval debulking surgery; OC – ovarian cancer; OS – overall survival; PFS – progression-free survival; POD-0 – 1st day of the postoperative period; SCS – surgical complexity score; SL – serum lactate.

administration. In addition, intravenous chemotherapy was tolerated by patients better [7].

A randomized clinical trial of the HIPEC effect on recurrent EOC [8] has received widespread criticism [7, 9, 10], and meta-analysis of retrospective studies on advanced stages of EOC or its relapses [11] did not show any survival benefit, but reported an increase in side effects such as anemia or acute kidney injury [12, 13] making it impossible to include HIPEC into treatment standards.

OVHIPEC Phase III multicenter open-label study [14] compared two groups of patients with stage III EOC: a group with an abdominal lesion too extensive for primary debulking surgery or after primary debulking surgery with a residual tumor with more than 1 cm in size and a group after 3 cycles of NAPCT for performing interval debulking surgery (IDS) followed by HIPEC or without it. The addition of HIPEC to IDS led to a significant increase in PFS and OS without toxicity increase. However, according to the opinion of most authors [15–18] it is impossible to extrapolate these results to all patients with advanced stages of OC. The authors also believe that the toxicity of HIPEC appears to have been underestimated, because of longer operation duration, longer hospitalizations, more perioperative gastrostomies/stomas and vague reports on known complications (e.g. acute renal failure) in the HIPEC group [17–20].

The survival analysis in the randomized study of Lim *et al.* [12] in patients with stage III–IV OC also has not demonstrated superiority of the HIPEC over CRS without HIPEC in treating the residual tumor less than 1 cm in size.

Still, NCCN since version 1 of 2019 [21] recommends performing HIPEC with cisplatin at a dose of 100 mg/m^2 in patients with stage III of disease after interval CRS.

The aim of the study is to analyze the short-term results of HIPEC in patients with primary (non-recurrent) advanced serous OC according to the following indicators: degree of HIPEC aggressiveness, postoperative complications, length of stay in intensive care unit and hospital, timing of adjuvant chemotherapy initiation in comparison with the group of patients after standard CRS of high and medium complexity according to surgical complexity scoring (SCS) scale.

MATERIALS AND METHODS

The treatment analysis of 35 patients with advanced serous OC treated at the Oncogynecology Department of the National Cancer Institute from December 2018 to April 2020 was performed. All patients were thoroughly informed about the study that was approved by the Institutional ethics committee. The clinical characteristics of patients with advanced serous OC, stages III–IV are shown in Table 1. 15 patients (42.9%) with primary advanced serous OC received standard treatment (CRS group). HIPEC was performed in 20 patients (57.1%) (CRS + HIPEC group).

The amount of cytoreduction was documented according to the requirements of the protocol of the European Society of Gynecological Oncologists — ESGO (ESGO Guidelines, Recommendations and Assurance Quality Committee, 2016) [22].

To assess the volume of performed surgical interventions and to predict possible postoperative complications, SCS system was used, providing quantification for each surgical procedure [23]. The points were given according to the volume of performed surgery.

HIPEC was carried out after CRS in patients with peritoneal carcinomatosis. The treatment was performed with the Performer HT apparatus (RanD, Italy) — a multifunctional system for local specialized chemotherapy focusing on support of multiple therapy regimens based on extracorporeal blood/fluid circulation.

After reaching an intraabdominal temperature of 41 °C, cisplatin 100 mg/m^2 was dissolved in 5000 ml of perfusate, which circulated at a rate of 700–800 ml/min for 60 min. The average volume of perfusate in the abdominal cavity was 3000 ml simultaneously. The intra-abdominal temperature ranged from 41 °C to 43 °C. The cooling phase of the abdominal cavity and the washing phase from chemotherapy lasted 5–10 min at maximum. The patient was transferred to the intensive care unit for intensive care and observation.

The maintenance therapy of surgical treatment was based on the protocols of multimodal analgesia, antibacterial therapy, ERAS 2016, MASCC and ESMO, as well as the protocol of anesthesia and intensive care developed at the National Cancer Institute.

Adjuvant polychemotherapy (APCT), according to the TC protocol, as standard-of-care in first-line OC treatment [2], included every 3 weeks intravenous carboplatin (AUC6) and paclitaxel (175 mg/m^2).

