Skip to main content

Cisplatin for Injection (Platinol)

??? ??????: 30 ??????/?????? 2017

Nephrotoxicity

Dose-related and cumulative renal insufficiency, including acute renal failure, is the major dose-limiting toxicity of PLATINOL. Renal toxicity has been noted in 28% to 36% of patients treated with a single dose of 50 mg/m². It is first noted during the second week after a dose and is manifested by elevations in BUN and **Renal toxicity becomes more prolonged and severe with repeated courses of the drug.** creatinine, serum uric acid and/or a decrease in creatinine clearance. Elderly patients may be more susceptible to nephrotoxicity (see **Renal function must return to normal before another dose of PLATINOL can be given.**).**Geriatric Use** :**PRECAUTIONS**

Impairment of renal function has been associated with renal tubular damage. The administration of PLATINOL using a 6- to 8-hour infusion with intravenous hydration, and mannitol has been used to reduce nephrotoxicity. However, renal toxicity still can occur after utilization of these procedures.

Ototoxicity

Ototoxicity has been observed in up to 31% of patients treated with a single dose of PLATINOL 50 mg/m², and is manifested by tinnitus and/or hearing loss in the high frequency range (4000 to 8000 Hz). The prevelance of hearing loss in children is particularly high and is estimated to be 40-60%. Decreased ability to hear normal conversational tones may occur. Deafness after the initial dose of PLATINOL has been reported. Ototoxic effects may be more severe in children receiving PLATINOL.

Hearing loss can be unilateral or bilateral and tends to become more frequent and severe with repeated cisplatin doses. It is unclear whether PLATINOL-induced ototoxicity is reversible. Vestibular toxicity has also been reported. Ototoxic effects may be related to the peak plasma concentration of cisplatin. Ototoxicity can occur during treatment or be delayed. Audiometric monitoring should be performed prior to initiation of therapy, prior to each subsequent dose, and for several years post therapy.

The risk of ototoxicity may be increased by prior or simultaneous cranial irradiation, and may be more severe in patients less than 5 years of age, patients being treated with other ototoxic drugs (e.g. aminoglycosides and vancomycin), and in patients with renal impairment. Variants in the thiopurine S-methyltransferase gene).**CLINICAL PHARMACOLOGY**(TPMT) have been reported to be associated with an increased risk of ototoxicity in children treated with cisplatin (see

Other genetic factors may also contribute to the cisplatin-induced ototoxicity.

Hematologic

Myelosuppression occurs in 25% to 30% of patients treated with PLATINOL. The nadirs in circulating platelets and leukocytes occur between days 18 to 23 (range 7.5 to 45) with most patients recovering by day 39 (range 13 to 62). Leukopenia and thrombocytopenia are more pronounced at higher doses (> 50 mg/m²). Anemia (decrease of 2 g hemoglobin/100 mL) occurs at approximately the same frequency and with the same timing as leukopenia and thrombocytopenia. Fever and infection have also been reported in patients with neutropenia. Potential fatalities due to infection (secondary to myelosuppression) have been reported. Elderly).**Geriatric Use** :**PRECAUTIONS**patients may be more susceptible to myelosuppression (see

In addition to anemia secondary to myelosuppression, a Coombs' positive hemolytic anemia has been reported. In the presence of cisplatin hemolytic anemia, a further course of treatment may be accompanied by increased hemolysis and this risk should be weighed by the treating physician.

The development of acute leukemia coincident with the use of PLATINOL has been reported. In these reports, PLATINOL was generally given in combination with other leukemogenic agents.

Gastrointestinal

Marked nausea and vomiting occur in almost all patients treated with PLATINOL, and may be so severe that the drug must be discontinued. Nausea and vomiting may begin within 1 to 4 hours after treatment and last up to 24 hours. Various degrees of vomiting, nausea and/or anorexia may persist for up to 1 week after treatment.

Delayed nausea and vomiting (begins or persists 24 hours or more after chemotherapy) has occurred in patients attaining complete emetic control on the day of PLATINOL therapy.

Diarrhea has also been reported.

