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Case Series

Paclitaxel Induced Peripheral Neuropathy in Patients with Ovarian Carcinoma in South India: A Case Series

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Abstract

Introduction: Ovarian carcinoma is a major gynaecological malignancy in India, frequently diagnosed at advanced stages requiring systemic chemotherapy. The combination of paclitaxel and carboplatin remains the standard first-line regimen and has significantly improved patient survival. However, paclitaxel is commonly associated with chemotherapy-induced peripheral neuropathy (CIPN), a dose-dependent adverse effect primarily affecting sensory nerves. This condition manifests as paraesthesia, numbness, burning pain, and impaired proprioception in a characteristic glove-and-stocking distribution. Despite its clinical importance, data regarding paclitaxel-induced peripheral neuropathy (PIPN) in South Indian populations remain limited. This study aims to describe the clinical presentation, associated risk factors, and management outcomes of PIPN in ovarian carcinoma patients treated at a tertiary care centre in South India.

Case description: A case series was conducted in the Departments of Pharmacology and Medical Oncology at a tertiary care teaching hospital in South India. Five adult female patients with histologically confirmed epithelial ovarian carcinoma who developed peripheral neuropathy following paclitaxel-based chemotherapy were included. Patients received paclitaxel (175 mg/m²) and carboplatin (AUC 5-6) administered every 21 days for up to six cycles. Baseline neurological assessments were performed, and patients were monitored during each chemotherapy cycle for symptoms of neuropathy.

Results: All five patients developed predominantly sensory neuropathy characterized by tingling, numbness, and paraesthesia involving distal extremities. Neuropathy typically appeared after multiple chemotherapy cycles, indicating a relationship with cumulative paclitaxel exposure. Clinical evaluation revealed a symmetrical glove-and-stocking distribution. Management included symptomatic treatment, close neurological monitoring, and chemotherapy dose modification when necessary.

Conclusion: PIPN is a clinically significant complication of paclitaxel-carboplatin chemotherapy in ovarian carcinoma patients. Vigilant monitoring, timely recognition, and coordinated management are essential to prevent severe neurotoxicity and ensure uninterrupted cancer treatment.

Keywords: Paclitaxel-Induced Peripheral Neuropathy, Ovarian Cancer Chemotherapy, Chemotherapy-Induced Peripheral Neuropathy (CIPN), Carboplatin-Paclitaxel Regimen, Adverse Drug Reaction, Case Series.

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Introduction

Problem Statement: Ovarian cancer is the third most common gynaecological malignancy in India, with an age-adjusted incidence rate of 5.3 per 100,000 women. In South India, ovarian cancer accounts for approximately 6-8% of all female cancers, with patients presenting at a younger median age (50-55 years) compared to Western populations. The majority of these patients (70-80%) are diagnosed in advanced stages (FIGO III-IV), which necessitates aggressive systemic chemotherapy following optimal cytoreductive surgery.[1]

The landmark GOG-158 trial established the combination of carboplatin and paclitaxel as the standard first-line chemotherapy regimen for advanced epithelial ovarian cancer. Paclitaxel works by stabilizing microtubules and disrupting cell division, which has led to significant improvements in overall survival. However, its clinical utility is frequently limited by the development of paclitaxel-induced peripheral neuropathy (PIPN). PIPN is a dose-dependent, predominantly sensory neuropathy affecting up to 97% of patients receiving paclitaxel. Clinical manifestations present as a "glove and stocking" distribution of numbness, tingling, pain, and loss of proprioception. The Gynaecologic Oncology Group (GOG) reported that roughly 20% of ovarian cancer patients treated with this regimen experience grade 2 or higher neuropathy. [2,3]

