Technical innovations

Intra-operative intra-peritoneal chemotherapy with cisplatin in patients with peritoneal carcinomatosis of ovarian cancer

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Abstract

Background: Intra-peritoneal (i.p.) chemotherapy is an encouraging treatment option for ovarian cancer with peritoneal involvement in addition with intravenous (i.v.) chemotherapy. Intra-operative i.p. chemotherapy is an interesting method of administration by enhancing the diffusion of chemotherapy. This study had assessed the feasibility of intra-operative i.p. chemotherapy in patients with peritoneal carcinoma of ovarian cancer.

Methods: From January 2003 to February 2006, 47 patients with stage III ovarian cancer were treated with standard paclitaxel carboplatin intravenous chemotherapy and debulking surgery with intra-operative i.p. chemotherapy. After optimal cytoreductive surgery, defined by no unresectable residual disease > 1 cm, i.p. chemotherapy was performed during surgery. The peritoneal cavity was filled by 3 litres of isotonic saline pre-heated at 37 degrees and 90 mg of cisplatin. The sequence was repeated twice during 2 hours based on previous published studies which optimized the cisplatin dosage and exposure duration. Optimal diffusion was obtained by stirring by hands during the 2 hours.

Results: Median age was 59.6 years. No severe haematological or non-haematological toxicity induced by intra operative i.p. chemotherapy was reported. No patient died due to the complications of surgery or the i.p. chemotherapy. No neurotoxicity occurred, and one patients had renal impairment.

Conclusion: This study demonstrates the feasibility of intra-operative i.p. chemotherapy with cisplatin after optimal resection of peritoneal tumor nodules. Further randomized trials are planned to investigate the clinical benefit of this therapeutic modality.
**Background**

Ovarian cancer is the leading cause of gynaecologic cancer-related death in most industrialized countries and the fifth cause of cancer death among women [1-3]. Approximately 60% of women have an advanced FIGO stage III-IV ovarian cancer at diagnosis and the 30% 5-year survival rate is dramatically poor. The peritoneal cavity is the main site of disease involvement in ovarian cancer [4,5]. Standards treatments include exploratory laparotomy with cytoreductive surgery followed by intra-venous (i.v.) platinum-taxane-based chemotherapy [6-8]. Nevertheless, additional intra-peritoneal (i.p.) chemotherapy is an encouraging treatment option for ovarian cancer with peritoneum involvement [9,10]. The rationale for i.p. chemotherapy is based on high drug concentration exposure in the peritoneal cavity leading to an increased cytotoxicity and avoiding a high level of systemic toxicity [11-16]. However, despite the advantage of a high concentration of anticancer drugs, the results obtained with i.p. chemotherapy are still debatable in terms of complete and lasting responses [17]. One of the reasons suggested to explain those failures was the difficulty for i.p. chemotherapy to diffuse widely in the peritoneal cavity due to adhesion and/or anatomic niches. Intra-operative i.p. chemotherapy was suggested with the aim to improve its results [18,19]. The administration of i.p. chemotherapy during surgery allows an optimal peritoneal cavity exposure controlled by the surgeon who stirs the cisplatin containing solution by hand. The goal of this present report was to analyze the feasibility and the toxicity of this method of intra-operative i.p. chemotherapy.

**Patients and methods**

Between January 2003 and February 2006, 47 patients with advanced epithelial ovarian cancer classified FIGO stage IIIC were included and treated in our institution, University Hospital of Besançon (France). In 31 patients, treatment consisted in 4 cycles of induction i.v. chemotherapy with 175 mg paclitaxel per square meter of body surface area (mg/m²) over 3 hours and area under the (AUC) curve targeted to 5 for carboplatin over 30 minutes (66%) had initial chemotherapy followed by debulking surgery. The median duration of surgery was 7 hours and 10 minutes (range: 5 hours 10 minutes to 9 hours and 30 minutes) including the 2 hours of the administration of i.p. chemotherapy (table 2). The median hospitalization duration in intensive care unity and surgery unity was 3 days (range: 1 to 21 days) and 18 days (range: 12 to 66 days), respectively. The median delay between the surgery...
and the resumption of feeding was 7 days (range: 3 to 28 days). Rehospitalization in the surgery unit was required for 16 patients (median: once, range: 0 to 3 times), for restoring bowel continuity (in 7 patients), infection (3 patients), abdominal pain (3 patients), bowel occlusion (2 patients) and renal failure (1 patient).

