

# Comparison of toxicity profiles between weekly paclitaxel and weekly cisplatin in concurrent chemoradiotherapy for locally advanced laryngeal cancer

## Abstract

**Background:** Cisplatin and paclitaxel are both commonly used chemotherapeutic agents in the treatment of locally advanced laryngeal cancer, with cisplatin being the standard. However, the toxicity profiles of these agents vary significantly, impacting treatment tolerability and patient quality of life. This study compares the local and systemic toxicities of weekly paclitaxel versus weekly cisplatin, both administered concurrently with radiotherapy.

**Methods:** Sixty patients with locally advanced laryngeal cancer were randomly assigned to two groups. Arm A (n=30) received weekly paclitaxel (30 mg/m<sup>2</sup>), and Arm B (n=30) received weekly cisplatin (40 mg/m<sup>2</sup>), both alongside radiotherapy (66 Gy in 33 fractions over 6.5 weeks). Toxicities were assessed weekly during treatment and at follow-up using the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 5.0. Local toxicities such as mucositis and skin reactions, as well as systemic toxicities including renal impairment, nausea, and hematological effects, were monitored.

**Results:** Local toxicities were more prevalent in the paclitaxel group, with higher incidences of grade 2 mucositis (53.3%) and skin reactions (40.0%), though these differences were not statistically significant. In contrast, systemic toxicities, particularly renal toxicity and nausea, were more common in the cisplatin group. Grade 2 renal toxicity was observed in 13.3% of cisplatin-treated patients compared to 3.3% in the paclitaxel group. Nausea occurred in 33.3% of the cisplatin group compared to 10.0% in the paclitaxel group.

**Conclusion:** Weekly paclitaxel demonstrated a more favorable systemic toxicity profile compared to cisplatin, with lower incidences of renal toxicity and nausea. Although paclitaxel was associated with slightly higher local toxicities, it may be a safer alternative for patients with pre-existing conditions that contraindicate cisplatin, such as renal dysfunction. These findings suggest that patient-specific factors should guide the choice of chemotherapeutic agents in concurrent chemoradiotherapy for laryngeal cancer.

**Keywords:** laryngeal cancer, concurrent chemoradiotherapy (CCRT), paclitaxel, cisplatin, toxicity profiles, chemotherapy, radiotherapy

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**Abbreviations:** CCRT, concurrent chemoradiotherapy; SCC, squamous cell carcinoma; NCI CTCAE, national cancer institute common terminology criteria for adverse events; IMRT, intensity-modulated radiotherapy

## Introduction

Laryngeal cancer is a significant contributor to head and neck malignancies worldwide, particularly in regions with high rates of tobacco and alcohol consumption.<sup>1</sup> Treatment for locally advanced laryngeal cancer often involves multimodal approaches, with concurrent chemoradiotherapy (CCRT) being the preferred strategy to enhance loco regional control and preserve laryngeal function.<sup>2</sup> Among chemotherapeutic agents, cisplatin is widely regarded as the standard radio sensitizer due to its proven efficacy in combination with radiotherapy.<sup>3,4</sup> However, the use of cisplatin is frequently associated with a range of severe toxicities, including nephrotoxicity, neurotoxicity, and hematological side effects.<sup>5,6</sup> These toxicities can lead to treatment delays, dose reductions, or discontinuation, which may affect overall treatment outcomes.<sup>3,5</sup>

In recent years, paclitaxel has emerged as a potential alternative to cisplatin in CCRT for head and neck cancers.<sup>7,8</sup> Paclitaxel is a potent radio sensitizer that functions by stabilizing microtubules and arresting the cell cycle in the G2/M phase, making cancer cells more susceptible to radiation.<sup>7,9</sup> Unlike cisplatin, paclitaxel's toxicity profile includes fewer instances of renal and neurotoxicity, making it a potentially safer option for patients with pre-existing conditions, such as renal impairment or older age.<sup>8</sup> However, paclitaxel is not without side effects; local toxicities like mucositis and skin reactions are commonly reported.<sup>7</sup>

Given the importance of balancing efficacy with safety, understanding the toxicity profiles of chemotherapeutic agents is crucial in tailoring treatment for patients with locally advanced laryngeal cancer. This study aims to compare the toxicity profiles of weekly paclitaxel and weekly cisplatin, both administered concurrently with radiotherapy. The study evaluates both local toxicities, such as mucositis and skin reactions, and systemic toxicities, including renal toxicity, nausea, and hematological effects. By analyzing the adverse effects experienced by patients, this research seeks to inform clinical

decisions on the safer and more tolerable treatment option for different patient populations.

