Paclitaxel/carboplatin versus cyclophosphamide/carboplatin in peritoneal carcinomatosis of the ovary

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Summary

The preceding platinum-based combination chemotherapy could possibly reduce tumor masses, allowing for adequate surgical debulking in advanced ovarian cancer. In this study, a total of 18 patients with peritoneal carcinomatosis of the ovary were evaluated between 1996 and 2003. All patients underwent open biopsy for the histopathologic confirmation of ovarian tumor. Forty-one percent of the patients (8/18) were administered six cycles of carboplatin /cyclophosphamide (CP) and the rest were administered six cycles of paclitaxel/carboplatin (TP) as a neoadjuvant chemotherapy (10/18).

After six cycles of chemotherapy metastases to the peritoneum, Douglas' pouch, diaphragm, and liver serosa were higher in the CP group than the TP group ($p < 0.05$). All patients also had a better performance status (WHO performance status 0 or 1), but no statistical difference was observed between either group ($p > 0.05$). Optimal debulking surgery rates were significantly higher in the TP group ($p < 0.05$).

In conclusion, we suggest paclitaxel/carboplatin in peritoneal carcinomatosis of the ovary as a neoadjuvant chemotherapy. However, large prospective, randomized studies should be performed in patients with peritoneal carcinomatosis of the ovary.

Key words: Peritoneal carcinomatosis; Ovary; Paclitaxel; Carboplatin; Cyclophosphamide; Debulking surgery.

Introduction

Ovarian cancer spreads early in the disease to the abdomen. At surgery, large pelvic tumor lesions are found together with multiple tumor lesions involving the omentum, bowel, and mesentery together with diffuse peritoneal carcinomatosis and diaphragmatic involvement. Approximately 70% of patients present with advanced ovarian cancer, a stage when total resection of all tumor is usually impossible.

The size of residual disease after surgery is one of the most important prognostic factors for survival. Hacker *et al.* [1] revealed that even more cytoreduction – leaving tumors smaller than 0.5 cm – was of additional benefit when compared to 0.5-1.5 cm and > 1.5 cm, leading to an increased overall survival of 40, 18 and six months, respectively.

Neoadjuvant chemotherapy refers to administration of chemotherapy before surgery is performed. Several studies have been published on the rationale for interval debulking surgery which is a surgical procedure with debulking followed by chemotherapy [2-5]. These studies suggest that neadjuvant chemotherapy is most beneficial for women who are medically impaired and unable to tolerate aggressive cytoreductive surgery.

In this study we prospectively compared the use of paclitaxel/carboplatin and cylophosphamide/carboplatin in 18 patients with peritoneal carcinomatosis of the ovary. The efficacy of optimal debulking surgery and performance status were examined.

Patients and Methods

A total of 18 patients with peritoneal carcinomatosis of the ovary were evaluated between 1996 and 2003. All patients had large abdominal ascites and were examined by computed tomography (CT) and ultrasound of the pelvis and abdomen. The CT scan and ultrasound revealed multiple metastases in the pelvis and abdomen including the diaphragm and liver parenchyma. Thirteen of 18 patients had pleural effusion at chest-X-ray. All patients were medically unfit for primary surgery, such as those with WHO performance status 2 or 3. All patients underwent open biopsy for histopathologic confirmation of ovarian tumor.

Forty-one percent of the patients (8/18) were administered six cycles of carboplatin 6 AUC/cyclophosphamide (600 mg/m^2) (CP) and the rest were administered six cycles of paclitaxel (175 mg/m^2)/carboplatin 6AUC (TP) as neoadjuvant chemotherapy (10/18).

All patients underwent laparotomy and tumor reductive surgery including total abdominal hysterectomy, pelvic lymph node dissection, omentectomy and appendectomy after six cycles of chemotherapy.

The same surgeon (OB) performed the surgical procedures. The performance status and surgical parameters were compared using the chi-square test.

Results

There were no significant differences between the two groups regarding age (57.5 ± 7.8 vs 56.7 ± 6.8) ($p > 0.05$). Histologic tumor types, age and tumor grading are shown in Table 1. Table 2 shows the degree of optimal debulking in the two groups and the distribution of residual tumor tissue diameters. After six cycles of chemotherapy, metastases to the peritoneum, Douglas pouch, diaphragm, and liver serosa were higher in the CP group than the TP group ($p < 0.05$). All patients also had a better performance status (WHO performance status 0 or 1), but no significant difference was observed between either group ($p > 0.05$). Optimal debulking surgery rates were significantly higher in the TP group than the CP group ($p < 0.05$).

