Toxicity and Tolerability of Paclitaxel and Carboplatin Regime in Patients with Epithelial Ovarian Cancer at a Tertiary Care Hospital

Praveen Jacob Ninan[#1], Dharam Prasath[#2], Mary James[#*3]
#1 Assistant Professor, Department of Radiotherapy, Government T.D Medical College, Alappuzha, Kerala, India.
#2 Senior Resident, Department of Pharmacology, Government T.D Medical College, Alappuzha, Kerala, India
#3 Assistant Professor, Department of Paediatrics, Government T.D Medical College, Alappuzha, Kerala, India
**Corresponding Author: Mary James*

Abstract

Epithelial Ovarian cancer treatment is based on cytoreductive surgery and combination chemotherapy with taxane and platinum compounds. The present study aims to analyse the toxicity and tolerability of Paclitaxel and Carboplatin regime in EOC.

This study was prospective observation study done in Govt. T.D. medical college, Alappuzha over a period of 18 months. All patients with epithelial ovarian cancer selected for first line chemotherapy with Paclitaxel and Carboplatin combination regimen irrespective of age. They were studied for toxicity pattern, tolerability of this regime, assess the performance of patients and to study the prevalence of neutropenia

The Mean age of patients was 51.15 years. Most common associated medical condition was Diabetes Mellitus. The most common histopathological type in this study is serous cancer. Majority patients had ECOG performance score 1 before chemotherapy and 3 after chemotherapy. The most common non- haematological toxicity was found to be Alopecia. Most common haematological toxicity was found to be Neutropenia.

ZZIn our study the toxicity profile of this regimen was well tolerated. Non- haematological toxicity like Alopecia, Vomiting, Myalgia, Nausea, Arthralgia, Fatigue, Peripheral Neuropathy, Diarrhoea, Pruritus, Oral Mucositis, Stomatitis and haematological toxicity like Neutropenia, Anaemia and Thrombocytopenia were significant clinical parameters.

Keywords: *Epithelial Ovarian Cancer, Paclitaxel, Carboplatin, Toxicity, Tolerability*.

I. INTRODUCTION

Ovarian cancer ranks fifth as the cause of cancer deaths in women. A woman's risk of acquiring ovarian cancer is about 1 in 71. The risk of dying from ovarian cancer is 1 in 95[1]. The number of new cases of ovarian cancer was 11.9 per 100,000 women per year. The number of deaths was 7.5 per 100,000 women per year. These rates are age-adjusted and based on 2009-2013 cases and deaths[2]. 70% of ovarian cancers are diagnosed at advanced stage and the five-year survival rate of women is only 30%. About 20% of ovarian cancers are confined to the ovaries at diagnosis. The five-year survival rate for women with localized tumours exceeds 90%[3].

In the United States, the American Cancer Society estimates that in 2016, about 22,280 new cases of ovarian cancer will be diagnosed and 14,240 women will die of ovarian cancer in the United States[4].

Ovarian cancer is emerging as one of the most common malignancies in India. In India, during 2004-2005, proportion of ovarian cancer varied in India from 1.7% to 8.7% of all female cancers in various urban and rural population based registries operating under the net- work of the National Cancer Registry programme (NCRP) of Indian Council Medical Research. Pune and Delhi has the highest incidence according to cancer registries[5]

Age-standardized Incidence rates of ovarian cancer (ASR) during the period 2001-2006 ranged from 0.9 (Silchar town) to 8.4 per 100,000 women. Pune had the highest ASR of ovarian cancer[5]. ASR of Trivandrum and Karunagapally is 4.8 per 100,000 woman years of ovarian cancer in Indian registries[6]
The symptomatology of ovarian cancer is not very clear, it is usually diagnosed at an advanced stage[7]. About 90% of ovarian cancer is Epithelial Ovarian cancer (EOC) in which the most common histologic type is serous carcinoma which is followed by mucinous, endometrioid and clear cell carcinoma[8].

The types of EOC is based entirely on tumour cell morphology. The four major types of epithelial tumours are serous, endometrioid, clear cell, and mucinous. They bear strong resemblance to the

normal cells lining different organs in the female genital tract[9-10]

Epithelial Ovarian cancer treatment is based on cytoreductive surgery and combination chemotherapy with taxane and platinum compounds. Paclitaxel and Carboplatin regime is broadly accepted as first line chemotherapy for epithelial ovarian cancer[11].