Standard descriptive statistics methods were used to process the data; in particular, mean values were calculated with their standard errors. The difference between the study groups was assessed using the Student's *t*-test and the chi-square test ($\chi 2$). The calculations were performed on a personal computer using the Microsoft Excel and GraphPad Prism 6.01 software packages. The critical level of statistical significance was taken equal to 0.05.

RESULTS

Complete cytoreduction (R0) (Figure) was performed in 10 (50%) patients of CRS + HIPEC group

Table 1. General clinical characteristics of OC patients

Indexes	Number of patients	
	N	%
Age of patients (years)		
Average	50.9 ± 1.98	
Min	23	
Max	70	
Stage		
III	30	85.7
IV	5	14.3
Grade		
Moderate (G2)	5	14.3
High (G3)	22	62.9
Psammoma cancer (Gx)	8	22.8

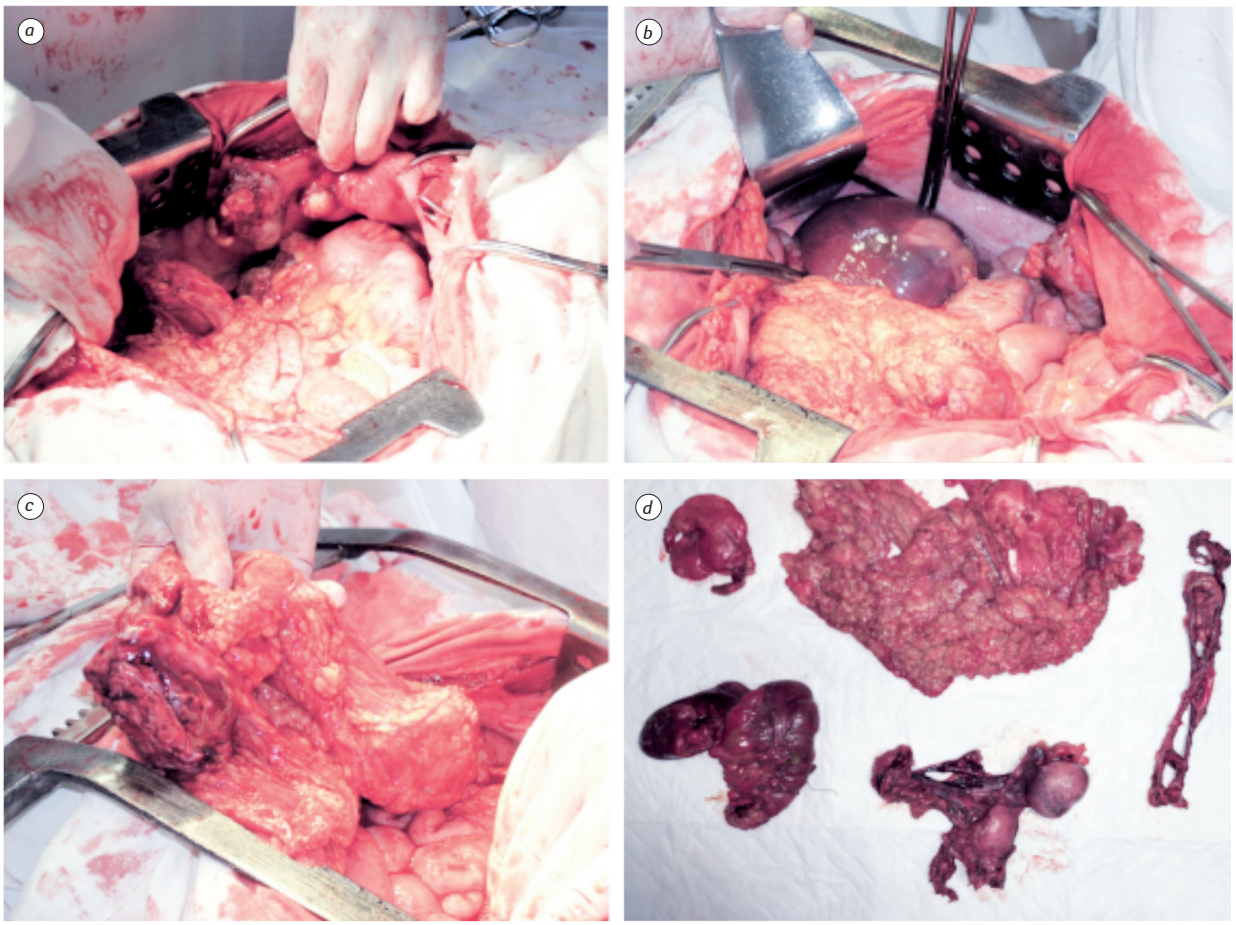

Figure. Patient B., 56 y.o; primary high grade EOC: *a, b* — tumor masses in the pelvis; *c* — omentum with tumor masses; *d* — uterus with fallopian tubes, ovarian tumors and pelvic peritoneum with metastasis. Omentum with metastasis; rectosigmoid part of colon with metastasis; diaphragmatic peritoneum with metastasis

and 10 (66.7%) patients in CRS group while optimal cytoreduction (R1) — in 10 (50%) patients of CRS + HIPEC group and 5 (33.3%) in CRS ($p > 0.05$). Since the patients of the study and control groups did not differ in the volume of CRS, the groups could be considered as homogeneous.

Operations of medium complexity included hysterectomy with bilateral adnexectomy, omentectomy, pelvic peritonectomy, diaphragm stripping, appendectomy, cholecystectomy (4–7 points).

High-complexity operations included hysterectomy with bilateral adnexectomy, omentectomy, diaphragm stripping with resection of the central tendon of the diaphragm, low anterior resection of the rectum, tumor foci removal on the mesenterium of the ileum and ascending colon, ileum resection and appendectomy (8–13 points).