Complications and toxicity
The safety analysis reported no severe haematological or non-haematological toxicity induced by intra operative i.p. chemotherapy. No patient died due to the complications of surgery or the i.p. chemotherapy. The most frequent complication was infection, including urinary or pulmonary infection which occurred in 9 and 3 patients, respectively (table 3). 13 of 47 patients require a re-laparotomy (4 patients needed 2 re-laparotomy) and we exclude from this total the 6 patients who had a surgical restoration after 30 days. Peritonitis and intra-abdominal abscess was observed in 5 and 3 patients respectively, they required a laparotomy to rinse and clean up the peritoneal cavity. This surgical intervention was also necessary for intra abdominal bleeding and intestinal necrosis which occurred in 7 and 2 patients, respectively. Two patients presented a bowel occlusion which recovered with medi-

Table 1: Characteristics of patients

| Characteristics of patients (N = 47) |  |
|-----------------------------------|---|
| Median age (years)               | 59 (Range: 35–75) |
| GOG Performans status 0          |  |
| ≥ 1                              | 40 (85%) |
|                                  | 7 (15%) |
| Histologic type                  |  |
| Serous adenocarcinoma            |  |
| Well differentiated              | 19 (40%) |
| Moderately/poorly differentiated | 20 (43%) |
| Endometrioid adenocarcinoma      | 5 (11%) |
| Mixed epithelial carcinoma       | 2 (4%) |
| Clear cell carcinoma             | 1 (2%) |
| Visible residual macroscopic disease |  |
| Yes                              | 20 (43%) |
| No                               | 27 (57%) |
| Induction Chemotherapy (paclitaxel – carboplatin regimen) | 31 (66%) |
| Initial surgery                  | 16 (44%) |
| Second look surgery              | 16/16* (100%) |
| Total number of i.v. cycles of chemotherapy | 6 (Range:5–8) |
| * Surgery during which was performed intra operative i.p. chemotherapy |

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Table 2: Duration of hospitalization

| Duration of surgery* (h = hours, mn = minutes) | Median | Range                  |
|------------------------------------------------|--------|------------------------|
|                                                | 7 h 10 mn | 5 h 10 mn- 9 h 30 mn   |
| Duration of hospitalization in intensive care unity | 3 Days   | 1–21 Days              |
| Duration of hospitalization in surgical unity   | 18 Days | 12–66 Days             |
| Delay between surgery and resumption of feeding | 7 Days  | 3–28 Days              |
| Number of rehospitalization                     | 1**     | 0–3 times              |

* including the 2 hours of IIP chemotherapy
** concerning 16 patients
cal treatment. Thromboembolic events occurred in 5 patients, including a pulmonary embolism in 1 patient. In 5 patients, grade 2 renal failures occurred during the first 10 days after surgery with i.p. cisplatin chemotherapy and they recovered after i.v. hydration with normal saline 2.2 mM Ca$^{2+}$ glucuronate, 1 g/l Mg$^{2+}$, 2 g/l KCl and 3 g/l NaCl. One patient presented a grade 3 renal failure with uncompleted recovery and which needed stringent follow up. No grade 4 haematological toxicity was observed. Six patients presented grade 3 anaemia and 5 patients presented grade 3 neutropenia without fever. Grade 2 thrombopenia occurred in only one patient. After a 30-day period, complications were surgery related (table 4). Chronic diarrhea, dysuria and abdominal pain were observed in 9, 8 and 2 patients, respectively. A surgical restoration was necessary for vesico-vaginal fistula, bowel fistula and entero-vesical fistula in 3, 2 and 1 patients, respectively.

