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# A STUDY ON CARBOPLATIN -PACLITAXEL INDUCED PERIPHERAL NEUROPATHY IN CANCER PATIENTS

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**ABSTRACT**

**Background:** Peripheral neuropathy is a common treatment related adverse effect and affects long term quality of life.

**AIM:** To study the Carboplatin-Paclitaxel induced peripheral neuropathy in patients with lung or ovarian cancer.

**Methods:** The study was carried out in the Department of Oncology, Government Rajaji Hospital, Madurai, after obtaining clearance from Institutional ethical committee, Government Rajaji Hospital, Madurai.Thirty newly diagnosed patients suffering from Lung or ovarian cancer attending Oncology department were selected. After satisfying inclusion and exclusion criteria,Patient received Injection Carboplatin AUC 6 and Injection Paclitaxel 175mg/m2 . Nerve conduction study was done to assess the peripheral neuropathy. It was done before starting the chemotherapy.Patients with grade 0 neuropathy were included for the study.Nerve conduction study was repeated after each cycle. The time taken to develop peripheral neuropathy was assessed using Cancer Institute – Common Toxicity Criteria version 3.0. The data were analyzed with SPSS statistical software package (Version 16.0 SPSS Inc., Chicago, USA ).

**Results:**There is a statistically significant reduction in sensory nerve (sural) amplitude (SNAP) and latency ($p<0.05$) indicating significant axonal damage. The time taken to develop peripheral neuropathy was 4 Cycles with Grade 2/4.

**Conclusions:** In this present study , the neurotoxicity induced by Carboplatin–Paclitaxel in patients with lung or ovarian carcinoma was observed. More effective dosing- schedules of treatment decreases the incidence of long lasting peripheral neurotoxicity thus providing better results withlonger survival rate and less disability.

**KEYWORDS :** Carboplatin, Paclitaxel, Peripheral neuropathy, chemotherapy, nerve conduction study, neurotoxicity

## INTRODUCTION

Chemotherapy induced peripheral neuropathy is the most common neurological complication of cancer chemotherapy.[1] It may be due to direct nerve compression by tumor or its infiltration; nutritional deficiencies; metabolic derangements.[2] It has been estimated that there are 28 million cancer survivors worldwide. 67% of patients outlast at 5 years. Assessing the long-term adverse effects of cancer chemotherapy is crucial due to their effect on cancer survivorship. Of particular importance is chemotherapy-induced peripheral neuropathy (CIPN), which may lead to permanent disability in 40% of cancer survivors.[3] CIPN may be a significant disability after the treatment of large number of cancer, including breast, testicular,lung, ovarian, colorectal and hematological malignancies and have an impact on quality of life .Peripheral neuropathy is common in ovarian and lung cancer. The incidence of CIPN was found to be 21.5 in ovarian cancer and 18.3 in patients with lung cancer(per 1000 person-years) who received combination chemotherapy with Platinum-Paclitaxel. 54% of patients after 6 cycles of chemotherapy and 23% after a median follow up of 18 months were found to have residual neuropathy.[3] Chemotherapy Induced Peripheral Neuropathy(CIPN)is an unmet clinical need in an approach to the cancer patients. More effective dosing- schedules of treatment decreases the incidence of long lasting peripheral neurotoxicity thus providing better results with longer survival rate and less disability.[4]

Hence, a study was planned to assess the Neurotoxicity of Carboplatin–Paclitaxel in patients with lung or ovarian carcinoma. More effective dosing- schedules of treatment decreases the incidence of long lasting peripheral neurotoxicity thus providing better results withlonger survival rate and less disability.

## MATERIALS AND METHODS

The study was carried out in the Department of Oncology and Department of Neurology Government Rajaji Hospital, Madurai, from December 2014 to June 2016 after obtaining clearance from Institutional ethical committee Ref number (13432/E1/8/2014), Government Rajaji Hospital, Madurai. ASingle center Open label Prospective Observational study carried out in 30 patients.

