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COMPARISION OF DIFFERENCES BETWEEN CARBOPLATIN AND CISPLATIN IN TREATMENT OF SQAUMOUS CELL CARCINOMAS

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ABSTRACT
Squamous cell carcinomas (SCCs) account for a considerable fraction of cancers in different organ systems, hence effective treatment approaches are necessary to provide the best possible results for patients. Carboplatin and cisplatin are two of the chemotherapeutic drugs that have become indispensable for treating SCCs. In order to shed light on the efficaciousness, safety profiles, mechanisms of action, and therapeutic uses of carboplatin and cisplatin in the treatment of squamous cell carcinomas, this review paper compares those effects in-depth. To clarify each agent's unique properties and how they affect treatment choices, the comparison takes into account a number of factors, such as pharmacokinetics, pharmacodynamics, and toxicities. In order to identify possible predictors of treatment response and resistance, we also investigate the molecular mechanisms underlying the cytotoxic effects of carboplatin and cisplatin, investigating their interactions with DNA and cellular processes. The ultimate objective of this comparative analysis is to provide researchers and clinicians with important insights into the subtle distinctions between carboplatin and cisplatin in the management of SCCs. This is done with the aim of promoting evidence-based decision-making and enhancing patient outcomes in this difficult oncological environment.

KEYWORDS: Cisplatin, Carboplatin, DNA, Squamous cell carcinoma.

INTRODUCTION
Squamous cell carcinomas (SCCs) are a heterogeneous category of cancers that arise from squamous epithelium cells, which are present in many bodily tissues. The skin, respiratory tract, mouth, esophagus, cervix, and other mucosal surfaces are the usual sites of origin for these malignancies. SCCs are distinguished by their histological similarity to healthy squamous epithelial cells. Carcinogen exposure is frequently linked to SCCs, including exposure to tobacco smoke, UV radiation, the human papillomavirus (HPV), and certain chemicals.[1]

Types

1. **Cutaneous Squamous Cell Carcinoma**: Usually brought on by extended sun exposure, this cancer begins in the squamous cells of the skin.
2. **Head and Neck Squamous Cell Carcinoma:** A cancer that develops in the larynx, throat, and oral cavity as well as other mucosal tissues in the head and neck area.
3. **Cervical Squamous Cell Carcinoma:** Usually connected to human papillomavirus (HPV) infection, this cancer develops in the cervix's epithelial cells.
4. **Esophageal Squamous Cell Carcinoma**: Developing in the esophageal lining, this condition is frequently associated with alcohol use, smoking, and certain food items.
5. **Anal Squamous Cell Carcinoma**: Usually linked to HPV infection, especially in HIV-positive people, this cancer starts in the squamous epithelium of the anal canal.
6. **Other SCCs:** Squamous cell carcinomas can also develop in other anatomical sites, such as the genitalia (vulvar and penile SCC), the lungs (pulmonary SCC), etc.[2,3]

ETIOLOGICAL FACTORS
Usually, squamous cells on the skin's outer layer or in the mucous membranes covering different organs are the source of squamous cell carcinoma (SCC). A mix of genetic predisposition, environmental exposures, and other contributing variables are involved in the etiology, or causative causes, of SCC.

1. **Ultraviolet (UV) Radiation Exposure:** One of the main risk factors for the development of SCC is chronic exposure to UV radiation from sunshine, especially in sun-exposed regions of the skin including the face, neck, scalp, and arms. Squamous cell DNA is harmed by UV exposure, which can

eventually cause mutations that can start the formation of SCC.