### Table 3: Early complication and toxicity by patient including intraoperative toxicity (within 30 days after surgery and i.p. chemotherapy)

| Type of complication            | Number of patients | % of patients |
|---------------------------------|--------------------|--------------|
| **Post operative pain**         | 10                 | 21.3         |
| **Infectious Peritonitis**      | 5                  | 10.6         |
| **Intraabdominal abscess**      | 3                  | 6.4          |
| **Others infectious complications* | 12               | 25.5         |
| **Intraabdominal bleeding**     | 7                  | 14.9         |
| **Intestinal necrosis**         | 2                  | 4.3          |
| **Bowel occlusion**             | 2                  | 4.3          |
| **Thromboembolic events**       | 5                  | 10.6         |

#### Renal failure
- **Grade 1**: 6 patients (12.8%)
- **Grade 2**: 5 patients (10.6%)
- **Grade 3**: 1 patient (2.1%)
- **Grade 4**: 0 patients (0%)

#### Anaemia grade 3
- 5 patients (10.6%)

#### Neutropenia grade 3
- 4 patients (8.5%)

#### Febrile Neutropenia
- 0 patients (0%)

#### Thrombopenia grade 2
- 1 patient (2.1%)

* including 9 urinary infection and 3 pulmonary infection

** including: deep venous thrombosis of the leg and the arm in 3 and 1 patients respectively and a pulmonary embolism in 1 patient.

**Efficacy**

After a median follow up of 23.3 months, a recurrence of the disease was observed in ten patients. The median disease free progression duration was 14.3 months (range: 9.6 – 23.3 months). Sites of relapse were peritoneal carcinomatosis in 4 patients, peritoneal nodes in 4 patients, pleural effusion in 3 patients, liver metastasis in one patient. At 24 months, the rate of patients alive without recurrence was 62.5% [95% CI, 55% to 70%] (Figure 1). No data in term of OS was of value due to the length of follow-up.

**Discussion**

Intra-peritoneal administration of chemotherapy is commonly performed at a distance from surgery by an i.p. catheter with artificial ascites [9,24]. Women who have a successful optimal resection of their cancers with microscopic residual tumour and no bowel resection are the best candidates for i.p. chemotherapy [25]. It seems favo-
rable if possible to perform a supra-cervical hysterectomy and not to enter the vagina because when the vagina is opened leakage of chemotherapy via the vagina is mostly risked. However, even if there is no absolute contraindication to placement of this access device, complications could occur such as catheter infection or intra-abdominal abscess, bowel injuries, kinking of the catheter or inflow obstruction and leakage of chemotherapy around the port or into the surrounding subcutaneous tissue [24]. Abdominal pain is the most common i.p. chemotherapy-related risk. In most cases it is due to the distension of the abdomen but it is very important not to underestimate the risk of peritonitis or bowel injuries which is a medical and surgical emergency. Others i.p. chemotherapy complications included those linked to the drug administered. The most frequently used drug is cisplatin [26-30]. Nausea, vomiting and renal toxicity must be prevented by effective anti-emetics drugs and suitable i.v. hyperhydration considering the systemic exposure to the agent after i.p. comparable to i.v. administration [20]. Since the emergence of this concept of i.p. administration with chemotherapy reported by Dedrick et al in 1978 [31], several phase II studies have confirmed the favorable trends obtained by these treatments in terms of overall and/or progression – free survival [32,33]. Comparison between i.p. and i.v. treatments was undertaken in several randomized phase III clinical trials [26-28]. Recently, Armstrong et al [28] reported a highly significantly improvement in progression-free (24 months versus 18.3 months; \( p = 0.027 \)) and overall survival (65.6 months versus 49.7 months; \( p = 0.017 \)) with i.p. therapy. Because of the need to recover from surgery, the beginning of the i.p. chemotherapy is often delayed and performed at distance of surgery. The

