Editorial-1

Adjuvant Chemotherapy for Epithelial Ovarian Cancer (EOC)

The prognosis of patients with EOC has improved over the past two decades following platinum based chemotherapy. While patients with low risk early stage EOC (stage IA & IB with tumour grade I or II) can be kept under observation following initial optimum debulking surgery, patients with high risk disease i.e. stage IA, IB with high grade tumour or clear cell histology and those with stage IC (irrespective of grade) should receive adjuvant chemotherapy. Similarly, patients with advanced EOC (stage II- IV) should receive post operative chemotherapy.[1] For advanced disease, amount of residual disease following initial surgery is the most important prognostic factor,[2] patients with optimum residual disease (£ 1 cm) have better outcome than those with sub-optimal debulking (residual tumour >1cm) .

Use of chemotherapy has varied from cisplatin plus cyclophosphamide +/- doxorubicin in early 1990's to paclitaxel and cisplatin or carboplatin based chemotherapy during the past decade following a series of studies by Gynecologic Oncology Group (GOG),[3] Intergroup[4] and German Group (AGO)[5] studies. Whether to use single agent (e.g. carboplatin based on ICON trial data)[6] or paclitaxel & platinum based combination remains debatable. General consensus is in favour of using 6 cycles of paclitaxel + carboplatin or cisplatin following surgery among patients with advanced EOC. Carboplatinum is preferred over cisplatinum due to better toxicity profile.

Compared to developed countries, situation is not so simple in developing countries. In this issue of the journal, Lal et al [7] gives an audit of cases seen at their institute, a tertiary care centre in northern India. The picture described by them is reflective of situation in many parts of India including teaching (medical college) and non teaching hospitals. Most patients with advanced EOC undergo sub-optimal debulking primarily due to lack of trained gynecologic Oncologists or surgical oncologists. Sub-optimum chemotherapy (dose and schedule) is another common occurrence, again due to lack of trained medical oncologists. There is clear evidence that appropriate management of this disease by team of specialists (gynecologic or surgical and medical oncology) can improve the outcome and survival.[8]

Presence of large volume or inoperable abdomino-pelvic disease ± gross pleural effusion and poor performance status at diagnosis make these patients at high risk for surgery. Such patients after confirmation of diagnosis and staging work up can be benefited with neoadjuvant chemotherapy followed by debulking surgery. Data from non randomized studies indicate that this is a reasonable approach in patients deemed inoperable based on clinical and CAT scan findings. Such approach results in optimum debulking in more than half of the patients with decreased operative morbidity and mortality.[9] Overall and progression free- survival of these patients treated with neoadjuvant chemotherapy is comparable to those treated with conventional approach ie. surgery followed by chemotherapy. Currently, the role of neo-adjuvant chemotherapy in advanced EOC is being evaluated in two International randomized trials, one by EORTC group (European Organization for Research and Treatment of Cancer) [10] and another by GOG. At AIIMS, we are involved in one such study in which patients

of EOC with stage III C & IV (pleural effusion only) are being randomized to receive upfront debulking surgery followed by 6 cycles of paclitaxel plus carboplatin versus upfront chemotherapy- (3 cycles of paclitaxel + carboplatin) followed by debulking surgery followed by 3 cycles of chemotherapy , 90 patients have been recruited so far. Final results are likely to be available by the end of this year.

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REFERENCES:

1. *Cannistra SA. Cancer of ovary. N Eng J Med 2004;351:2519-2529.*

2. *Brislow RE, Tomacruz RS, Armstrong DK, et al. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: A meta-analysis. J Clin Oncol 2002;20:1248-1259.*

3. *McGuire WP, Hoskins WJ, Brady MF et al. Cyclophosphamide and cisplatin compared with paclitaxel and cisplatin in patients with stage III and IV ovarian cancer. N Eng J Med 334;3-6,1996.*

4. *Piccart M, Bertelsen K, James K, et al. Randomized intergroup trial of cisplatin –paclitaxel versus cisplatin cyclophosphamide in women with advanced epithelial ovarian cancer : Three year results. J Nat Cancer Inst 2000;92:699-708.*

5. *The International Collaborative Ovarian Neoplasms (ICON) Group : Paclitaxel plus carboplatin versus standard chemotherapy with either single agent carboplatin or cyclophosphamide, doxorubicin and cisplatin in women with ovarian cancer. The ICON 3 randomized trial. Lancet 2002;360:505-515.*

6. *du Bois A, Luck HJ, Meier W Carboplatin plus paclitaxel as first-line chemotherapy in previously untreated advanced ovarian cancer. German AGO Study Group Ovarian Cancer. Arbeitsgemeinschaft Gynakologische Onkologie. Semin Oncol. 1997;24(4Suppl 11):S11-28-S11-33.*

7. *Lal P, Tiwari A, Rastogi N, & Kumar Sh. Epithelial ovarian cancer : an audit of patients treated over 15 years. Ind J Med & Paed Oncol 2006;27:15-22.*

8. *Junor EJ, Hole DJ, McNulty L, et al. Specialist gynecologists and survival outcome in ovarian cancer: A Scottish national study of 1866 patients. Br J Obstet Gynecol 1999;106:1130-1136.*

9. *Schwartz PE, Rutherford TJ, Chambers JT et al. Neoadjuvant chemotherapy for advanced ovarian cancer: Long term survival Gyneco Oncol 1999;72:93-99.*

10. *Vergote IB, de Wever I, decloedt J, Tjalma W, et al. Neoadjuvant chemotherapy versus primary debulking surgery in advanced ovarian cancer. Sem Oncol 2000;27(suppl.7):31-36.*