Drugs used were Injection Carboplatin AUC 6,Injection Paclitaxel 175mg/m2. All the patients received premedications consisting of single dose of dexamethasone (20mg) and ranitidine(50mg) administered 30 minutes before start of Paclitaxel infusion and anti emetic prophylaxis with ondansetron . Chemotherapy cycles were repeated every 3 weeks.

**INCLUSION CRITERIA**: Newly diagnosed patients with lung or ovarian cancer ,Age group: 18 to 60 years, Patients with grade 0 peripheral neuropathy (National Cancer Institute – Common Toxicity Criteria version 3.0.)

**EXCLUSION CRITERIA:** Those with pre-existing peripheral neuropathy, Patients with any other comorbid conditions were excluded. Patients with extensive CNS metastasis, pregnancy and breastfeeding patients when the patient was found to develop another illness or worsening of existing illness or requiring additional drugs ,they were withdrawn from the study .The study was carried out in 30 patients who satisfied the inclusion /exclusion criteria after getting written and informed consent

**INVESTIGATIONS** : Complete Haemogram, Blood sugar, Renal function test ,Liver function test , Thyroid Profile Nerve conduction study- to assess the peripheral neuropathy, Nerve conduction study was done before starting the chemotherapy. Patients with grade 0 neuropathy were included for the study Patients were followed up after each cycle till the end of 6 cycles and examined for signs and symptoms of peripheral neuropathy. Nerve conduction study was repeated after each cycle. Time taken by each group to develop peripheral neuropathy were assessed using Cancer Institute – Common Toxicity Criteria version 3.0. The data were analyzed with SPSS statistical software package (Version 16.0 SPSS Inc., Chicago, USA ). The nerve conduction study variables were compared before and after chemotherapy using students t test and $p<0.05$ will be considered as statistically significant.

## RESULTS:

All the patients were reviewed once in three weeks and there was no drop out in the study, all the 30 patients were analyzed for the time taken to develop neuropathy. Among thirty patients analyzed (37%) were males and rest were females (63%), The age wise distribution was 10 (33%) patients belonged to 30-39 years, 20 (67%) were between 40-49 years. The tumor type includes (36%) were mucinous cystadenoma ovary, (30%) were serous cyst adenocarcinoma,(14%) were nonsmall cell carcinoma,(20 %) were squamous cell carcinoma. The mean latency of sural nerve before chemotherapy was 3.543±0.4826and latency was 3.670±0.503after they developed neuropathy .The mean amplitude of sural nerve before chemotherapy was 7.573±0.8505and 5.960±1.9204after they developed neuropathy. The conduction velocity of sural nerve before chemotherapy was 45.67±3.17and was 48.33±3.29 after they developed neuropathy.The mean latency of peroneal nerve before chemotherapy was 3.557±0.432and latency was

3.743±0.432after they developed neuropathy .The mean amplitude of peroneal nerve before chemotherapy was 3.407±0.6175 and 3.233±0.6008after they developed neuropathy. The conduction velocity of peroneal nerve before chemotherapy was 46.80±2.041 and was 49.20±1.804 after they developed neuropathy. The nerve conduction study variables were compared before and after neuropathy using students t test and the results were statistically significant ($p< 0.05$) imparting that there was significant difference before and after chemotherapy. The time taken to develop peripheral neuropathy in carboplatin-paclitaxel group was 4.76±1.95 cycles. The grading of peripheral neuropathy was found to be Grade II.

**Table-1:comparison Of Nerve Conduction Study Variables Before Chemotherapy And After They Developed Neuropathy Carboplatin-paclitaxel Group**

| **SURAL NERVE** | BEFORE (MEAN±SD) | AFTER (MEAN±SD) |
|---|---|---|
| LATENCY | 3.543±0.4826 | 3.670±0.503* |
| AMPLITUDE | 7.573±0.8505 | 5.960±1.9204* |
| CONDUCTION VELOCITY | 45.67±3.17 | 48.33±3.29* |
| **PERONEAL NERVE** | BEFORE (MEAN±SD) | AFTER (MEAN±SD) |
| LATENCY | 3.557±0.432 | 3.743±0.432* |
| AMPLITUDE | 3.407±0.6175 | 3.233±0.6008* |
| CONDUCTION VELOCITY | 46.80±2.041 | 49.20±1.804* |