| Type of complication   | Number of patients | % of patients |
|------------------------|--------------------|--------------|
| Vesico-vaginal fistula | 3                  | 6.4          |
| Bowel fistula          | 2                  | 4.3          |
| Entero-vesical fistula | 1                  | 2.1          |
| Chronic diarrhea       | 9                  | 19.1         |
| Chronic dysuria        | 8                  | 17           |
| Chronic abdominal pain | 2                  | 4.3          |
| Loss of weight *       | 4                  | 8.5          |

* more than 10% of the weight 3 months after surgery

% of patient alive

Figure 1
Disease free survival in intraoperative i.p. chemotherapy group and control group.
occurrence of adhesion barriers will be embarrassing for an optimal distribution of chemotherapy in the abdominal cavity. One should consider that the most frequent sites of recurrences are those where i.p. chemotherapy is unable to reach. Advocates of adhesion formation barriers could be used to limit their incidence but efficacy is not clearly demonstrated in this situation. Relying on these considerations, i.p. chemotherapy during surgery was suggested with the aim to improve results. The administration of i.p. chemotherapy during the surgery allows an optimal peritoneal cavity exposure warranted by the control of the surgeon who stirs the cisplatin liquid by hand inside the peritoneal cavity. This method presents the advantage to not require an i.p. catheter and to provide optimal diffusion. The aim of our study was to analyze its feasibility. One of our questions was to determine the optimal dose of i.p. cisplatin, knowing that standard regimen in i.p. clinical trial uses a dose of 50 to 100 mg/m² cisplatin [24]. A search for optimizing the dose and schedule of intraperitoneal cisplatin was performed, with the aim to increase the intraperitoneal concentration and to limit the systemic spread. The addition of epinephrin in preclinical model have shown to achieve this goal and warrant further clinical studies [22]. The dose used in the present study issued from studies performed in 2005 regarding serum and i.p. pharmacokinetics of platin with intra-operative chemotherapy. This study concluded that cisplatin administered at the dose of 50 mg/m² during 2 hours i.p. chemotherapy resulted in an early dramatic decrease in i.p. drug concentration, below the targeted threshold for activity within 15 minutes. The author suggested that performing twice 1 hour i.p. cisplatin chemotherapy should increase the length of peritoneal exposure to a local cytotoxic dose [21]. Relying on these results, we proposed in our study to perform i.p. chemotherapy in 2 consecutive one-hour administrations with cisplatin given at a dose of 90 mg. The present paper is the first demonstration of the feasibility for this modality of intra-operative i.p. chemotherapy. The described modalities of administration for i.p. chemotherapy enhance the distribution of cisplatin in the peritoneal cavity without inducing severe and non-manageable toxicities. Those results suggest further randomized clinical studies aimed to establish its benefit in terms of survival.

Competing interests
The authors declare that they have no competing interests.

Authors' contributions
EG conceived and participated to the design of the study, included patients, performed data analysis and interpretation, followed-up patients and write the manuscript DD included patients, performed surgery and intra-peritoneal chemotherapy, followed-up patients and participate to the data collection BH included patients, performed sur-