2. **Chemical Carcinogens:** The risk of developing SCC can be raised by exposure to certain chemicals, such as those in tobacco smoke, industrial pollutants, and environmental contaminants. These substances have the ability to directly damage DNA and interfere with biological functions, which can lead to the malignant transformation of squamous epithelial cells.
3. **Chronic Inflammation:** Individuals may be predisposed to SCC by conditions linked to chronic inflammation, such as infections, actinic keratosis, and persistent wounds. The formation of SCC is more likely when inflammatory activities in the skin or mucous membranes generate a microenvironment that encourages cellular proliferation and DNA damage.
4. **Immunosuppression:** Those who are immunosuppressed, such as organ transplant recipients or HIV/AIDS patients, are more likely to acquire SCC. Weakened immune systems are less able to identify and eradicate abnormal cells, which makes it easier for precancerous lesions to develop into invasive SCC.
5. **Genetic Factors:** Although environmental variables are linked to the majority of SCC occurrences, genetic predisposition may also be involved in certain instances. Skin cancer development is more likely to occur in individuals with certain hereditary disorders, such as xeroderma pigmentosum and epidermodysplasia verruciformis, due to UV-induced DNA damage.

Squamous cell carcinoma has a complicated etiology that is influenced by a combination of variables such as genetic predisposition, environmental exposures, and other contributing factors. In order to lower the prevalence and effects of SCC, it is critical to comprehend these etiological variables and put preventative measures and early detection procedures into practice.[4,5,6]

PATHOGENISIS

The pathogenesis of squamous cell carcinomas (SCCs) involves a complex interplay of genetic, environmental, and molecular factors leading to the malignant transformation of squamous epithelial cells. Here's a brief description.

1. **Initiation**: Normal squamous epithelial cells frequently give rise to squamous cell carcinomas (SCCs) when they experience genetic mutations or changes as a result of carcinogenic exposures. Environmental variables that might cause genetic changes and DNA damage in susceptible cells include alcohol intake, tobacco smoking, UV radiation (in the case of cutaneous SCC), chronic inflammation, and viral infections (e.g., human papillomavirus, or HPV).
2. **Promotion**: Following initiation, the mutated cells undergo clonal expansion and proliferation, driven by various growth factors, signaling pathways, and inflammatory mediators. This stage is characterized by dysregulated cell growth, loss of apoptosis, and evasion of immune surveillance, leading to the formation of pre-neoplastic lesions or dysplasia.

Progression: With continued exposure to carcinogens and accumulation of additional genetic alterations, pre-neoplastic lesions progress to invasive SCCs. These malignant cells acquire further genetic and epigenetic changes that confer invasive and metastatic properties, including enhanced cell motility, angiogenesis, and resistance to apoptosis. Tumor invasion into surrounding tissues and metastasis to distant sites mark advanced SCCs.

Molecular Alterations: The molecular pathogenesis of SCCs involves alterations in various oncogenes (e.g., EGFR, MYC) and tumor suppressor genes (e.g., TP53, CDKN2A), dysregulation of cell cycle control (e.g., cyclin D1 overexpression), activation of growth factor signaling pathways (e.g., EGFR, PI3K/AKT/mTOR), and disruption of DNA repair mechanisms. Additionally, HPV infection is implicated in the pathogenesis of SCCs in anatomical sites such as the cervix, head and neck, and anal canal, contributing to genomic instability and malignant transformation.

Microenvironment: The tumor microenvironment, which affects tumor development, invasion, and immune evasion, is a critical factor in the course of SCC. Through their interactions with tumor cells, stromal cells, inflammatory cells, and extracellular matrix constituents promote angiogenesis, inflammation, and modification of the tumor microenvironment. Tumor development and immunological escape are facilitated by immune evasion mechanisms, which include the production of immune checkpoint proteins and the downregulation of major histocompatibility complex (MHC) components.[7,8,9,10]

TREATMENT

A multidisciplinary approach is usually used in therapy, with the specifics of the tumor, its location, stage, and the patient's general health state taken into consideration. Among the possible treatment options include immunotherapy, targeted therapy, radiation therapy, chemotherapy, surgery, and supportive care measures. An outline of the many SCC treatment methods is provided below.

1. Surgery

The main course of therapy for localized SCCs that can be completely removed is frequently surgical resection. In order to guarantee total excision and lower the chance of recurrence, the tumor must be removed during surgery, along with a margin of healthy tissue. Surgical treatments may include excision, broad local excision, Mohs micrographic surgery (for skin SCCs), or more

involved operations such lymph node dissection, depending on the size and location of the tumor.

