NIPEC with Single Dose Intra-peritoneal Cisplatin and Paclitaxel In Stage IIIc Epithelial Ovarian Cancer

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INTRODUCTION

- EOC is essentially peritoneal disease and standard treatment involves around surgical staging, maximal CRS and taxane/platinum-based chemotherapy. [1]
- GOG 172 trial compared IV chemotherapy with IP chemotherapy arms in advanced EOC concluded that the median PFS of 18.3 and 23.8 months, OS as 49.7 and 65.6 months, proving prognostic advantage of IP route.[2]
- Subset analysis of GOG 172 and the MSKCC studies revealed that the patients receiving 1–2 courses of IP chemotherapy also had significant OS advantages compared with IV arm.[3]

AIMS AND OBJECTIVES

- To assess the effectiveness of single dose IP chemotherapy in optimally debulked patients in advanced EOC and DFS.

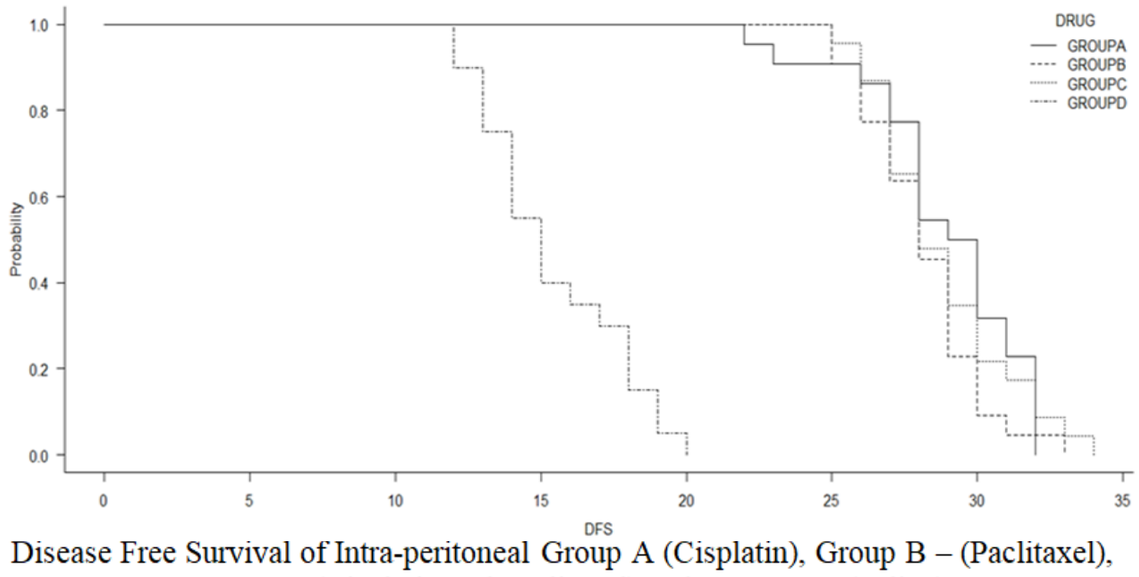
PATIENTS AND METHODS

- Prospective randomized study of 87 patients with advanced IIIc EOC
- 261 cases underwent CRS, 87(44.6%) consented for the study.
- **Inclusion criteria for PDS:** ECOG 0–1, resectability based on CT scan and serum albumin > 3 g/dl.
- Those not meeting criteria were given 3 courses of NACT reassessed for IDS
- **Exclusion criteria :** Poor ECOG score,non-consenting patients
- Surgical staging with ascitic or peritoneal lavage fluid cytology (sample 1).
- PCI index was calculated, CRS done.
- Patients consenting for the study were randomized into four groups.
  - Group A - Receiving Intra Peritoneal Cisplatin dose of 100mg/m^2 (diluted in 1000 ml N.S).
  - Group B - Receiving Intra Peritoneal Paclitaxel dose of 60mg/m^2 (diluted in 1000 ml N.S).
  - Group C - Receiving Intra Peritoneal Paclitaxel and Cisplatin in the dose as mentioned above.
  - Group D - Control group of saline instillation
- IP agent circulated in abdomen, left intraperitoneally with a sealed drain for absorption and was released after 24 hr.
- After 48 hours of surgery, drain fluid cytology (sample 2) sent after being clamped for 6-8 hours.
- Patients received 6 courses of IV chemotherapy and one IP chemotherapy.
- Patients were followed up for 36 months to assess the response and DFS.

RESULTS

GROUP	CHEMOTHERAPY AGENT	NUMBER	CYTOLOGY POSITIVE	CYTOLOGY POSITIVE	p VALUE
GROUP A	CISPLATIN	22	22	2	< 0.001
GROUP B	PACLITAXEL	22	22	0	0.996
GROUP C	CISPLATIN + PACLITAXEL	23	23	0	0.996
GROUP D	SALINE	20	20	14	< 0.0003

GROUP	IP CHEMOTHERAPY AGENT	NUMBER	ILEUS	NEUTROPENIA	LYMPHORRHOEA
GROUP A	CISPLATIN	22	2	1	2
GROUP B	PACLITAXEL	22	1	0	1
GROUP C	CISPLATIN + PACLITAXEL	23	2	2	2
GROUP D	SALINE	20	0	0	0



Disease Free Survival of Intra-peritoneal Group A (Cisplatin), Group B – (Paclitaxel), Group C – (Cisplatin and Paclitaxel) and Group D – (Saline).

DISCUSSION

- Due to peritoneal-plasma barrier, high doses of IP chemotherapy can be administered safely
- The efficiency of IP chemotherapy - depth of tissue penetration & physical properties,high molecule weight and hydrophilic properties.
- Post-IP peritoneal cytology fluid was positive in 70% (14/20) of cases in saline, 9% (2/22) in case of cisplatin IP agent, negative in paclitaxel and cisplatin/paclitaxel combination IP agent.
- Neither were the complications significant. 5 patients had prolonged ileus and lymphorrhoea. No mortality in our study.
- DFS in saline group - 15 months while in IP group - 28 months and was statistically significant based log rank test.
- There was no significant difference in DFS between IP groups.
- Although CRS and HIPEC have proven its efficacy in ovarian cancers, it has got a learning curve, not easily available or affordable, is associated with significant morbidity and mortality.[4]
- Single-dose IP chemotherapy after optimal CRS can be practiced in the centers without HIPEC facility and has got acceptable morbidity, mortality and with comparable DFS.

CONCLUSION

- Complete or optimal CRS in advanced EOC does have a possibility of microscopic peritoneal residue.
- Adjuvant loco-regional strategies should be considered to prolong disease free survival.
- Single dose normothermic IP chemotherapy can be offered to patients with minimal morbidity and prognostic benefits comparable to HIPEC.
- Future clinical trials are required to validate these protocols.

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