Operations of medium complexity (4–7 points) were performed in 8 (40%) patients of CRS + HIPEC group and 1 (6.7%) patient in CRS group. Operations of high complexity (⩾ 8 points) were performed in 12 (60%) patients of CRS + HIPEC group and 14 (93.3%) patients in CRS group ($p < 0.05$). Therefore, in the control group, the level of operation complexity by SCS scale was significantly higher.

To evaluate HIPEC toxicity we analyzed changes in body temperature, arterial blood gases (ABGs), serum lactate (SL) level, and vasopressor requirements during the procedure. As can be seen from Table 2, HIPEC resulted in elevated body temperature exceeding 38 °C in 10 patients (50%), including 2 patients (10%) with body temperature above 39 °C. Vasodilation and arterial hypotension during HIPEC required norepinephrine support in 11 patients (55%) with a mean dose of 0.16 μg/kg/min.

Most patients developed metabolic acidosis within the HIPEC procedure or worsened the metabolic acidosis developed at the end of the surgery. Only one patient (5%) had base excess (BE) below –10 mmol/l at the beginning of HIPEC, while at the end of the procedure 5 patients (25%) had BE below –10 mmol/l despite of Na-bicarbonate infusion (270 mmol in average) in 6 patients (30%) during the HIPEC. Although the increase of SL level at the end of HIPEC was not statistically significant, there is an increased risk of postoperative complications

Table 2. Body temperature, ABGs, and SL level before and after HIPEC procedure in CRS + HIPEC group (n = 20)

№	Indicator	Start of HIPEC	End of HIPEC
1	pH	7.32 ± 0.01	7.31 ± 0.01
2	BE, mmol/l	–5.60 ± 0.63	–8.11 ± 0.55*
3	$PaCO_2$ mmHg	34.15 ± 0.88	31.90 ± 1.09
4	Body temperature, °C	36.20 ± 0.15	38.12 ± 0.16*
5	SL, mmol/l	1.91 ± 0.45	2.23 ± 0.57

Note: * $p < 0.05$ as compared to the indexes at the start of HIPEC.

after CRS + HIPEC with SL levels above 2 mmol/l according to literature data [24]

Therefore, HIPEC negatively affects metabolism and aggravates the severity of disorders that develop during the CRS phase. Nevertheless, the intensive care (body cooling, hyperventilation, the use of norepinephrine and Na-bicarbonate infusion) may compensate mentioned disorders and increase the safety of HIPEC.