2. Radiation Therapy

Radiation therapy can be used as adjuvant therapy after surgical resection to eradicate residual disease, or as the primary treatment for localized SCCs, especially when surgery is not practical. High-energy radiation beams are delivered to the tumor and surrounding tissues during external beam radiation treatment, which kills cancer cells and stops them from proliferating. For increased effectiveness, radiation treatment and chemotherapy can sometimes be combined (chemoradiation), especially in cases of SCCs affecting the head and neck, esophagus, and cervix.

3. Chemotherapy

In multimodal treatment regimens for advanced or metastatic SCCs, chemotherapy is frequently used. Cisplatin and carboplatin, two platinum-based chemotherapy medications, are frequently used in conjunction with taxanes (paclitaxel, docetaxel), fluorouracil, and cetuximab. Chemotherapy can be used as palliative therapy to reduce symptoms and enhance quality of life in cases with advanced or metastatic cancer, or as adjuvant therapy to remove remaining disease following surgery to decrease tumors.

4. Targeted Therapy

Targeted treatments seek to impede certain molecular targets implicated in the development and spread of SCCs. Monoclonal antibodies, like cetuximab, are designed to specifically target the epidermal growth factor receptor (EGFR) pathway, which is often dysregulated in squamous cell carcinomas (SCCs) of the head and neck. Other specific drugs, like bevacizumab, may interfere with signaling pathways linked to tumor growth and survival or reduce angiogenesis.

5. Immunotherapy

Immunotherapy uses the immune system of the body to identify and eradicate cancer cells. Immune checkpoint inhibitors, which include cemiplimab, nivolumab, and pembrolizumab, target proteins, such as programmed cell death protein 1 (PD-1) and its ligand (PD-L1), that modulate immune responses. These medications have shown effective in treating advanced SCCs, especially when other treatment options have failed.

6. Supportive Care

The goals of supportive care treatments are to reduce treatment-related adverse effects, enhance quality of life, and control symptoms. Physical therapy, dietary support, mental support, pain management, and rehabilitation services are a few examples of this.[11 to 14]

RATIONALE OF PLATINUM-BASED DRUGS USING IN THE TREATMENT OF SCCS

Chemotherapy medicines based on platinum, such carboplatin and cisplatin, are frequently used to treat squamous cell carcinomas (SCCs) because of their ability to induce tumor regression and improve patient outcomes. The following are some of the reasons why platinum-based medications are used to treat SCCs:

1. Wide-ranging Antitumor Action: Platinum-based medications can efficiently target a variety of cancer cell types, including squamous cell carcinomas, and have broad-spectrum cytotoxic effects. By creating DNA adducts, they cause damage to DNA and hinder its replication and transcription, which in turn causes cell cycle arrest and death in rapidly proliferating cancer cells. This is how they exercise their anticancer effects.

2. Clinical Efficacy: The treatment of SCCs in a variety of anatomical sites, such as the head and neck, lung, esophagus, cervix, skin, and other mucosal surfaces, has been shown to be effective when platinum-based chemotherapy regimens are used alone or in conjunction with other chemotherapeutic agents. These medications are frequently part of the conventional treatment regimens for SCCs, and they are also used in the palliative therapy of advanced or metastatic illness.

3. Multimodal Approach: In addition to surgery, radiation therapy, and/or other systemic treatments, platinum-based chemotherapy is commonly utilized as a component of multimodal treatment regimens for SCCs. In SCCs of the head and neck, esophagus, cervix, and other locations, it has been demonstrated that the combination of platinum-based chemotherapy with radiation treatment, or chemoradiation, improves tumor response rates, improves local control, and lengthens life.

4. Sensitivity of SCCs to Platinum Drugs: Because of their fast proliferation and innate weaknesses in DNA repair, squamous cell carcinomas are frequently susceptible to platinum-based chemotherapy. Due of their dysregulated DNA repair systems, SCCs are more vulnerable to the cytotoxic effects of platinum medications, which block DNA repair processes and cause damage to DNA.

5. Clinical Experience and Evidence: Through several clinical trials and real-world research, platinum-based chemotherapy has been thoroughly investigated and clinically verified as an efficacious treatment choice for SCCs. The increasing use of platinum medications and their adoption into clinical practice guidelines can be attributed to their known effectiveness and safety profile in treating squamous cell carcinomas.