References
1. Almadrones LA: Treatment advances in ovarian cancer. Cancer Nurs 2003, 26:165-205.
2. Ozols RF: Update on the management of ovarian cancer. Cancer 2002, 8(Suppl 1):S22-30.
3. Carmignani CP, Sugarbaker PH: Comprehensive approach to advanced primary and recurrent ovarian cancer: a personal experience. Expert Rev Anticancer Ther 2004, 4:477-487.
4. Cannistra SA: Cancer of the ovary. N Engl J Med 2004, 351:2519-2529.
5. Thiggen T: The if and when of surgical debulking for ovarian carcinoma. N Engl J Med 2004, 351:2544-2546.
6. Stuart GC: First-line treatment regimens and the role of consolidation therapy in advanced ovarian cancer. Gynecol Oncol 2003, 90:58-15.
7. McGuire WP, Hoskins WJ, Brady MF, Kucera PR, Partridge EE, Look KY, Clarke-Pearson DL, Davidson M: Cyclophosphamide and cisplatin compared with paclitaxel and cisplatin in patients with stage III and stage IV ovarian cancer. N Engl J Med 1996, 334:1-6.
8. Ozols RF, Bundy BN, Greer BE, Fowler JM, Clarke-Pearson D, Burger RA, Mannel RS, DeGeest K, Hartenbach EM, Baergen R: Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study. J Clin Oncol 2003, 21:3194-3200.
9. Markman M: Intraperitoneal antineoplastic drug delivery: rationale and results. Lancet Oncol 2003, 4:277-283.
10. Rossi CR, Mocellin S, Pilati P, Follett M, Quintieri L, Palatini P, Lise M: Pharmacokinetics of intraperitoneal cisplatin and doxorubicin. Surg Oncol Clin N Am 2003, 12:781-794.
11. Capor ES, Kelsen DP, Alcock NW, Lewis JL Jr: Ip cisplatin in patients with malignant ascites: pharmacokinetic evaluation and comparison with the iv route. Cancer Treat Rep 1983, 67:235-238.
12. Lopez JA, Krikorian JG, Reich SD, Smyth RD, Lee FH, Issell BF: Clinical pharmacology of intraperitoneal cisplatin. Gynecol Oncol 1985, 20:1-9.
13. Pretorius RG, Hacker NF, Berek JS, Ford LC, Hoeschel JD, Butler TA, Lagasse LD: Pharmacokinetics of Ip cisplatin in refractory ovarian carcinoma. Cancer Treat Rep 1983, 67:1085-1092.
14. Markman M, Rowinsky E, Hakes T, Reichman B, Jones W, Lewis JL Jr, Rubin S, Curtis J, Barakat R, Phillips M, et al.: Phase I trial of intra-peritoneal taxol: a Gynecologic Oncology Group study. J Clin Oncol 1992, 10:1485-1491.
15. Francis P, Rowinsky E, Schneider J, Hakes T, Hoskins W, Markman M: Phase I feasibility and pharmacologic study of weekly intraperitoneal paclitaxel: a Gynecologic Oncology Group pilot Study. J Clin Oncol 1995, 13:2961-2967.
16. DeGregorio MW, Lum BL, Holleran WM, Willber BJ, Sirkic BI: Preliminary observations of intraperitoneal carboplatin pharmacokinetics during a phase I study of the Northern
California Oncology Group. Cancer Chemother Pharmacol 1986, 18:235-238.

17. Piccart MJ, Floquet A, Scarfone G, Willems PH, Emerich J, Vergote I, Giugas L, Coens C, Awada A, Vermorken JB. Intraperitoneal cisplatin versus no further treatment: 8-year results of EORTC 5 a randomized phase III study in ovarian cancer patients with a pathologically complete remission after platinum-based intravenous chemotherapy. Int J Gynecol Cancer 2003, 13(Suppl 2):196-203.

18. Segna RA, Dottino PR, Jennings TS, Cohen CJ. Feasibility of intraoperative administration of chemotherapy for gynecologic malignancies: assessment of acute postoperative morbidity. Gynecol Oncol 1993, 48:227-231.

19. Ahmad SA, Kim J, Sussman JJ, Soldano DA, Pennington LJ, James LE, Lowy AM: Reduced morbidity following cytoreductive surgery and intraperitoneal hyperthermic chemoperfusion. Ann Surg Oncol 2004, 11:387-392.