The effect of HIPEC on metabolism was assessed not only at the end of the procedure, but also at the end of the first postoperative day (POD-0), comparing these data with the CRS group without HIPEC. As can be seen from Table 3, body temperature at the end of POD-0 in the HIPEC group was higher, although the level of hyperthermia was subfebrile.

In addition to the difference in body temperature there was a difference in the severity of metabolic acidosis, although acidosis remained at a compensated level. Besides, both groups differed significantly in alanine aminotransferase & aspartate aminotransferase levels, indicating hepatotoxicity, probably due to chemotherapy and hyperthermia itself.

Thus, negative effects of HIPEC, which developed at the end of the procedure, may persist at the end of the first postoperative day (POD-0). While metabolic acidosis diminishes at the end of POD-0, signs of hepatotoxicity persist.

We have identified the most common surgical and non-surgical complications in both groups of patients. Pleurisy was one of the most frequently encountered surgical complications (Table 4) diagnosed on days 2–5 in patients of both groups without statistically significant difference ($p > 0.05$). Such complication required the intervention of a thoracic surgeon. Surgical complications of IIIb severity according to Clavien — Dindo requiring repeated laparotomy associated with stump failure and stoma necrosis after CRS were diagnosed in 1 (5%) case in CRS + HIPEC group and in 1 (1.6%) case in CRS group.

Among the most frequent non-surgical complications (Table 5) in the postoperative period, we identified mild and moderate anemia and toxic liver damage that occurred in 14 (70%) patients in CRS + HIPEC group and 3 (20%) in CRS group ($p < 0.05$). It should be noticed that 30-day mortality was recorded only in one (5%) case in the group of patients with HIPEC.

We analyzed the immediate (short-term) results of treatment of patients of both groups in terms of such indicators as the length of stay in the intensive care unit, the duration of inpatient treatment after surgery, as well as the timing of APCT initiation (Table 6).

According to the results of the analysis, there was no significant difference between the groups of patients regarding the duration of their stay in the intensive care unit and the hospital, however, APCT reliably ($p < 0.05$) began later in the group of patients with HIPEC. Thus, in CRS + HIPEC group, APCT began on average in 31.9 ± 4.4 days postoperatively while in CRS group — in 18.6 ± 1.6 days ($p < 0.05$) evidencing that HIPEC delayed the APCT onset.

Table 3. Body temperature, ABGs, creatinine, albumin, ALT and AST at the end of the POD-0 in CRS + HIPEC group and CRS group

Indicator	CRS + HIPEC (n = 20)	CRS without HIPEC (n = 15)
pH	7.33 ± 0.01*	7.37 ± 0.02
BE, mmol / l	–3.80 ± 0.98	–3.21 ± 0.19
$PaCO_2$ mmHg	34.3 ± 1.3	35.8 ± 0.83
Body temperature, °C	37.37 ± 0.14*	36.99 ± 0.10
Creatinine, µmol /l	87.1 ± 3.3	88.63 ± 5.34
Albumin, g/l	28.20 ± 1.19	28.00 ± 1.05
Alanine aminotransferase, U/l	139.62 ± 21.10*	52.6 ± 12.61
Aspartate aminotransferase, U/l	144.57 ± 19.40*	43.2 ± 7.28

Note: *Difference between groups is significant, $p < 0.05$.

Table 4. Surgical complications in the postoperative period

Complication	Clavien – Dindo severity grade	With HIPEC (n = 20)	Without HIPEC (n = 15)
Pleurisy	IIIa	10 (50%)*	4 (26.7%)
Failure of the stump	IIIb	1 (5%)	0
Stoma necrosis	IIIb	0	1 (6.7%)

Note: *$p = 0.08$; χ^2 test.

Table 5. Non-surgical complications in the postoperative period

Complication	Clavien – Dindo severity grade	With HIPEC (n = 20)	Without HIPEC (n = 15)
Anemia I-II	I	12 (60%)	8 (53.3%)
Toxic liver damage	II	14 (70%)*	3 (20%)
Acute kidney injury	II	8 (40%)	4 (26.7%)
Anemia III	II	8 (40%)	**7** (46.7%)
Gastrostasis or ileus paralytic	II	1 (5%)	3 (20%)
Pancreatitis	II	2 (10%)	2 (13.3%)

Note: *$p < 0.05$ – the difference between the study and control group is statistically significant.

