J Bionic Mem 2025; 5(2): 24-31 DOI: 10.53545/jbm.2025.46

Journal of Bionic Memory Original article

Comparative analysis of cisplatin tolerability in head and neck, bladder, and cervical cancers: Does the primary tumor site influence toxicity profiles?

Mustafa Ersoy

Department of Internal Medicine, Kütahya Health Sciences University, Faculty of Medicine, Kutahya, Türkiye

ABSTRACT

Aim: This study aims to investigate whether there is a difference in the tolerance of the cisplatin-radiotherapy regimen between head and neck cancers and bladder/cervical cancers. This will help determine if the typical tolerability issues associated with the cisplatin-radiotherapy combination are the primary barrier to delivering the desired cisplatin dose, or if the sensitive anatomical location of head and neck cancers leads to even poorer tolerance compared to other tumor sites.

Method: Our study included 60 patients who received cisplatin and radiotherapy between 2017 and 2025. Of these, 34 had head and neck cancer, 21 had cervical cancer, and 5 had bladder cancer. We examined whether there was a difference in the patients' ability to receive the planned cisplatin dose.

Results: The results showed that the proportion of head and neck cancer patients who were unable to complete the full treatment regimen was statistically significantly lower compared to the cervical and bladder cancer groups. The most common toxicity that hindered treatment in head and neck cancer was mucositis, while in the other groups it was nephrotoxicity. Among the head and neck cancer patients, 9 out of 17 were able to receive alternative therapies, with 7 receiving carboplatin and 2 receiving cetuximab. In the other group, 6 patients who did not receive treatment also could not access alternative therapies.

Conclusions: The results of our study indicate that the poor tolerability of cisplatin in head and neck cancers can be attributed to the high prevalence of site-specific mucositis, which hinders its administration. Consequently, we believe the promotion of alternative clinical trials, particularly those evaluating carboplatin, is warranted for this patient population.

Keywords: Head and neck cancer, cisplatin, carboplatin, cervix cancer, bladder cancer.

✉ *Mustafa Ersoy*

Department of Internal Medicine, Kütahya Health Sciences University, Faculty of Medicine, Kutahya, Türkiye

E-mail: mustafa.ersoy@ksbu.edu.tr

Received: 2025-07-26

Accepted: 2025-08-14 / Published: 2025-08-20

Introduction

Cisplatin has been extensively utilized for an extended period as a definitive, adjuvant, and palliative treatment option across a wide range of cancer types, including head and neck, gynecological, bladder, and various other malignancies [1]. The extensive body of data demonstrating its survival benefits has solidified cisplatin's critical role in daily clinical practice [2]. Cisplatin binds to DNA strands, forming intra-strand and inter-strand crosslinks, which subsequently inhibit DNA replication and transcription processes [1]. Additionally, cisplatin has been demonstrated to influence the radiation sensitivity of various cell types, and several potential mechanistic explanations have been proposed. These include radiation-induced increases in cisplatin

uptake, efficient blockade of DNA repair pathways, and prolonged cell cycle arrest [3].

Patients treated with concurrent cisplatin-based chemoradiotherapy have demonstrated longer survival times compared to those treated with radiotherapy alone, particularly in cervical cancer, head and neck cancer, non-small cell lung cancer, and esophageal cancer [4].

Another platinum-based agent, carboplatin, also exhibits a similar mechanism of action [5]. However, while it can be utilized as a radiosensitizer similar to cisplatin, cisplatin remains the standard of care for many patients, as there is less extensive evidence supporting the efficacy of carboplatin in this capacity compared to cisplatin [6].

In head and neck cancer, the ability to deliver the full intended cisplatin dose is crucial, as it has been shown to impact patient survival [7]. Common factors leading to discontinuation of cisplatin treatment in this population may include the typical toxicities associated with this agent, as well as issues specific to the anatomical location, such as mucositis and impaired oral intake resulting in cisplatin-related nephrotoxicity [8]. Additionally, a decline in performance status due to tumor-related factors and the associated caloric deficit can contribute to a worsened ECOG performance score [9]. Carboplatin, as a potential alternative, demonstrates a more favorable toxicity profile in comparison [10].

The aim of our study is to compare the treatment completion rates among patients with head and neck, cervical, and bladder cancer who received similar cisplatin dosages. While cisplatin is an effective therapy when administered at full dose, we will examine whether there are any notable differences in real-world treatment completion rates across these cancer types. This could provide insights into the potential tolerability challenges with cisplatin in head and neck cancer patients, potentially due to the unique mucosal toxicity profile exacerbated by concurrent radiotherapy given the anatomical location of these tumors. This information could illuminate the possible utility of alternative agents like carboplatin in this patient population and pave the way for future prospective studies comparing the efficacy of cisplatin and alternative treatment options, potentially offering a solution to this clinically significant problem.