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Table 1. — *Histologic tumor types, tumor grading, and age of patient.*

		TP (n: 10)	CP (n: 8)
Histologic type	Serous	8	6
	Endometrioid	2	2
Age (years)		57.5 ± 7.8	56.7 ± 6.8
Tumor grading	G2	3	2
	G3	7	6

TP: paclitaxel-carboplatin; CP: cyclophosphamide-carboplatin.

Table 2. — *Degree of optimal debulking surgery.*

	TP (n: 10)	CP (n: 8)
No residual tumor	3 (30%)	1 (12.5%)
< 1 cm	6 (60%)	4 (50%)
> 1 cm	1 (10%)	3 (37.5%)

TP: paclitaxel-carboplatin; CP: cyclophosphamide-carboplatin.

Discussion

Cytoreductive surgery is the cornerstone of treatment for women suspected of having advanced ovarian cancer. Platinum-based chemotherapy is the traditional treatment, with response rates of 70-80% and pathologic complete remission in 20-25% of patients [6]. However, a combination of paclitaxel and platinum analog is currently the standard first-line chemotherapy for women with ovarian cancer with response rates of 20-37% [7]. Despite advances in surgery, it is still not possible in most patients with ovarian cancer to remove the tumor completely. For these patients, the concept of primary chemotherapy followed by interval debulking has emerged. Lawton *et al.* [8] treated 36 patients with advanced, unresected epithelial ovarian cancer using chemotherapy combined with intervention debulking surgery in 1989. Of these patients, 78% underwent interval debulking surgery and 98% could be optimally (residual tumor size was less than 2 cm) debulked.

In 1991 Jacob *et al.* [5] treated 22 patients with FIGO Stage III and IV epithelial ovarian cancer using cisplatin-based chemotherapy after initial laparotomy and biopsy only. In that study the planned treatment was two to four cycles of chemotherapy, interval debulking surgery, six more chemotherapy cycles and second-look laparotomy. Optimal cytoreduction to less than or equal to 2 cm was achieved for 77% of the study group vs 39% of the immediate-reexploration group (18 patients). In another recent retrospective study by Kayikcioglu *et al.* [9], neoadjuvant chemotherapy followed by interval surgery was performed in 45 of 205 patients with advanced ovarian cancer and medically unfit for primary surgery. In that study, optimal cytoreductive surgery rates were significantly higher in the neoadjuvant CT group. Chan *et al.* [10] treated 17 patients with advanced ovarian cancer using neoadjuvant chemotherapy based on the extent of disease on CT. All patients received three or six cycles of combined platinum/paclitaxel chemotherapy. In that study the rate of optimum debulking to residual disease less than 2 cm after chemotherapy was 76.9%, and 38.5% had no gross residual disease after surgery.

In our study, we found that the degree of debulking was significantly higher in the TP group of patients than the CP group. The performance status was better in all patients, but no significant difference was observed between groups. Neoadjuvant chemotherapy was employed in women who, by diagnostic analysis, were unlikely to undergo successful optimal cytoreductive surgery. The current data are derived mainly from single institution experiences and suggest that this approach may increase disease-free survival but does not improve overall survival of patients [11]. With neoadjuvant approaches to patients with bulky disease several advantages may be added; reduction in tumor volume, ascites or plural effusions could improve patient performance status before surgery, and preceding debulking of the tumor with combination chemotherapy might result in an increased rate of maximal cytoreduction with less blood loss, reduced operative morbidity, and shorter operations, intensive care unit stays and overall hospitalizations [12].

In conclusion, neoadjuvant chemotherapy is most beneficial for women who are medically impaired and unable to tolerate aggressive surgery due to large pleural effusion, parenchymal liver metastasis, and peritoneal carcinomatosis. We also suggest paclitaxel/carboplatin in these patients as a neoadjuvant chemotherapy. However, large prospective randomized studies should be performed in patients with peritoneal carcinomatosis of the ovary.

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