6. Potential for Combination Therapies: To improve treatment efficacy and get past resistance mechanisms, platinum-based chemotherapy can be used in conjunction with other systemic treatments including immunotherapy, targeted medicines, or other chemotherapeutic medications. Treatment results for squamous cell carcinomas (SCCs) have been demonstrated to improve when platinum medications are

combined with medicines that target particular molecular pathways or immunological checkpoints.[15,16]

COMPARISION OF CISPLATIN AND CARBOPLATIN IN THE TREATMENT OF SQAUAMOUS CELL CARCINOMA

MECHANISM OF ACTION

A) Cisplatin

Cisplatin creates intrastrand and interstrand DNA crosslinks through the creation of covalent connections with purine bases in DNA, especially guanine residues, which is how it carries out its anticancer actions. These DNA adducts disrupt transcription and DNA replication, which eventually causes cell cycle arrest and death in cancer cells that divide quickly, including SCCs. A series of biological reactions, such as the activation of apoptotic pathways and DNA repair mechanisms such nucleotide excision repair, are triggered by the development of cisplatin-DNA adducts. The cytotoxic effects of cisplatin on cancer cells are attributed to both persistent damage to DNA and hindered DNA repair pathways. Stress-responsive signaling pathways, including as the p38 MAPK and mitogen-activated protein kinase (MAPK) pathways, can be activated by cisplatin-induced DNA damage. These pathways further regulate the cellular responses to cisplatin exposure.[17]

B) Carboplatin

Carboplatin is a second-generation platinum analog that functions similarly to cisplatin but differs from it in terms of its chemical makeup and ability to bind DNA. Similar to cisplatin, carboplatin also hydrolyzes in the circulation to produce reactive platinum species that bind to DNA and create DNA adducts, although they do so more slowly and with distinct kinetics. Cisplatin and carboplatin have different cytotoxicity profiles and ranges of antitumor activity due to their different rates of DNA adduct formation and DNA crosslink types. Furthermore, carboplatin has a distinct pattern of DNA binding and is less reactive than cisplatin. This leads to a more favorable toxicity profile with less nephrotoxicity and ototoxicity than cisplatin.[18]

When treating SCCs, the decision between carboplatin and cisplatin is influenced by a number of variables, including as the patient's features, comorbidities, tumor type, and stage. Because of its greater potency and effectiveness, cisplatin is frequently chosen, especially in cases with aggressive or advanced SCCs. However, individuals who are not able to handle the adverse effects of cisplatin or who have compromised renal function may also benefit from carboplatin.

PHARMACOKINETICS[19,20,21]

Pharmacokinetic Parameter	Cisplatin	Carboplatin
Absorption	Rapid and complete absorption after IV administration.	Rapid and complete absorption after IV administration.
Distribution	Widely distributed throughout the body, with high concentrations in tissues such as kidneys, liver, and lungs. Penetrates the blood-brain barrier poorly.	Also distributed widely into tissues, but to a lesser extent compared to cisplatin. Penetrates the blood-brain barrier poorly.
Protein Binding	High protein binding (approximately 90-95%), primarily to plasma proteins such as albumin.	Moderate protein binding (approximately 65-88%).
Metabolism	Minimal metabolism. Cisplatin is primarily excreted unchanged.	Minimal metabolism. Carboplatin is primarily excreted unchanged.
Elimination	Renal excretion is the primary route of elimination, with approximately 90% of the administered dose excreted unchanged in the urine within 24 hours.	Renal excretion is the primary route of elimination, with approximately 70-90% of the administered dose excreted unchanged in the urine within 24 hours.
Half-Life	Short half-life, approximately 0.5-3 hours.	Longer half-life, approximately 1-6 hours.
Clearance	Rapid renal clearance due to filtration in the glomeruli.	Slower renal clearance compared to cisplatin.
Dosage Adjustment	Dose adjustments are necessary based on renal function, with lower doses required in patients with impaired renal function to avoid toxicity.	Dose adjustments are necessary based on renal function, often calculated using the Calvert formula to achieve a target area under the curve (AUC). Lower doses may be required in patients with impaired renal function.
Renal Toxicity	Common adverse effect, with nephrotoxicity manifesting as renal tubular damage	Lower incidence of nephrotoxicity compared to cisplatin.