Patients with Stage IA or IB disease with Grade I and II tumour have a greater than 90% cure rate, and require no further postoperative treatment, while patients with a Stage I Grade 3 lesion or Stage II disease have a recurrence rate of approximately 25%–40% and will need additional postoperative chemotherapy[12].

The present study aims to analyse the toxicity and tolerability of Paclitaxel and Carboplatin regime in EOC and this study is not done previously in our hospital.

II. METHODS

This prospective observation study was conducted for a period of 18 months from March 2015 - September 2016 in the outpatient and inpatient department of Radiotherapy, Government T.D Medical College, Alappuzha after getting approval from Institutional Human Ethics Committee as well as from Institutional Research Committee.

Total 33 cases of Epithelial Ovarian Cancer receiving Carboplatin and Paclitaxel regime as first line chemotherapy were studied. The patients will be categorized according to the demographic details, histological type of epithelial ovarian cancer and FIGO staging of ovarian cancer. Performance status of the patient will be assessed before and after a chemotherapy session by ECOG-Performance status. The regime consists of 6 cycles of chemotherapy at 21 days interval.

One treatment cycle consists of Paclitaxel 175 mg/m^2 intravenously 3-hour infusion followed by intravenous carboplatin (area under the plasma concentration time curve of 5). The response to chemotherapy was found by measuring CA125 and USG scan. The toxicity to this chemotherapy regimen is noted and grading is done by NCI-CTCAE. The haematological toxicity is found by complete blood count after a chemotherapy session. Details were recorded in the proforma and analysed

Statistical Analysis

The data was sorted, coded and entered into Microsoft Excel sheet 2007 and subsequently analysed. Descriptive statistics was used for data analysis. Quantitative Variables like age were expressed as Mean. The toxicity to Carboplatin and Paclitaxel regime was assessed by National Cancer Institute – Common Terminology Criteria for Adverse Effects (NCI-CTCAE). The performance status of the patient was assessed before and after a chemotherapy session by ECOG Performance Status.

III. RESULTS

Total 33 cases of Epithelial Ovarian Cancer receiving Carboplatin and Paclitaxel regime as first line chemotherapy were studied in Department of Radiotherapy (both IPD and OPD) of Govt. T.D. Medical College, Alappuzha over a period of 18 months

Table 1: Age wise distribution of study population

Age (years)	Female N (%)
21-30	1 (3.03 %)
31-40	3 (9.09 %)
41-50	9 (27.27 %)
51-60	**14 (42.42 %)**
> 60	6 (18.18 %)
Total	**33 (100 %)**

The age range of study population was between 30 years to 66 years. The Mean age of the patient was 51.15 years. Table 1 shows the maximum number of cases (42.42 %) in the age interval 51-60 years.

Table 2: OPD/IPD wise distribution

Patients	Cases	Percentage
Out-patients	24	72.72%
In-patients	9	27.27%
Total	33	100%

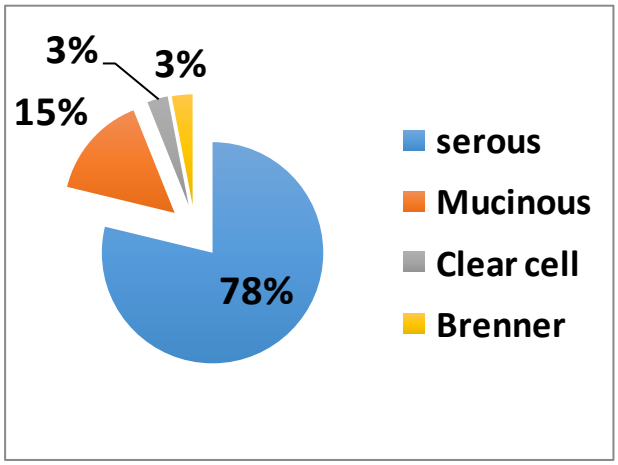
Total OPD and IPD cases were found to be 24 (72.72%) and 9 (27.27%)

Table 3: Associated medical condition

Medical Condition	**Patients**
Diabetes Mellitus	11 (33.33%)
Hypertension	6 (18.18%)
Coronary Artery Disease	1 (3.03%)
Deep Vein Thrombosis	1 (3.03%)