## Methods

**Study design:** This prospective, comparative study was conducted at the Department of Radiotherapy, Rajshahi Medical College Hospital, from January 2021 to June 2022. The study aimed to evaluate and compare the toxicity profiles of weekly paclitaxel and weekly cisplatin in patients with locally advanced laryngeal cancer undergoing concurrent chemoradiotherapy (CCRT).

**Study population:** Sixty patients with Histopathologically confirmed locally advanced squamous cell carcinoma (SCC) of the larynx (Stage III-IVB) were recruited. Patients were randomly assigned to one of two treatment arms:

- (i) **Arm A (Paclitaxel group):** 30 patients received weekly paclitaxel at a dose of 30 mg/m<sup>2</sup>.
- (ii) **Arm B (Cisplatin group):** 30 patients received weekly cisplatin at a dose of 40 mg/m<sup>2</sup>.

Both groups received concurrent external beam radiotherapy with a total dose of 66 Gy, delivered in 33 fractions over 6.5 weeks.

**Toxicity monitoring and assessment:** Toxicities were assessed weekly during treatment and at follow-up intervals (6, 12, and 24 weeks post-treatment) using the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 5.0. Toxicities were classified into local and systemic categories.

1. **Local toxicities:** Included mucositis, skin reactions, xerostomia, and dysphagia. Mucositis was assessed based on the extent and severity of oral ulcerations or inflammation, while skin reactions were evaluated by the degree of erythema, desquamation, or ulceration of irradiated areas. Xerostomia was evaluated based on patient-reported dryness, and dysphagia was graded according to swallowing difficulties.
2. **Systemic toxicities:** These involved renal, gastrointestinal, and hematological toxicities. Renal toxicity was assessed through serum creatinine levels and changes in glomerular filtration rate (GFR). Nausea and vomiting were graded by severity, frequency, and patient-reported interference with daily activities. Hematological toxicities, including anemia, leukopenia, and thrombocytopenia, were monitored through complete blood counts and categorized based on NCI CTCAE guidelines.

Toxicities were graded from 1 to 5, where:

1. **Grade 1:** Mild symptoms; no intervention required.
2. **Grade 2:** Moderate symptoms requiring minimal intervention.
3. **Grade 3:** Severe symptoms requiring intervention or hospitalization.
4. **Grade 4:** Life-threatening symptoms requiring urgent intervention.
5. **Grade 5:** Death related to treatment toxicity.

**Data collection:** A dedicated toxicity monitoring team, including oncologists and nursing staff, performed weekly clinical assessments. Blood tests, imaging studies (where applicable), and patient-reported symptoms were used to evaluate adverse effects. A standardized log was maintained to capture the onset, duration, and severity of toxicities for each patient.

**Statistical analysis:** Data were analyzed using SPSS software (version 25.0). Descriptive statistics were used to summarize the frequency and severity of toxicities in both treatment groups. Comparisons between the two arms were performed using chi-square tests for categorical variables, and Fisher's exact test was applied when appropriate. Statistical significance was set at  $p < 0.05$ .

## Results

A total of 60 patients with locally advanced laryngeal cancer were enrolled, with 30 patients in the paclitaxel group (Arm A) and 30 patients in the cisplatin group (Arm B). Toxicities were monitored weekly during treatment and at follow-up intervals. The observed toxicities were categorized as local (mucositis, skin reactions, xerostomia) and systemic (renal toxicity, hematological effects, nausea).