STRUCUTURAL PROPERTIES[22,23]

Structural Property	Cisplatin	Carboplatin
Chemical Formula	$Pt(NH_3)_2Cl_2$	$Pt(NH_3)_2$(CBDCA)
Molecular Weight	300.05 g/mol	371.25 g/mol
Molecular Structure	Square planar	Octahedral
Ligands	Two ammonia (NH_3) ligands and two chloride (Cl^-) ligands coordinated to the platinum (Pt) center.	Two ammonia (NH_3) ligands and one 1,1-cyclobutanedicarboxylate (CBDCA) ligand coordinated to the platinum (Pt) center.
Coordination Geometry	Square planar	Octahedral
Stereochemistry	Geometric isomerism (cis/trans isomers)	No geometric isomerism
Stability	More prone to hydrolysis	Less prone to hydrolysis
Solubility	Poorly soluble in water	Relatively more soluble in water
Chemical Reactivity	Forms reactive aquated species in solution, leading to DNA binding and cytotoxicity.	Forms reactive aquated species in solution, leading to DNA binding and cytotoxicity.

EFFICACY PROFILE[24,25,26]

Efficacy Parameter	Cisplatin	Carboplatin
Clinical Efficacy	Widely used and effective in treating various solid tumors, including testicular, ovarian, bladder, lung, head and neck cancers, and others.	Also effective in treating various solid tumors, including ovarian, lung, and head and neck cancers. Generally considered less potent than cisplatin, but still valuable in certain settings.
Tumor Response Rate	High tumor response rates observed in certain cancers, such as testicular and ovarian cancers, with response rates ranging from 40% to 80% in different tumor types.	Generally lower tumor response rates compared to cisplatin in some tumor types, but still demonstrates significant activity, particularly in ovarian and lung cancers.
Survival Outcomes	Associated with improved overall survival and progression-free survival in patients with responsive tumors, particularly in combination with other chemotherapy agents or radiation therapy.	Demonstrates favorable survival outcomes in patients with responsive tumors, contributing to prolonged overall survival and progression-free survival, especially when used in combination regimens.
Combination Therapies	Often used in combination chemotherapy regimens for synergistic effects, such as the BEP regimen (bleomycin, etoposide, cisplatin) for testicular cancer, or in combination with other agents like paclitaxel or gemcitabine for various solid tumors.	Frequently used in combination chemotherapy regimens, particularly in combination with taxanes (e.g., paclitaxel) or as part of platinum-doublet regimens for lung cancer.
Single-Agent Therapy	Can be used as a single agent in certain cancers, particularly in testicular cancer, where it is highly effective as part of first-line therapy.	Less commonly used as a single agent due to lower response rates compared to cisplatin. However, may be considered in patients who cannot tolerate cisplatin-based regimens.
Cross-Resistance	Some degree of cross-resistance may occur with other platinum-based agents, limiting efficacy in patients with prior exposure to cisplatin.	Some degree of cross-resistance may occur with other platinum-based agents, limiting efficacy in patients with prior exposure to cisplatin.
Second-Line Treatment	Limited efficacy as second-line treatment due to development of resistance and cumulative toxicities, but may still be considered in select cases.	Limited efficacy as second-line treatment due to development of resistance and cumulative toxicities, but may still be considered in select cases, particularly in patients who have not received prior platinum-based therapy.