Rationale & Pathophysiology: The primary site of pathogenesis for paclitaxel-associated peripheral neuropathy remains incompletely defined. In tissue culture, paclitaxel promotes the formation of abnormal microtubule bundles within the cytoplasm, leading to the disruption of normal cell function. In patients, paclitaxel accumulates in the dorsal root ganglia and can access the brain at very low concentrations. Intermediate concentrations are present in the sciatic nerve and spinal cord. PIPN is likely driven by dysfunctional microtubules in the dorsal root ganglia, axons, and Schwann cells. In vivo studies show that paclitaxel injection into the rat sciatic nerve causes unusual microtubule aggregates, demyelination, and loss of axoplasmic transport. It is highly probable that paclitaxel induces both a sensory axonopathy and ganglion neuropathy, particularly at higher cumulative doses. [4,5]

Novelty and Objective: Despite the significant impact of PIPN on treatment delivery and patient quality of life, there is limited published data on its prevalence and clinical characteristics in the South Indian population. Management strategies currently include dose modifications, treatment delays, drug discontinuation, and supportive care. This case series aims to describe the clinical features, incidence, risk factors, and management outcomes of a series of 5 cases of PIPN in ovarian carcinoma patients treated at a tertiary cancer centre in South India.[6]

Materials and Methods

Study Design and Site

Study Design: Case Series.

Study Site: Department of Pharmacology and Medical Oncology, Sri Venkateswara Institute of Medical Sciences (SVIMS), Tirupati, Andhra Pradesh, India.

Sample Size: 5 cases of paclitaxel-induced peripheral neuropathy.

Patient Selection Criteria [7]

Inclusion Criteria:

- Adult females (age ≥18 years) with histologically confirmed epithelial ovarian carcinoma.
- Patients who received at least one cycle of paclitaxel-carboplatin chemotherapy.
- Complete medical records with adequate follow-up data.
- Performance status ECOG 0-2 at treatment initiation.

Exclusion Criteria:

- Pre-existing peripheral neuropathy of any aetiology.
- Concurrent use of other neurotoxic agents.
- Previous taxane exposure.
- Incomplete treatment records or inadequate follow-up (<3 months).

Study Procedure and Treatment Protocol

All patients received the standard paclitaxel-carboplatin regimen, which consisted of:

- Paclitaxel 175 mg/m² administered intravenously over 3 hours on day 1.
- Carboplatin AUC 5-6 administered intravenously over 30-60 minutes on day 1.
- Cycles repeated every 21 days for a total of 6 cycles.

Standard premedication (dexamethasone, diphenhydramine, and ranitidine) was provided to prevent hypersensitivity reactions.

Patients underwent baseline neurological assessment before treatment initiation and were monitored for neuropathy development at each cycle. Clinical features, onset of neuropathy, risk factors, and management strategies were documented and analysed descriptively. Data entry was performed in Microsoft Excel 2019.[8]

Table 1: Treatment guidelines for paclitaxel induced neuropathy [9,10,11]

Category	Intervention / Agent	Standard of Care & Clinical Notes	Guideline Source
Primary Treatment	**Duloxetine (SNRI)**	**First-line choice** for painful CIPN. Typical dosing: 30 mg/day for 1 week, then 60 mg/day.	ASCO / ESMO (High)
Prevention (non-pharmacological)	**Cryotherapy (Cooling)**	Use of cooling gloves/socks (e.g., Hilotherm) during infusion to induce vasoconstriction. Significant reduction in Grade 2 neuropathy.	ESMO / NCCN (Moderate)
Prevention (non-pharmacological)	**Compression Therapy**	Wearing surgical gloves (often 0.5 to 1 size smaller) or compression stockings during infusion to limit distal drug delivery.	Emerging Evidence (2025)
Prevention (Pharmacologic)	**None Recommended**	**Strong recommendation against** use of Vitamin E, L-glutamine, Acetyl-L-carnitine, or Ca/Mg infusions for prevention.	ASCO (Strong Against)
Second-line / Refractory	**Venlafaxine / Gabapentinoids**	May be considered if Duloxetine is poorly tolerated or ineffective. Weak evidence for efficacy compared to Duloxetine.	ESMO (Weak)
Oncology Management	**Dose Modification**	**Gold standard for limiting progression.** Consider dose delay, reduction, or discontinuation if functional impairment occurs.	NCCN / Expert Opinion
Regimen Substitution	**Docetaxel / Nab-paclitaxel**	In severe cases, substituting Paclitaxel with Docetaxel or Liposomal Doxorubicin is supported to mitigate neurotoxicity.	GOG / NCCN
Supportive Care	**Physical Activity**	Low-impact exercise (walking, balance training) is moderately recommended to improve functional status and reduce fall risk.	ASCO