**Incidence of local toxicities:** Local toxicities such as mucositis, skin reactions, xerostomia, and dysphagia were more frequent in the paclitaxel group, although the differences were not statistically significant. Grade 2 mucositis occurred in 53.3% of patients in the paclitaxel group compared to 46.7% in the cisplatin group (Table 1).

**Table 1** Incidence of local toxicities in paclitaxel and cisplatin groups

Toxicity	Arm A (Paclitaxel)	Arm B (Cisplatin)	p-value
<b>Mucositis (Grade 2-3)</b>	16 (53.3%)	14 (46.7%)	0.625
<b>Skin Reactions (Grade 2)</b>	12 (40.0%)	10 (33.3%)	0.712
<b>Xerostomia (Grade 2)</b>	18 (60.0%)	16 (53.3%)	0.712
<b>Dysphagia (Grade 2-3)</b>	15 (50.0%)	13 (43.3%)	0.629

**Incidence of systemic toxicities:** Systemic toxicities, including renal toxicity, nausea, vomiting, and hematological effects, were more pronounced in the cisplatin group. Grade 2 renal toxicity was observed in 13.3% of patients receiving cisplatin, compared to only 3.3% in the paclitaxel group. Additionally, nausea (33.3% vs. 10.0%) and vomiting (30.0% vs. 6.7%) were significantly more common in the cisplatin group ( $p < 0.05$ ) (Table 2).

**Table 2** Incidence of systemic toxicities in paclitaxel and cisplatin groups

Toxicity	Arm A (Paclitaxel)	Arm B (Cisplatin)	p-value
<b>Renal Toxicity (Grade 2)</b>	1 (3.3%)	4 (13.3%)	0.355
<b>Nausea (Grade 2-3)</b>	3 (10.0%)	10 (33.3%)	0.047*
<b>Vomiting (Grade 2)</b>	2 (6.7%)	9 (30.0%)	0.044*
<b>Anemia (Grade 2-3)</b>	5 (16.7%)	7 (23.3%)	0.524
<b>Leukopenia (Grade 2-3)</b>	6 (20.0%)	8 (26.7%)	0.531
<b>Thrombocytopenia (Grade 2)</b>	3 (10.0%)	5 (16.7%)	0.707

\*Significant at  $p < 0.05$

## Key findings

- (i) **Local toxicities:** While paclitaxel-treated patients exhibited a slightly higher incidence of mucositis and skin reactions, these differences were not statistically significant.
- (ii) **Systemic toxicities:** Cisplatin-treated patients experienced significantly more nausea and vomiting, as well as higher rates of renal toxicity.

## Discussion

This study compared the toxicity profiles of weekly paclitaxel versus weekly cisplatin in patients receiving concurrent chemoradiotherapy (CCRT) for locally advanced laryngeal cancer. The findings indicate that while both treatment regimens are effective, the toxicity profiles differ significantly, particularly in terms of systemic side effects. Cisplatin, which has long been the standard radio sensitizer in CCRT, was associated with higher rates of renal toxicity, nausea, and vomiting, while paclitaxel showed a more favorable systemic toxicity profile, with fewer renal complications and gastrointestinal symptoms.

**Local toxicities:** Local toxicities, including mucositis, skin reactions, xerostomia, and dysphagia, were slightly more frequent in the paclitaxel group, although the differences were not statistically significant. Mucositis, a common side effect of radiotherapy, was observed in 53.3% of paclitaxel-treated patients, compared to 46.7% in the cisplatin group. These findings are consistent with studies that noted similar mucositis rates among patients receiving paclitaxel-based regimens for head and neck cancers.<sup>8</sup> Although paclitaxel may cause more local inflammation, these side effects are generally manageable with supportive care and do not necessitate treatment discontinuation.