Materials and Methods

Study participants

The study retrospectively analyzed the medical records of patients treated at the Medical Oncology Clinic of Kütahya Evliya Çelebi Training and Research Hospital and Kütahya City Hospital between 2017 and 2025. A total of 60 individuals were included in the investigation. Demographic and clinical characteristics, such as birth date, weight, medications, chronic illnesses, smoking history, and cancer stage, were obtained from the patients' oncology files.

The study population encompassed patients with head and neck cancers, including malignancies arising from the oral cavity, oropharynx, nasopharynx, hypopharynx, and larynx. The cervical cancer cohort comprised both squamous cell carcinoma and adenocarcinoma subtypes. The bladder cancer group consisted of patients receiving either trimodal or palliative treatment. The study included patients receiving adjuvant, curative, or palliative therapies.

The inclusion criteria were: being 18 years of age or older, receiving the complete treatment at the study centers, and being eligible for cisplatin.

The exclusion criteria were: having received prior cisplatin treatment and being unable to

complete the desired treatment due to chemotherapy allergy.

Chemotherapy regimen

All patients received concurrent radiotherapy as part of their treatment. Radiotherapy was permitted to be administered at external centers in addition to the Kütahya Evliya Çelebi Education and Research Hospital Department of Radiation Oncology.

Cisplatin was administered using the following regimens: for head and neck cancer, 40 mg/m2 weekly for 6 weeks or 100 mg/m2 every 21 days for 2 cycles; for cervical cancer, 40 mg/m2 weekly for 6 weeks; and for bladder cancer, 35 mg/m2 weekly for 6 weeks or 20 mg/m2 given twice weekly on days 1 and 2 for 6 weeks. Patients unable to receive cisplatin, but deemed appropriate based on their overall condition, were prescribed carboplatin at an AUC of 2, administered weekly for a duration tailored to their remaining treatment plan. For head and neck cancer patients who became ineligible for platinum-based therapy due to toxicity, cetuximab was given as a 400 mg/m2 loading dose, followed by 250 mg/m2 weekly, based on the remaining chemotherapy regimen. Patients were categorized according to whether they were able to complete the planned treatment.

Eligibility criteria for cisplatin and carboplatin

For cisplatin, patients needed to have a creatinine clearance of at least 60 mL/min, an ECOG performance status of 1 or better, grade 1 or milder neuropathy, grade 1 or milder deafness, New York Heart Association heart failure of class II or lower with a cardiac ejection fraction of at least 50%, and normal blood parameters.

The eligibility criteria for carboplatin were a creatinine clearance of at least 30 mL/min, an ECOG performance status of 2 or better, grade 2 or milder neuropathy, grade 2 or milder deafness, New York Heart Association heart failure of class II or lower with a cardiac ejection fraction of at least 50%, and normal blood parameters. Hematological parameters were critical for all treatment regimens, with particularly stringent requirements for carboplatin-based chemotherapy.

Toxicity interpretation

The toxicities that prevented patients from completing the full course of treatment were assessed by the physician at each visit and documented in an adverse event form. For patients with multiple toxicities who were unable to continue treatment, the primary limiting toxicity was determined by Dr. Mustafa Ersoy and recorded in the patient's file. Upon review of the records, the toxicities that hindered treatment continuation were observed to be mucositis, nephrotoxicity unresponsive to intravenous fluid replacement, nausea resistant to antiemetics, neuropathy, and a decline in ECOG performance status. The decision to continue or discontinue cisplatin and carboplatin therapies was made based on the eligibility criteria outlined above.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0. Descriptive statistics were used to summarize the data, with categorical variables reported as frequencies and percentages, and continuous variables as means with standard deviations and medians. To compare the categorical variables across the study groups, which were divided into bladder+cervical and head and neck groups, the chi-square test was employed. Statistical significance was established at a p-value less than 0.05, indicating the observed differences between the groups were unlikely to have occurred by chance alone.

Results

Table 1 summarizes the clinical characteristics of the patients. The patient population was predominantly female, comprising 57% of the cohort. The most common primary tumor site was head and neck, accounting for 56% of cases. The majority of patients, 63%, had stage 3 disease. Notably, a substantial proportion, 38%, experienced toxicities that led to incomplete treatment.