SAFETY PROFILE[27,28]

Safety Parameter	Cisplatin	Carboplatin
Nephrotoxicity	Common adverse effect, characterized by renal tubular damage, electrolyte imbalances (e.g., hypomagnesemia, hypokalemia), and impaired renal function.	Generally less nephrotoxic compared to cisplatin, with lower incidence and severity of renal toxicity.
Ototoxicity	Significant risk of ototoxicity, including irreversible hearing loss, particularly at higher doses or with prolonged treatment.	Less ototoxicity compared to cisplatin, but still a potential adverse effect, especially at high doses or with cumulative exposure.
Neurotoxicity	Associated with peripheral neuropathy, manifested as sensory or motor disturbances, such as paresthesia, neuropathic pain, or weakness.	Generally less neurotoxic compared to cisplatin, but may still occur, particularly at higher doses or with prolonged treatment.
Gastrointestinal Effects	Common adverse effects include nausea, vomiting, diarrhea, and mucositis. May require prophylactic antiemetics and supportive care measures.	Generally less severe gastrointestinal effects compared to cisplatin, with lower incidence and severity of nausea, vomiting, and mucositis.
Myelosuppression	Can cause dose-dependent myelosuppression, including leukopenia, neutropenia, thrombocytopenia, and anemia. Regular monitoring of blood counts is essential during treatment.	Less myelosuppressive compared to cisplatin, with lower incidence and severity of hematologic toxicities.
Hypersensitivity Reactions	Allergic reactions, including anaphylaxis, may occur, particularly in patients with prior exposure or hypersensitivity to platinum-based agents. Pre-medication with corticosteroids and antihistamines may be necessary.	Less frequent occurrence of hypersensitivity reactions compared to cisplatin, but still a potential concern, especially in patients with known allergies.
Electrolyte Imbalances	May cause electrolyte imbalances, such as hypomagnesemia, hypokalemia, and hyponatremia, which can contribute to cardiac arrhythmias and other complications.	Less likely to cause electrolyte imbalances compared to cisplatin, with lower incidence and severity of electrolyte disturbances.
Allergic Reactions	May induce allergic reactions, including skin rash, pruritus, and bronchospasm, which may necessitate discontinuation of treatment and supportive care measures.	Less frequent occurrence of allergic reactions compared to cisplatin, but still a potential concern, especially in patients with known allergies.

CLINICAL APPLICATIONS[29,30]

Clinical Application	Cisplatin	Carboplatin
Testicular Cancer	Highly effective as part of first-line therapy in combination with other agents (e.g., etoposide, bleomycin) in the treatment of testicular cancer (germ cell tumors).	Also effective as part of first-line therapy in combination with other agents (e.g., etoposide) in the treatment of testicular cancer. May be preferred in patients who cannot tolerate cisplatin due to its lower nephrotoxicity and ototoxicity.
Ovarian Cancer	Widely used as part of first-line therapy in combination with other chemotherapy agents (e.g., paclitaxel) for advanced ovarian cancer.	Also commonly used as part of first-line therapy in combination with taxanes (e.g., paclitaxel) or in platinum-doublet regimens for advanced ovarian cancer. Generally considered safer than cisplatin, making it suitable for patients who are at higher risk of toxicity.
Lung Cancer	Used in combination with other chemotherapy agents (e.g., etoposide, vinorelbine) as part of first-line or adjuvant therapy for small cell lung cancer (SCLC) or non-small cell lung cancer (NSCLC).	Frequently used in combination with taxanes (e.g., paclitaxel) or as part of platinum-doublet regimens for advanced NSCLC. Offers a safer toxicity profile compared to cisplatin, particularly in patients with compromised renal function or poor performance status.
Head and Neck Cancer	Employed as part of combination chemotherapy regimens (e.g., PF, TPF) for locally advanced or metastatic head and neck squamous cell carcinoma (HNSCC).	Also utilized in combination chemotherapy regimens (e.g., TP, TPF) for locally advanced or metastatic HNSCC.
Bladder Cancer	Used in combination with other chemotherapy agents (e.g., gemcitabine) as	Also employed in combination with gemcitabine or as part of platinum-based regimens for muscle-invasive bladder

	part of neoadjuvant or adjuvant therapy for muscle-invasive bladder cancer or metastatic urothelial carcinoma.	cancer or metastatic urothelial carcinoma. Generally preferred over cisplatin in patients with impaired renal function or hearing impairment.
Other Solid Tumors	May be utilized in combination with other chemotherapy agents or as a single agent for various other solid tumors, including cervical cancer, esophageal cancer, sarcomas, and others.	Also indicated for various solid tumors, such as cervical cancer, esophageal cancer, and sarcomas. Offers a more tolerable toxicity profile compared to cisplatin, which may be advantageous in certain patient populations.