Results (Case Series Summary): The study included five adult female patients (age ≥18 years) with histologically confirmed epithelial ovarian carcinoma who were undergoing first-line systemic chemotherapy. All patients were treated with a standard regimen consisting of paclitaxel (175 mg/m2) administered intravenously over three hours, followed by carboplatin (AUC 5–6), with cycles repeated every 21 days for a maximum of six cycles.

To minimize the risk of hypersensitivity, standard premedication with dexamethasone, diphenhydramine, and ranitidine was administered. Following the initiation of treatment, all five patients developed predominantly sensory peripheral neuropathy characterized by symptoms of tingling, numbness, and paraesthesia.

Clinical evaluation revealed a symmetrical "glove-and-stocking" distribution of these symptoms involving the distal extremities. The onset of neuropathy typically occurred after multiple chemotherapy cycles, suggesting a direct correlation with cumulative paclitaxel exposure. Management of the neurotoxicity involved a combination of symptomatic treatment, close clinical monitoring, and chemotherapy dose modifications when necessary. These early interventions allowed for the successful continuation of the oncological treatment while preventing progression to severe, irreversible neurotoxicity.

Causality Assessment: All five cases were officially reported as adverse drug reactions (ADRs) to the Pharmacovigilance Programme of India (PvPI) through the Adverse Drug Reaction Monitoring Centre (AMC) at SVIMS. According to the WHO-UMC causality assessment criteria, the relationship between paclitaxel administration and the development of peripheral neuropathy was determined to be "probable" in all five instances. No cases of mortality were reported within this series. [12,13,14]

Discussion

The development of PIPN observed in this case series aligns closely with the established literature regarding taxane-induced neurotoxicity. Paclitaxel-induced peripheral neuropathy (PIPN) is recognized as a dose-dependent complication, with symptoms predominantly affecting sensory nerves.[15]