When examining the demographic and clinical characteristics of the patients based on primary cancer site, the cervical cancer patients were generally younger and had fewer smoking histories compared to the other patient groups. However, the groups were similar in terms of chronic comorbidities, medication usage, and disease stage.

Table 1. The clinical characteristics of the patients.

Characteristic	N	Percentage
Gender		
Male	26	43%
Female	34	57%
Primary Site		
Head and Neck	34	56%
Cervical	21	35%
Bladder	5	8%
Stage		
2	12	20%
3	38	63%
4	10	17%
Toxicity leading to incomplete treatment		
Yes	23	38%
No	37	62%

Note. N: Number of patients.

Table 2 shows the comparison of treatment completion rates across different primary tumor sites. Patients with head and neck cancers had a higher rate of toxicity leading to incomplete treatment (17 patients) compared to those with cervical (5 patients) and bladder (1 patient) cancers. This difference was statistically significant ($p = 0.034$).

Table 2. Comparison of treatment completion rates.

Toxicity leading to incomplete treatment	Primary Site			$p^{\#}$
	Head and Neck	Cervical	Bladder	
Yes	17	5	**1**	0.034
No	17	16	4	

Note. # : Pearson chi-square test, p< 0.05 considered statistically significant..

Table 3 outlines the specific toxicities that led to incomplete treatment across the different primary tumor sites. While some patients experienced multiple toxicities, the key factors that prevented treatment completion were as follows. For head and neck cancers, the reported toxicities included mucositis in 9 cases, nephrotoxicity in 5 cases, and a decline in ECOG performance status in 2 cases. Additionally, nausea was observed in 1 case. In cervical cancers, nephrotoxicity was reported in 3 cases, and neuropathy was seen in 1 case. Among bladder cancers, only 1 case of nephrotoxicity was noted.

Table 3. Number of toxicities leading to incomplete treatment by primary tumor site.

Toxicity	Primary Site		
	Head and Neck	Cervical	Bladder
Mucositis	9	0	0
Nephrotoxicity	5	3	1
Nausea	1	1	0
Neuropathy	0	1	0
Decline in ECOGPS	2	0	0

Note. ECOGPS: Eastern Cooperative Oncology Group Performance Status.

Table 4 presents the alternative therapy received by patients across the different primary tumor sites. Among patients with head and neck cancers, 9 completed the alternative therapy, while 8 did not receive any alternative treatment. The primary alternative therapies used for head and neck cancers were carboplatin in 7 patients and cetuximab in 2 patients. None of the patients with cervical or bladder cancer who were unable to tolerate cisplatin received any alternative therapy at the planned dose.

Table 4. Patients receiving alternative therapy and the specific treatments received.

Alternative therapy status	**Primary Site**		
	Head and Neck	**Cervical**	**Bladder**
Alternative therapy received			
Completed	9	0	0
Incomplete	8	5	1
Alternative therapy			
Carboplatin	7	0	0
Cetuximab	2	0	0

Among the patients who were unable to complete cisplatin treatment due to toxicity, 4 out of the 9 patients who were unable to receive treatment due to mucositis did not receive any alternative therapy, while the remaining 5 were able to receive carboplatin. Of the 5 patients who were unable to receive treatment due to nephrotoxicity, 2 did not receive any alternative therapy, while 3 were able to receive alternative treatment. One patient received carboplatin, and 2 patients received cetuximab. The 2 patients who were unable to receive treatment due to a decline in ECOG performance status also did not receive any alternative therapy. The patient who was unable to receive treatment due to nausea was able to receive carboplatin.

Discussion

In head and neck cancer, the standard concurrent chemoradiotherapy regimen is high-dose cisplatin at 100 mg/m2 administered in two or three cycles [6]. However, in our study, only 2 out of 34 patients were prescribed the high-dose regimen, while the majority received weekly cisplatin. Similarly, a retrospective multicenter international study from 2005-2019 found that only 8 out of 310 patients receiving single-agent cisplatin were prescribed the high-dose regimen [7]. In our study, two patients were unable to receive the second 100 mg/m2 dose of cisplatin, and one experienced an acute kidney injury requiring hospitalization. Based on these findings and the literature, it appears that clinicians may be hesitant to prescribe the high-dose cisplatin regimen due to concerns about its tolerability with concurrent radiotherapy, opting instead for a weekly cisplatin regimen to avoid severe toxicities.