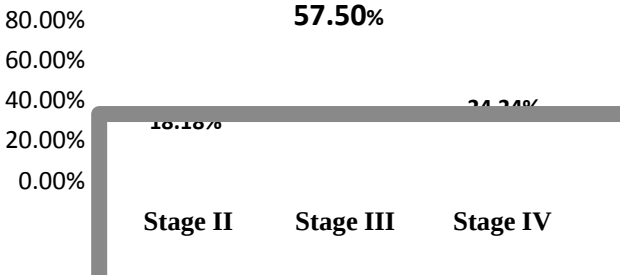
Most common associated medical condition was Diabetes Mellitus (33.33%) followed by Hypertension (18.18%), Coronary Heart Disease (3.03%) and DVT (3.03%)

Figure 1: **Histopathological types of Epithelial Ovarian Cancer**



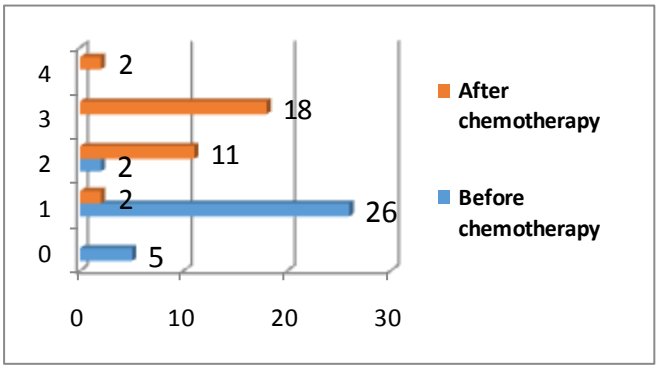
The most common histopathological type in this study is Serous cancer in 26 (78.78%) patients followed by Mucinous cancer in 5 (15.15%) patients. Clear cell and Brenner's tumour were found to be 1 patient (3.03%) each.

Figure 2: Staging of Ovarian Cancer



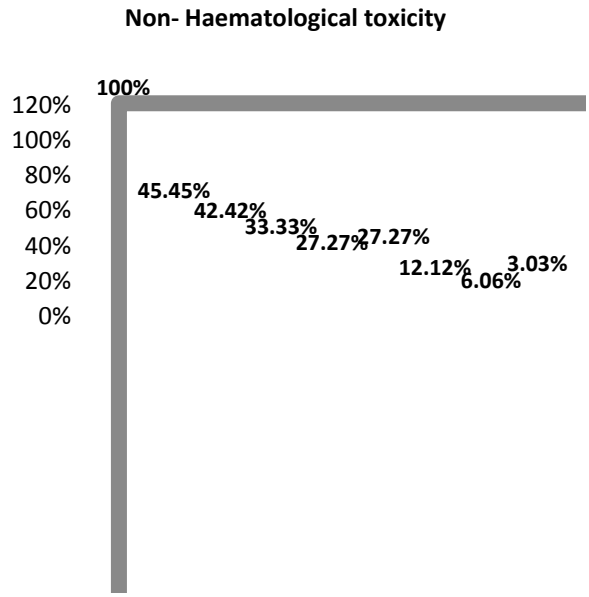
The FIGO staging in the patients was Stage II in 6 (18.18%) patients, Stage III in 19 (57.57%) patients and Stage IV in 8 (24.4%) patients.

Figure 3: ECOG Performance Status



The performance status of 33 patients was assessed before and after a chemotherapy session by ECOG (Eastern Cooperative Oncology Group) performance status. ECOG performance status before chemotherapy session was ≤2 and after chemotherapy session was 1 to 4

Figure 4: Non haematological Toxicity



Toxicity to carboplatin and paclitaxel regime was assessed using Common Terminology Criteria for Adverse Events (NCI-CTCAE). The most common non- haematological toxicity was found to be Alopecia (N= 33, 100%) followed by Vomiting (N= 15, 45.45%), Myalgia (N= 14, 42.42%), Nausea (N= 11, 33.33%), Arthralgia (N=9, 27.27%), Fatigue (N=9, 27.27%), Peripheral Neuropathy (N=4, 12.12%); Diarrhoea, Pruritus and Oral Mucositis was found to be 2 (6.06%) patients each and Stomatitis and URI in 1 (3.03%)

Table 4: Haematological Toxicity

Toxicity	Grade 1	Grade 2	Grade 3	Grade 4
Anaemia	0	1	1	0
Neutropenia	0	2	2	0
Thrombocytopenia	0	1	0	0

Most common haematological toxicity was found to be Neutropenia (N=4, 12.12%) followed by Anaemia (N=2, 6.06%) and Thrombocytopenia (N= 1, 3.03%). Grade 3 and grade 2 Neutropenia was present in 2 patients each, grade 3 and grade 2 Anaemia was present in 1 patient each and 1 patient showed grade 2 Thrombocytopenia.