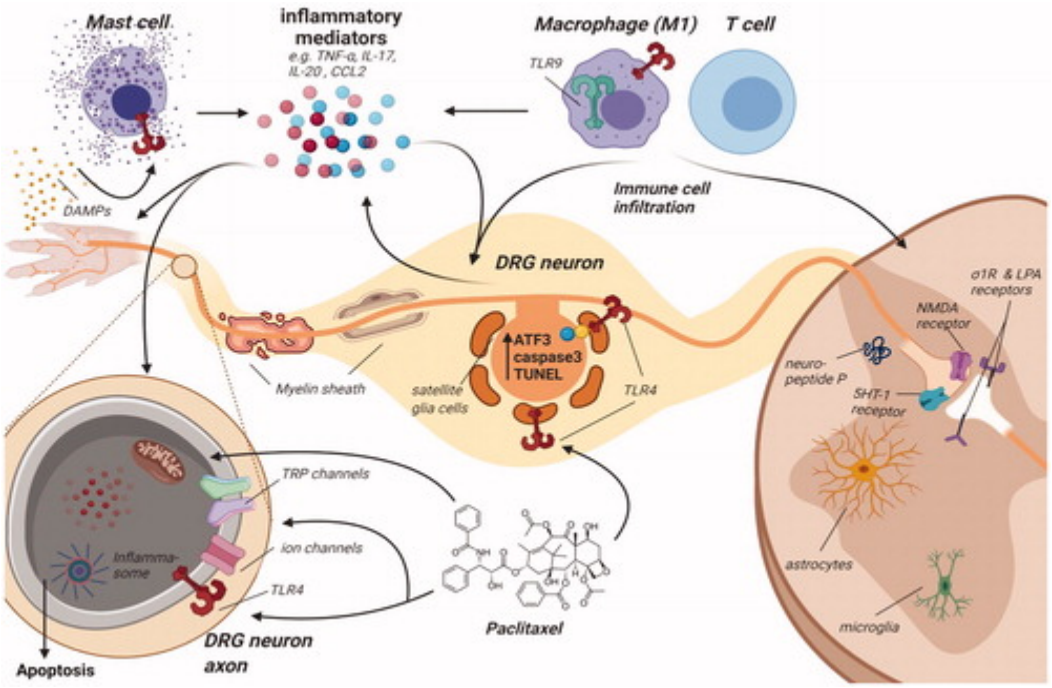

Figure 1: Schematic overview of dorsal root ganglion and spinal cord to indicate the various molecular mechanisms that contribute to paclitaxel-induced peripheral neuropathy.

Cornelia J. C. Vermeer et al explained about Paclitaxel induces peripheral neuropathy in rodents, characterized by distal nerve damage, demyelination, and reduced nerve conduction. This is primarily linked to neuronal injury (evidenced by increased ATF3 and apoptosis markers), mitochondrial dysfunction (swelling, reduced ATP, increased ROS), and altered sensory neuron excitability due to changes in ion channels (e.g., TRPV1, Nav1.7). Inflammation plays a key role, involving mast cell degranulation, direct activation of TLR4 by paclitaxel, DAMPs, and TLR9, leading to immune cell recruitment. Macrophages (M1) infiltrate the DRG, releasing pro-inflammatory mediators (cytokines, HMGB1) that activate neuronal TLR4 and cause pain. T cells may aid resolution. In the spinal cord, paclitaxel activates astrocytes, impairs glutamate uptake, and releases cytokines, and also dysregulates synaptic transmission through altered receptors (5-HT1a, substance P) and presynaptic NMDAR activation.[16]

Our findings are consistent with prior studies investigating CIPN in gynaecological cancers. Oneda et al. reported that CIPN occurs in roughly 20% of ovarian cancer patients treated with carboplatin/paclitaxel, heavily correlated with paclitaxel dosage, and can lead to dose reductions or early termination of treatment.[17] Furthermore, a study by Umamaheshwari et al. on patients receiving cisplatin and paclitaxel highlighted statistically significant axonal damage evidenced by reductions in sensory nerve amplitude and latency, with severe neuropathy commonly developing by the third cycle. [18]. Similarly, Forsyth et al. demonstrated in a prospective study that paclitaxel-induced peripheral neuropathy is primarily sensory, often beginning early in the treatment cycle, and characterized by paraesthesia. [19] Pansari et al. also noted that tingling sensations were the most common symptom in patients receiving weekly paclitaxel, confirming the sensory-dominant nature of this toxicity.[20]

The underlying pathophysiology involves the disruption of axonal transport, mitochondrial dysfunction, and microtubule stabilization in peripheral neurons, heavily impacting the dorsal root ganglia. Risk factors such as pre-existing diabetes mellitus have been shown in the broader literature to increase both the incidence (from 58.4% to 74.4%) and severity of paclitaxel-induced neuropathy. In our series, early identification and proactive management (including dose modifications and symptomatic care) were pivotal in mitigating severe neurotoxic decline.

Conclusion

Paclitaxel-induced peripheral neuropathy (PIPN) is a clinically significant complication of paclitaxel-carboplatin chemotherapy in ovarian carcinoma patients. This case series highlights the critical importance of vigilant monitoring, timely recognition, and coordinated management to prevent severe neurotoxicity and ensure uninterrupted cancer treatment. All reported cases demonstrated a "probable" causality under WHO-UMC criteria, with no associated mortality. Larger-scale prospective studies are required to further evaluate population-specific risk factors and

preventive strategies in the South Indian demographic.

Declarations

Ethical Considerations: The study was initiated following approval from the Institutional Ethics Committee (IEC) of Sri Venkateswara Institute of Medical Sciences (SVIMS). The research strictly adhered to the principles of the Declaration of Helsinki and good clinical practices.

Informed Consent: Written informed consent (provided in both English and the local language, Telugu) was obtained from all study participants, ensuring complete confidentiality and voluntary participation.

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