In our study, only 50% of the head and neck cancer patients receiving cisplatin were able to tolerate the full prescribed dose. Similarly, a multicenter study of 697 patients found that 53% of those receiving weekly cisplatin were able to complete at least 5 weeks of treatment, while in our cohort, patients were considered to have fully received the therapy if they completed 6 weeks [7]. A study evaluating 109 patients found that only 45% of those planned for 6 weeks of weekly cisplatin treatment were able to receive the full prescribed dose [11]. Another study involving 300 patients receiving concurrent chemoradiotherapy reported that 84.6% of those administered 100 mg/m2 cisplatin every 21 days and 71.6% of those receiving 30 mg/m2 weekly cisplatin

experienced grade 3 or higher acute toxicities [12]. Additionally, the literature indicates that increasing the cumulative cisplatin dose, even in 10 mg increments, and exceeding a total of 200 mg can contribute to improved survival outcomes [7, 13]. The findings from our study align with the existing literature, suggesting that the inability to deliver the full desired cisplatin dose is a significant long-term challenge for head and neck cancer patients.

Our study found that the completion rate of weekly cisplatin therapy was higher among patients with cervical and bladder cancers compared to those with head and neck cancers. Due to the limited number of bladder cancer cases in our cohort, they were combined into a single group, and 77% of these patients were able to complete the prescribed treatment. Conversely, a previous study involving 112 cervical cancer patients reported a 45% full-dose completion rate for weekly cisplatin therapy [14]. Additionally, another investigation on bladder cancer revealed that 40 out of 43 patients tolerated concurrent weekly cisplatin well [15]. The existing literature suggests that the rate of treatment completion can vary significantly based on the patient population under examination. Notably, our single-center study, with a patient cohort similar in all characteristics except age and gender, demonstrated that head and neck cancer patients were less likely to receive the full intended cisplatin dose. Given that radiation therapy toxicity can differ depending on the treatment facility, equipment, and personnel, a single-institution study focused on a sensitive anatomical region like the head and neck may provide valuable insights into the comparative tolerability of cisplatin across various primary cancer sites.

In our study, 3 out of 5 patients in the cervical cancer cohort and 1 patient in the bladder cancer cohort were unable to receive the intended cisplatin dose due to nephrotoxicity. In the head and neck cancer group, 9 out of 17 patients were unable to receive the full planned treatment, with severe mucositis being the primary limiting factor rather than nephrotoxicity. Overall, nephrotoxicity was observed in 5 patients. While potential obstruction-related renal impairment in bladder and cervical cancers may have contributed to a more toxic cisplatin course, our findings indicate that nephrotoxicity occurred at a similar frequency of approximately 15% in these two groups. Additionally, excluding patients with a baseline glomerular filtration rate below 60 may have helped mitigate more extensive nephrotoxicity. Inadequate fluid intake in head and neck cancer patients may have also contributed to the nephrotoxicity observed, as seen in the other groups with potential obstructive issues.

While none of the patients in the bladder and cervical cancer cohorts were able to receive alternative treatment after being unable to tolerate the intended cisplatin regimen, 9 out of the 17 head and neck cancer patients were able to receive alternative therapy. Notably, 7 of these 9 patients were able to receive the desired dose of carboplatin, in contrast to the other groups where patients generally could not receive any treatment at all. This suggests that the toxicity issues were not specific to cisplatin but rather reflected a more general treatment intolerance in the cervical and bladder cancer populations, with cisplatin posing particular challenges for the head and neck cancer group. The observation that carboplatin was well-tolerated, as has been reported in the literature, raises the question of whether initiating carboplatin as the primary treatment for patients who were originally planned for cisplatin but were unable to complete the intended therapy

and did not receive any alternative treatment could have been a more effective approach [16].

Limitations

This retrospective study involved 60 patients, with the comparison focused solely on whether the intended treatment dose was achieved or not. Long-term outcomes, such as local recurrence, systemic control, and overall survival, were not monitored, and the relationship between treatment dose and these endpoints could not be directly assessed.

Conclusion

Although cisplatin is the standard radiosensitizing agent used in head and neck cancers, the rates of achieving the desired dosing levels are not optimal, and the negative impact of insufficient dosing on survival has been well-documented. Our study findings suggest that cisplatin was less well-tolerated in head and neck cancer patients compared to those with bladder and cervical cancer who received similar doses. Given that carboplatin was shown to be well-tolerated in a subset of patients unable to receive cisplatin, initiating treatment with an effective and more tolerable agent such as carboplatin may be warranted, particularly for patients initially thought to be unable to receive cumulative cisplatin doses over 200 mg. Therefore, new randomized studies comparing the long-term outcomes of head and neck cancer patients who were able to receive the full dose of carboplatin versus those who were unable to receive the full dose of cisplatin, but had similar characteristics, would be valuable.