20. Royer B, Guardiola E, Polycarpe E, Hoizey G, Delroeux D, Combe M, Chaigneau L, Samain E, Chauffert B, Heyd B, Kantelip JP, Pivot X: Serum and intraperitoneal pharmacokinetics of cisplatin within intraoperative intraperitoneal chemotherapy: influence of protein binding. Anticancer Drugs 2005, 16:1009-1016.

21. Dedrick RL, Myers CE, Bungay PM, DeVita VT Jr: Intraperitoneal cisplatin in small-volume stage III ovarian carcinoma: why, how, and when? Semin Oncol 1985, 12:43-46.

22. Carson LF, Wadler S, Sickel J: Intraperitoneal cisplatin in small-volume stage III ovarian carcinoma: an intergroup study of the Gynecologic Oncology Group. Obstet Gynecol Surv 1978, 33:457-481.

23. Kaplan EL, Meier P: Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958, 53:457-481.

24. Markman M, Walker JL: Intraperitoneal chemotherapy of ovarian cancer: a review, with a focus on practical aspects of treatment. J Clin Oncol 2006, 24:988-994.

25. Walker JL, Armstrong DK, Huang HQ, Fowler J, Webster K, Burger RA, Clarke-Pearson D: Intraperitoneal catheter outcomes in a phase III trial of intravenous versus intraperitoneal chemotherapy in optimal stage III ovarian and primary peritoneal cancer: a Gynecologic Oncology Group Study. Gynecol Oncol 2006, 100:27-32.

26. Alberts DS, Liu PY, Hannigan EV, O’Toole R, Williams SD, Young JA, Franklin EW, Clarke-Pearson DL, Maliya VK, Dusheker B. Intraperitoneal cisplatin plus intravenous cyclophosphamide versus intravenous cisplatin plus intravenous cyclophosphamide for stage III ovarian cancer. N Engl J Med 1996, 335:1950-1955.

27. Markman M, Bundy BN, Alberts DS, Fowler JM, Clark-Pearson DL, Carson LF, Wadler S, Sickel J: Phase III trial of standard-dose intraperitoneal cisplatin plus paclitaxel versus moderately high-dose carboplatin followed by intravenous paclitaxel and intraperitoneal cisplatin in small-volume stage III ovarian carcinoma: an intergroup study of the Gynecologic Oncology Group, Southwestern Oncology Group, and Eastern Cooperative Oncology Group. J Clin Oncol 2001, 19:1001-1007.

28. Armstrong DK, Bundy B, Wenzel L, Huang HQ, Baergen R, Lele S, Copeland LJ, Walker JL, Burger RA: Intraperitoneal cisplatin and paclitaxel in ovarian cancer. N Engl J Med 2006, 354:34-43.

29. Markman M: Intraperitoneal chemotherapy as treatment of ovarian carcinoma: why, how, and when? Obstet Gynecol Surv 1987, 42:533-539.

30. van Bakel Huinink WW, Dubbelman R, Aartsen E, Franklin H, McVie JG: Experimental and clinical results with intraperitoneal cisplatin. Semin Oncol 1985, 12:43-46.

31. Dedrick RL, Myers CE, Bungay PM, DeVita VT Jr: Pharmacokinetic rationale for peritoneal drug administration in the treatment of ovarian cancer. Cancer Treat Rep 1978, 62:1-11.

32. Look M, Chang D, Sugarbaker PH: Long-term results of cytoreductive surgery for advanced and recurrent epithelial ovarian cancers and papillary serous carcinoma of the peritoneum. Int J Gynecol Cancer 2004, 14:335-41.

33. Topuz E, Eralp Y, Saglam S, Saip P, Aydiner A, Berkman S, Yayuc E: Efficacy of intraperitoneal cisplatin as consolidation therapy in patients with pathologic complete remission following front-line therapy for epithelial ovarian cancer. Consolida-

Conclusions: Intraperitoneal cisplatin in ovarian cancer. Gynecol Oncol 2004, 92:147-151.