DISCUSSION

The issue of the HIPEC application in OC treatment remains debatable as HIPEC has both positive and negative sides.

The advantages of HIPEC include the possibility of creating a high local concentration of the chemotherapeutic agent in the tumor immediately after CRS, which is aimed to battle micrometastases and prevent recurrences. This statement is confirmed by data of Bhatt and Glehen, who recommend using the peritoneal carcinomatosis index (PCI) as a tool for the patient selection and as a prognostic marker [25], which partially echoes the suggestion of using SCS system in our study for similar purposes. Also, Halkia and Spiliotis confirm the benefits of HIPEC as a method of obtaining a higher degree of cytoreduction by the attempt to eliminate the microscopic component of the tumor, which is responsible for the development of recurrences [26]. This opinion is consistent with the results of a study by Ukrainian authors [27], which confirms safety of HIPEC use in patients with

Table 6. Immediate (short-term) results of treatment in the study and control group

Indicators	with HIPEC (n = 20)	without HIPEC (n = 15)
Length of stay in intensive care unit (number of days after surgery)	1.46 ± 0.13	1.85 ± 0.33
Length of hospital stay (number of days after surgery)	11.32 ± 0.74	11.93 ± 1.23
Onset of APCT terms (number of days after surgery)	31.9 ± 4.4*	18.6 ± 1.6

Note: *$p < 0.05$ – the difference between the study and control group is statistically significant.

OC IIIA-IIIC stage, who underwent optimal (28%) and suboptimal cytoreduction (72%) with improved life quality of such patients for 6 months after treatment.

Once again, the result of the OVHIPEC study should be commented, in which 245 patients with initially presumed inoperable EOC were randomly assigned either to undergo HIPEC or not at their IDS, if not having the disease progression after three cycles of neoadjuvant chemotherapy [14]. The study reported a statistically significant PFS and OS benefit of HIPEC + IDS without significant increase of surgical morbidity and mortality. This study was criticized [17] due to its design, lack of surgical morbidity description, absence of established surgical morbidity classification score (e.g. Clavien — Dindo). Van Driel *et al*. [14] reported equivalent toxicity in both arms of the study, which caused bewilderment among critics, as the group with HIPEC patients received an additional course of cisplatin chemotherapy.

At the same time, the majority of other authors' data [25–27] indicate a good tolerability of the HIPEC procedure. Nevertheless, the results of our study demonstrate a significantly more frequent diagnosis of toxic liver damage after HIPEC.

Hyperthermia should also be noted as a negative side of HIPEC. According to the data of Tkachenko *et al.* [27], hyperthermic reaction after HIPEC was observed in 24.3% of cases, which was subsequently managed by taking non-steroid anti-inflammatory drugs. The authors also testify to the presence of pain syndrome in the area of drainage tubes removal syndrome in the area of the lavage drains introduction in 13.5% of patients. These data coincide with ours, among which we identified hyperthermia, the presence of metabolic acidosis, toxic liver damage, which we diagnosed in patients of the study group at the end of the 1st day of the postoperative period (POD-0). However, the above violations were successfully corrected by the use of appropriate drug treatment in adequate doses.

Thus, in light of the conflicting scientific evidence available today, the attitude of the medical community towards the use of HIPEC for the treatment of patients with OC differs in Europe and the United States. European medical community does not yet recommend the use of HIPEC as a standard treatment. Recommendation of ESMO — ESGO consensus conference (2019; recommendations 14.2) states that HIPEC is not a standard of care as first-line treatment (Level of evidence: II, strength of recommendation: A [2]. However, the accumulated existing data allowed the inclusion of HIPEC (cisplatin 100 mg/m^2, as in our study) to the NCCN guidelines for the treatment of OC patients with III stage after IDS (NCCN guidelines, version 1/2020) [21].

To sum up, despite the fact that HIPEC after CRS is a promising treatment option for peritoneal carcinomatosis in patients with advanced OC, this problem requires further study considering patient selection criteria, safety profile and analysis of long-term treatment results.