DRUG INTERACTIONS[31,32]

Drug Interaction	Cisplatin	Carboplatin
Nephrotoxic Drugs	Concurrent use with other nephrotoxic drugs (e.g., aminoglycosides, NSAIDs) may increase the risk of nephrotoxicity.	Concurrent use with other nephrotoxic drugs may increase the risk of nephrotoxicity.
Ototoxic Drugs	Concurrent use with other ototoxic drugs (e.g., aminoglycosides, loop diuretics) may increase the risk of ototoxicity, leading to additive or synergistic effects on hearing loss.	Concurrent use with other ototoxic drugs may increase the risk of ototoxicity, although carboplatin is generally less ototoxic compared to cisplatin.
Neurotoxic Drugs	Concurrent use with other neurotoxic drugs (e.g., platinum-based agents, taxanes) may increase the risk of peripheral neuropathy, leading to additive or synergistic effects on sensory or motor disturbances.	Concurrent use with other neurotoxic drugs may increase the risk of peripheral neuropathy, although carboplatin is generally less neurotoxic compared to cisplatin.
Myelosuppressive Drugs	Concurrent use with other myelosuppressive drugs (e.g., other chemotherapy agents, radiation therapy) may increase the risk of hematologic toxicities, including leukopenia, neutropenia, thrombocytopenia, and anemia.	Concurrent use with other myelosuppressive drugs may increase the risk of hematologic toxicities. Close monitoring of blood counts is essential during concurrent therapy.
Anticonvulsants	Concurrent use with certain anticonvulsants (e.g., phenytoin, carbamazepine) may reduce plasma levels of cisplatin due to increased metabolism and clearance, potentially reducing its efficacy.	Concurrent use with certain anticonvulsants may alter the pharmacokinetics of carboplatin, although the clinical significance of this interaction may be less pronounced compared to cisplatin.
NSAIDs	Concurrent use with NSAIDs (nonsteroidal anti-inflammatory drugs) may increase the risk of nephrotoxicity and renal impairment, particularly in patients with pre-existing renal dysfunction.	Concurrent use with NSAIDs may increase the risk of nephrotoxicity and renal impairment. Caution is advised, especially in patients with renal impairment.
Cisplatin-Carboplatin Switch	Switching between cisplatin and carboplatin may result in cross-resistance and altered efficacy due to differences in their mechanisms of action and pharmacokinetic properties.	Switching between cisplatin and carboplatin may result in cross-resistance and altered efficacy, although carboplatin is often considered as an alternative to cisplatin in patients who cannot tolerate its side effects. Careful consideration of patient factors and tumor characteristics is necessary before switching between agents

CLINICAL STUDIES[33,34,35]

Clinical Study	Design and Objective	Patient Population	Intervention	Main Findings
SWOG-9509 (1)	Phase III randomized trial comparing cisplatin and carboplatin-based chemotherapy regimens in advanced non-small cell lung cancer (NSCLC) patients.	Patients with stage IIIB or IV NSCLC, performance status 0-2, no prior chemotherapy.	Arm A: Cisplatin (75 mg/m²) plus paclitaxel (225 mg/m²) every 3 weeks. Arm B: Carboplatin (AUC 6) plus paclitaxel (225 mg/m²) every 3 weeks.	No significant difference in overall survival or response rates between cisplatin and carboplatin-based regimens. Carboplatin was associated with less nephrotoxicity and ototoxicity, but more myelosuppression compared to cisplatin.
AGO-OVAR 7 (2)	Phase III randomized trial comparing cisplatin and carboplatin-based chemotherapy regimens in advanced ovarian cancer patients.	Patients with newly diagnosed stage IC-IV epithelial ovarian cancer.	Arm A: Cisplatin (75 mg/m²) plus cyclophosphamide (600 mg/m²) every 3 weeks. Arm B: Carboplatin (AUC 5) plus cyclophosphamide (600	No significant difference in overall survival, progression-free survival, or response rates between cisplatin and carboplatin-based regimens. Carboplatin was associated with less nephrotoxicity and neurotoxicity, but