IV. DISCUSSION

This study analysed the toxicity profile of Carboplatin and Paclitaxel regime in 33 Epithelial

Ovarian Cancer (EOC) patients who received this regimen as a first line chemotherapy in Outpatient and Inpatient Departments of Radiotherapy at Govt. T.D Medical College, Alappuzha.

Age of study population varied from 30 years to 66 years with a mean age of 51.15 years. In a study done by H. Shawky et al[13], age range was 35-77 years with the mean age of 57.1 years.

Majority of the patients had FIGO stage III cancer and was comparable to study done by H. Shawky et al[13] and by P Georgeena et al[14].
Most of the patients had Serous cancer in 26 {78.78%), followed by Mucinous cancer in 5 (15.15%). In a study conducted by H. Shawky et al[13] 26 patients (81.2%) had Serous cancer and was comparable to the study conducted by S. Nagao et al[15].

The ECOG Performance status was found to be ≤2 before chemotherapy and ranged from 1 to 4 after chemotherapy. In H. Shawky et al[13] study the ECOG performance status was ≤2 before chemotherapy and >1 after chemotherapy.
The most common non- haematological toxicity was found to be Alopecia (N= 33, 100%) in which grade2 alopecia was present in 91% patients followed by Vomiting (N= 15, 45.45%), Myalgia (N= 14, 42.42%), Nausea (N= 11, 33.33%), Arthralgia (N=9, 27.27%), Fatigue (N=9, 27.27%), Peripheral Neuropathy (N=4, 12.12%) grade 3 PN was present in 1 patient. Diarrhoea, Pruritus and Oral Mucositis was found to be in 2 (6.06%) patients each and Stomatitis and URI in 1 (3.03%) patient.

In a study conducted by Andreas du Bois et al[16], grade 2 alopecia was the commonest non-haematological toxicity followed by vomiting, nausea, arthralgia, myalgia, Peripheral neuropathy. H. Shawky et al[13] study shows that Peripheral neuropathy was the most frequent grade 3 non-haematological toxicity which is similar to the present study. Sharma et al[17] recorded grade 3 neuropathy in 3 (14%) patients.

The haematological toxicity observed in our study are Neutropenia, Anaemia and Thrombocytopenia. Neutropenia (12.12%) is the most common in which grade 3 is present in (6.06%) and grade 2 in (6.06%). Grade 3 Anaemia was present in (3.03%) and grade 2 in (3.03%). Grade 2 Thrombocytopenia was present in (3.03%). In H. Shawky et al[13] study the haematological toxicity profile of this regimen was with only one (3.1%) and 8 (25.0%) patients suffering from grade 4 and grade 3 neutropenia. Grade 3 anaemia occurred in 2 patients (6.3%), and 2 patients (6.3%) experienced grade 3 thrombocytopenia.

In a study conducted by Sharma et al[17]. the most common haematological toxicity were grade 3/4 neutropenia in 30%, grade 3 anaemia in one (5%) patient and no grade 3 thrombocytopenia. van der Burg et al[18]. reported grade3 neutropenia and thrombocytopenia in 40% and 8.% of patients, respectively in the weekly phase. The toxicity observed in this study is somewhat similar to the above mentioned studies.

In a study conducted by Baruah U et al[19], Grade I haematological toxicity was observed in 28.84% of cases, Grade II in 5.7% of cases and Grade III in 1.92% of patients. There was no Grade IV haematological toxicity. Grade I non- haematological toxicity was noted in 19.23% patients and Grade II in 3.8% of cases. No Grade III or IV GI toxicity was noted

In the present study the toxicity profile of Carboplatin and Paclitaxel regimen in patients was well tolerated. No deaths reported due to toxicity of this regime.

V. CONCLUSION

Paclitaxel and Carboplatin regime is broadly accepted as first line chemotherapy, this study is useful in determining the toxicity and tolerability of this regime. The commonest cause of haematological and non- haematological toxicity are discussed in this study. Thereby this regime should be used cautiously in EOC patients.

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