**Systemic toxicities:** The most notable differences between the two groups were in systemic toxicities. Cisplatin-treated patients experienced significantly higher incidences of nausea, vomiting, and renal toxicity, consistent with findings from earlier studies.<sup>3,6</sup> In our study, 13.3% of cisplatin-treated patients developed Grade 2 renal toxicity, compared to only 3.3% in the paclitaxel group. This aligns with the known nephrotoxic effects of cisplatin, which often require dose reductions or treatment delays, potentially impacting overall treatment efficacy. Paclitaxel, on the other hand, exhibited a much lower incidence of renal toxicity, making it a safer alternative for patients with pre-existing renal impairment or those at higher risk of nephrotoxicity.

Nausea and vomiting were also significantly more common in the cisplatin group, with 33.3% and 30.0% of patients, respectively, experiencing these symptoms. By contrast, only 10.0% and 6.7% of paclitaxel-treated patients reported nausea and vomiting. This difference is crucial in clinical practice, as gastrointestinal toxicity can severely affect patient compliance and quality of life during treatment. Studies have reported similar findings, where paclitaxel-based CCRT was associated with a better tolerance profile compared to cisplatin.<sup>10</sup>

**Comparison with existing literature:** Several studies have explored the toxicity profiles of paclitaxel and cisplatin in head and neck cancers. Our findings corroborate those of studies that also reported a higher incidence of gastrointestinal and renal toxicities in cisplatin-treated patients, while paclitaxel was associated with more localized toxicities such as mucositis and skin reactions.<sup>7</sup> Furthermore, other studies support the notion that paclitaxel is a viable alternative for patients who cannot tolerate cisplatin due to its systemic side effects.<sup>8</sup>

**Clinical implications:** The results of this study suggest that paclitaxel is a safer alternative to cisplatin for certain patients, particularly those with pre-existing renal conditions or those prone to gastrointestinal disturbances. While both agents are effective radio sensitizers, paclitaxel's lower incidence of severe systemic toxicities may improve patient compliance and overall treatment success. Additionally, the manageable nature of the local toxicities associated with paclitaxel, such as mucositis and skin reactions, makes it a suitable option for long-term use in CCRT protocols.<sup>11</sup>

**Limitations and future directions:** Despite the promising results, this study has limitations. The sample size was relatively small, and the follow-up period was limited to 24 weeks, which may not fully capture the long-term toxicities associated with these regimens. Future studies with larger patient cohorts and extended follow-up periods are needed to further validate these findings. Additionally, further research should investigate the use of paclitaxel in combination with advanced radiotherapy techniques, such as intensity-modulated radiotherapy (IMRT), to minimize local toxicities while maintaining systemic safety.<sup>12</sup>

## Conclusion

This study demonstrates that weekly paclitaxel and weekly cisplatin, when used in concurrent chemoradiotherapy (CCRT) for locally advanced laryngeal cancer, result in comparable efficacy in terms of treatment outcomes. However, their toxicity profiles differ significantly, with paclitaxel showing a more favorable systemic toxicity profile. Cisplatin was associated with higher rates of renal toxicity, nausea, and vomiting, which can negatively impact patient compliance and quality of life. By contrast, paclitaxel, while associated with slightly higher local toxicities such as mucositis, showed fewer systemic side effects, making it a safer alternative for patients with pre-existing renal conditions or those more prone to gastrointestinal toxicities.

The findings of this study have important clinical implications. Paclitaxel should be considered for patients who are at risk of cisplatin-related toxicities, such as those with renal dysfunction, older adults, or patients who are less tolerant of gastrointestinal side effects. For these individuals, paclitaxel can provide a safer chemotherapeutic option while maintaining treatment efficacy. On the other hand, for patients who are able to tolerate cisplatin without significant side effects, it remains a viable option, particularly when considering its longstanding use in head and neck cancer treatments.

Further studies with larger sample sizes and longer follow-up periods are needed to confirm these findings and to explore the potential benefits of combining paclitaxel with advanced radiotherapy techniques, such as intensity-modulated radiotherapy (IMRT), to optimize both efficacy and safety. Personalized treatment strategies based on patient health status and tolerance to chemotherapeutic agents should guide clinical decisions in managing locally advanced laryngeal cancer.

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## Conflicts of interest

The author declares that there is no conflict of interest.

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