Funding: *The author(s) received no financial support for the research, authorship, and/or publication of this article.*

Conflict of Interest: *The authors declare that they have no conflict of interest.*

Ethical statement: *This study was approved by the Non-Interventional Research Ethics Committee of Bezmialem Vakif University on April 2, 2025, with the number 2025/82, and all procedures were carried out in accordance with the principles outlined in the Declaration of Helsinki.*

References

[1]Dasari S, Tchounwou PB. Cisplatin in cancer therapy: molecular mechanisms of action. Eur J Pharmacol. 2014;740:364-378.

[2]Gómez-Ruiz S, Maksimović-Ivanić D, Mijatović S, Kaluđerović GN. On the discovery, biological effects, and use of Cisplatin and metallocenes in anticancer chemotherapy. Bioinorg Chem Appl. 2012;2012:140284.

[3]Lawrence TS, Blackstock AW, McGinn C. The mechanism of action of radiosensitization of conventional chemotherapeutic agents. Semin Radiat Oncol. 2003;13(1):13-21.

[4]Mierzwa ML, Nyati MK, Morgan MA, Lawrence TS. Recent advances in combined modality therapy. Oncologist. 2010;15(4):372-381.

[5]Fong CW. Platinum based radiochemotherapies: Free radical mechanisms and radiotherapy sensitizers. Free Radic Biol Med. 2016;99:99-109.

[6]Lacas B, Carmel A, Landais C, et al. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): An update on 107 randomized trials and 19,805 patients, on behalf of MACH-NC Group. Radiother Oncol. 2021;156:281-293.

[7]Rühle A, Weymann M, Behrens M, et al. A Multicenter Evaluation of Different Chemotherapy Regimens in Older Adults With Head and Neck Squamous Cell Carcinoma Undergoing Definitive Chemoradiation. Int J Radiat Oncol Biol Phys. 2024;118(5):1282-1293.

[8]Falco A, de Oliveira TB, Cacicedo J, et al. Ibero-American Expert Consensus on Squamous Cell Carcinoma of the Head and Neck Treatment in Patients Unable to Receive Cisplatin: Recommendations for Clinical Practice. Cancer Manag Res. 2021;13:6689-6703.

[9]Corrêa GT, Bandeira GA, Cavalcanti BG, et al. Analysis of ECOG performance status in head and neck squamous cell carcinoma patients: association with sociodemographical and clinical factors, and overall survival. Support Care Cancer. 2012;20(11):2679-2685.

[10]Moncharmont C, Auberdiac P, Mélis A, et al. Cisplatine ou carboplatine, telle est la question [Cisplatin or carboplatin, that is the question]. Bull Cancer. 2011;98(2):164-175.

[11]Andhi, N., Sravya, A., Praneetha, S., et al. An Observational Study on Tolerability and Safety of Cisplatin Chemotherapy in Various Cancer. Indian J Pharm Pract, 15(3), 227–234.

[12]Noronha V, Joshi A, Patil VM, et al. Once-a-Week Versus Once-Every-3-Weeks Cisplatin Chemoradiation for Locally Advanced Head and Neck Cancer: A Phase III Randomized Noninferiority Trial. J Clin Oncol. 2018;36(11):1064-1072.

[13]Strojan P, Vermorken JB, Beitler JJ, et al. Cumulative cisplatin dose in concurrent chemoradiotherapy for head and neck cancer: A systematic review. Head Neck. 2016;38 Suppl 1:E2151-E2158.

[14]Serkies K, Jassem J. Concurrent weekly cisplatin and radiotherapy in routine management of cervical cancer: a report on patient compliance and acute toxicity. Int J Radiat Oncol Biol Phys. 2004;60(3):814-821.

[15]Gogna NK, Matthews JH, Turner SL, et al. Efficacy and tolerability of concurrent weekly low dose cisplatin during radiation treatment of localised muscle invasive bladder transitional cell carcinoma: a report of two sequential Phase II studies from the Trans Tasman Radiation Oncology Group [published correction appears in Radiother Oncol. 2007;83(2):215. Mameghan, Heidi [corrected to Mameghan, Hedy]]. Radiother Oncol. 2006;81(1):9-17.

[16]Ahmed Riad, M. A Comparative Study of Response and Toxicity between Weekly Cisplatin plus Radiotherapy Versus Weekly Carboplatin plus Radiotherapy in Locally Advanced Squamous Cell Carcinoma of Head-Neck. J Enam Med Coll. 2024;11(3):173–179.