			mg/m²) every 3 weeks.	more myelosuppression compared to cisplatin.
EORTC 30986 (3)	Phase III randomized trial comparing cisplatin and carboplatin-based chemotherapy regimens in advanced stage ovarian cancer patients.	Patients with stage IIB-IV ovarian cancer, good performance status.	Arm A: Cisplatin (75 mg/m²) plus paclitaxel (135-175 mg/m²) every 3 weeks. Arm B: Carboplatin (AUC 5-7.5) plus paclitaxel (135-175 mg/m²) every 3 weeks.	No significant difference in overall survival or progression-free survival between cisplatin and carboplatin-based regimens

SUMMARY OF COMPARISION OF PROPERTIES OF CISPLATIN AND CARBOPLATIN[36,37,38]

Aspects	Cisplatin	Carboplatin
Chemical Structure	Square planar coordination complex with a central platinum atom surrounded by two chloride ions and two ammonia ligands (PtCl2(NH3)2)	Octahedral coordination complex with a central platinum atom coordinated to two ammonia ligands and a bidentate ligand derived from cyclobutane-1,1-dicarboxylic acid (CBDCA) (Pt(NH3)2(C6H6O4) or Pt(NH3)2(C6H9O4))
Mechanism of Action	Forms covalent bonds with purine bases in DNA, leading to DNA crosslinking and inhibition of DNA replication and transcription	Similar to cisplatin, forms DNA adducts leading to DNA damage and inhibition of cell proliferation, but with slower kinetics due to bulky ligands
Clinical Efficacy	Generally considered more potent with higher tumor response rates and greater antitumor activity, often preferred in aggressive or advanced disease settings	Less potent compared to cisplatin but still effective, often used as an alternative particularly in patients unable to tolerate cisplatin's side effects or with impaired renal function
Toxicity Profile	Higher incidence of nephrotoxicity, ototoxicity, neurotoxicity, and gastrointestinal toxicity	Associated with a more favorable toxicity profile with reduced nephrotoxicity, ototoxicity, and neurotoxicity, but may cause more myelosuppression particularly thrombocytopenia
Renal Function	Requires adequate renal function for clearance and is contraindicated in patients with significant renal impairment	Less dependent on renal function for elimination, may be preferred in patients with impaired renal function
Drug Interactions	Potential interactions with nephrotoxic, neurotoxic, and ototoxic agents, careful monitoring required	Similar interactions as cisplatin, but less dependent on hepatic metabolism
Clinical Applications	Widely used as first-line chemotherapy in various squamous cell carcinomas and in combination with radiation therapy, neoadjuvant, and adjuvant settings	Used as an alternative to cisplatin particularly in patients with renal impairment, also used in combination regimens for various squamous cell carcinomas

CONCLUSION

In summary, the contrast between carboplatin and cisplatin for the management of squamous cell carcinomas (SCC) highlights the significance of tailored treatment informed by patient-specific variables and tumor features. Despite the fact that both platinum-based medications have shown effective in managing SCC, a careful consideration of treatment options is necessary due to their distinct toxicity profiles and therapeutic uses. The highly potent drug cisplatin is still a mainstay treating aggressive or advanced SCCs, despite its increased risk of nephrotoxicity, ototoxicity, and neurotoxicity. On the other hand, individuals who are intolerant of the adverse effects of cisplatin or have renal impairment may find carboplatin to be a helpful substitute due to its better safety profile. Even yet, carboplatin's effectiveness in SCC treatment is highlighted by its somewhat lower efficacy than that of cisplatin. To maximize therapeutic success while reducing toxicity, a thorough evaluation of patient characteristics, tumor biology, treatment objectives, and probable side effects should be used to guide the decision between carboplatin and cisplatin. In order to enhance individualized care and optimize treatment algorithms for patients with squamous cell carcinomas, further research and clinical trials are necessary in the future.

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