* p value < 0.05

**Figure 1: Amplitude Of Sural Nerve**

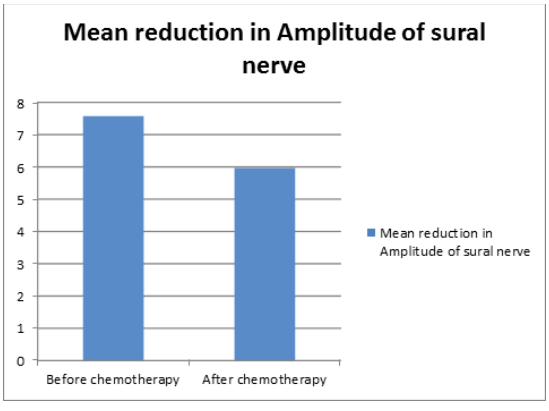
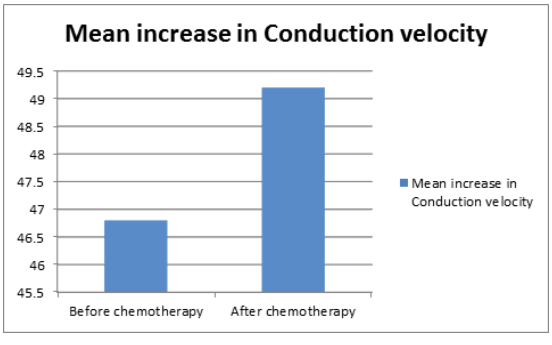



**Figure 2: Conduction Velocity Of Peroneal Nerve**




## DISCUSSION AND CONCLUSION:

The peripheral nervous system is affected more than central nervous system. The clinical features are dependent on the type of agent involved and its site of action.As a result of neurotoxicity, treatment with these drugs usually will be discontinued, which may prevent an effective treatment[5]. The dose-intensity mainly determines the severity of the neuropathy it may due to dose per cycle, or due to cumulative dose[6]. If it is accessable to prevent or reduce the neurotoxic adverse-effects of these drugs, this would have great impact on the efficacy of treatment and the quality of life of these patients[7]. In this present study , the neurotoxicity induced by Carboplatin–Paclitaxel in patients with lung or ovarian carcinoma was observed, so that early intervention can prevent the permanent neurotoxicity.[8] when nerve conduction variables are compared before and after chemotherapy there is a significant reduction in sensory nerve (sural) amplitude (SNAP) and latency ($p<0.05$)indicating significant axonal damage. According to the randomized study conducted by Du Bois et al the neurotoxicity of Carboplatin is generally considered to be less frequent, and less severe than Cisplatin. Grade 3/4 sensory neuropathy was 13.5% in the Cisplatin regimen versus 7.2% in the Carboplatin regimen[9]. In a randomized study by Daugaard GK et al Nerve conduction studies performed in patients treated with platinum drugs showed sensory axonal damage with reduction in amplitude of the sensory nerve action potentials (SNAP). Motor nerve conduction velocities (NCV), compound muscle action potentials (CMAP) and F-wave latencies remain unchanged during treatment.[10] In a study by Windebank AJ etal Electrophysiological abnormalities were decrease in SNAP indicating axonal sensory peripheral neuropathy. Reduction of CMAP occurs at the highest cumulative doses, while sensory and motor NCV are usually spared.[11]In this study,The time taken to develop peripheral neuropathy in Carboplatin-Paclitaxel group was 4 Cycles .In a study by Umamaheshwari et al the time taken to develop peripheral neuropathy in cisplatin- paclitaxel group was 3 cycles[12]. The occurrence of sensory neuropathy (which is proved by reduction in sensory nerve amplitude seen in nerve conduction study) is most commonly encountered than motor neuropathy. Since this is an observational study, dose relationship could not be explained for the development of adverse effects So, further studies are needed to confirm the dose adjustment for the reduction of neurological manifestations

## DECLARATIONS

*Funding: NIL*
*Conflict of interest: NIL*
*Ethical approval: OBTAINED*

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