Although HIPEC negatively affects metabolism and aggravates the severity of disorders that develop during the CRS phase, the intensive therapy methods make it possible to compensate for above-mentioned metabolic disorders and increase the safety of the HIPEC procedure. Toxic liver damage is the most frequent complication of the postoperative period and is reliably more often detected after HIPEC in comparison with standard CRS.

The use of HIPEC postpones the initiation of APCT, which is probably associated with a longer period of restoration of the functions of organs and systems of patients (in particular, liver function), which was revealed by the results of our study. Correction of all complications is possible, but only in highly specialized cancer centers with close cooperation of the attending physician with the anesthesiologist. The feasibility of the HIPEC use in the treatment of patients with advanced serous OC requires further study.

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ДОСВІД ВИКОРИСТАННЯ HIPEC ПРИ ЗАПУЩЕНОМУ СЕРОЗНОМУ РАКУ ЯЄЧНИКА ПІСЛЯ ПОВНОЇ ТА ОПТИМАЛЬНОЇ ЦИТОРЕДУКЦІЇ

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Стан питання: Рак яєчника (РЯ) — одна з найсерйозніших невирішених проблем онкогінекології. В Україні щорічно реєструється понад 3000 нових випадків захворювання, 24.6% хворих помирають протягом першого року після встановлення діагнозу. Це вказує на актуальність розробки нових і оптимізації існуючих програм лікування РЯ. ***Мета***: Проаналізувати короткотермінові результати застосування гіпертермічної внутрішньоочеревинної хіміотерапії (HIPEC) у пацієнток з первинним (нерецидивним) розповсюдженим серозним РЯ у порівнянні зі стандартними циторедуктивними операціями (ЦРО) високого та середнього ступеня складності за шкалою SCS за наступними показниками: вплив на метаболізм, післяопераційні ускладнення, тривалість перебування у відділенні реанімації та стаціонарі, термін початку ад'ювантної поліхіміотерапії. ***Матеріали та методи***: Проаналізовано 35 випадків розповсюдженого серозного РЯ. Хворі лікувалися у відділенні онкогінекології Національного інституту раку з грудня 2018 р. до квітня 2020 р. Для оцінки обсягів хірургічних втручань була використана шкала оцінки складності хірургічної операції (SCS). HIPEC було проведено 20 пацієнткам (57.1%), а 15 пацієнткам (42.9%) було виконано стандартну ЦРО. ***Результати***: На початку та в кінці процедури HIPEC було виявлено статистично значущу різницю ($p < 0.05$) у показниках кислотно-основного стану та температури тіла, що свідчить про зсув кислотно-основного стану та розвиток гіпертермії. Наприкінці 1-го дня післяопераційного періоду у пацієнток із групи HIPEC виявлено статистично значущі зміни ($p < 0.05$) за pH, показником кислотно-основного стану, температурою тіла, рівнями аланінамінотрансферази та аспартатамінотрансферази, що свідчить про розвиток метаболічного ацидозу та токсичного ураження печінки. Останнє є найчастішим ускладненням післяопераційного періоду і значно частіше ($p < 0.05$) виявляється після HIPEC у порівнянні зі стандартними ЦРО. Стандартна ад'ювантна хіміотерапія починалася в середньому через 31.9 ± 4.4 доби у групі HIPEC та через 18.6 ± 1.6 доби у групі без HIPEC ($p < 0.05$). ***Висновки***: Отримані дані вказують на те, що HIPEC негативно впливає на обмін речовин та посилює тяжкість розладів, що розвиваються на етапі ЦРО. Несприятливі ефекти HIPEC, що розвинулися в кінці процедури, можуть персистувати до кінця першої доби після операції. Хоча вираженість метаболічного ацидозу зменшується в цей термін, ознаки гепатотоксичності зберігаються. Застосування HIPEC відтерміновує початок ад'ювантної поліхіміотерапії, що, ймовірно, пов'язано з більш тривалим періодом відновлення функцій органів та систем хворих, зокрема функції печінки. Можливість застосування HIPEC у лікуванні розповсюдженого серозного РЯ потребує подальших досліджень.

Ключові слова: серозний рак яєчника, хірургічне лікування, циторедукція, гіпертермічна внутрішньочеревна хіміотерапія.