Other Toxicities

Vascular toxicities coincident with the use of PLATINOL in combination with other antineoplastic agents have been reported. The events are clinically heterogeneous and may include myocardial infarction, cerebrovascular accident, thrombotic microangiopathy (hemolytic-uremic syndrome [HUS]), or cerebral arteritis. Various mechanisms have been proposed for these vascular complications. There are also reports of Raynaud's phenomenon occurring in patients treated with the combination of bleomycin, vinblastine with or without PLATINOL. It has been suggested that hypomagnesemia developing coincident with the use of PLATINOL may be an added, although not essential, factor associated with this event. However, it is currently unknown if the cause of Raynaud's phenomenon in these cases is the disease, underlying vascular compromise, bleomycin, vinblastine, hypomagnesemia, or a combination of any of these factors.

Serum Electrolyte Disturbances

Hypomagnesemia, hypocalcemia, hyponatremia, hypokalemia, and hypophosphatemia have been reported to occur in patients treated with PLATINOL and are probably related to renal tubular damage. Tetany has been reported in those patients with hypocalcemia and hypomagnesemia. Generally, normal serum electrolyte levels are restored by administering supplemental electrolytes and discontinuing PLATINOL.

Inappropriate antidiuretic hormone syndrome has also been reported.

Hyperuricemia

Hyperuricemia has been reported to occur at approximately the same frequency as the increases in BUN and serum creatinine.

It is more pronounced after doses greater than 50 mg/m², and peak levels of uric acid generally occur between 3 to 5 days after the dose. Allopurinol therapy for hyperuricemia effectively reduces uric acid levels.

Neurotoxicity

.**WARNINGS** See

Neurotoxicity, usually characterized by peripheral neuropathies, has been reported. The neuropathies usually occur after prolonged therapy (4 to 7 months); however, neurologic symptoms have been reported to occur after a single dose. Although symptoms and signs of PLATINOL neuropathy usually develop during treatment, symptoms of neuropathy may begin 3 to 8 weeks after the last dose of PLATINOL. PLATINOL therapy should be discontinued when the symptoms are first observed. The neuropathy, however, may progress further even after stopping treatment. Preliminary evidence suggests peripheral neuropathy may be).**Geriatric Use** :**PRECAUTIONS**irreversible in some patients. Elderly patients may be more susceptible to peripheral neuropathy (see

Lhermitte's sign, dorsal column myelopathy, and autonomic neuropathy have also been reported.

Loss of taste, seizures, leukoencephalopathy, and reversible posterior leukoencephalopathy syndrome (RPLS) have also been reported.

Muscle cramps, defined as localized, painful, involuntary skeletal muscle contractions of sudden onset and short duration, have been reported and were usually associated in patients receiving a relatively high cumulative dose of PLATINOL and with a relatively advanced symptomatic stage of peripheral neuropathy.

Ocular Toxicity

Optic neuritis, papilledema, and cerebral blindness have been reported in patients receiving standard recommended doses of PLATINOL. Improvement and/or total recovery usually occurs after discontinuing PLATINOL. Steroids with or without mannitol have been used; however, efficacy has not been established.

Blurred vision and altered color perception have been reported after the use of regimens with higher doses of PLATINOL or greater dose frequencies than recommended in the package insert. The altered color perception manifests as a loss of color discrimination, particularly in the blue-yellow axis. The only finding on funduscopic exam is irregular retinal pigmentation of the macular area.

Anaphylactic-Like Reactions

Anaphylactic-like reactions have been reported in patients previously exposed to PLATINOL. The reactions consist of facial edema, wheezing, tachycardia, and hypotension within a few minutes of drug administration. Reactions may be controlled by intravenous epinephrine with corticosteroids and/or antihistamines as indicated. Patients receiving PLATINOL should be observed carefully for possible anaphylactic-like reactions and supportive equipment and medication should be available to treat such a complication.

Hepatotoxicity

Transient elevations of liver enzymes, especially SGOT, as well as bilirubin, have been reported to be associated with PLATINOL administration at the recommended doses.

Other Events

Cardiac abnormalities, hiccups, elevated serum amylase, rash, alopecia, malaise, asthenia, and dehydration have been reported.

Local soft tissue toxicity has been reported following extravasation of PLATINOL. Severity of the local tissue toxicity appears to be related to the concentration of the PLATINOL solution. Infusion of solutions with a PLATINOL concentration greater than 0.5 mg/mL may result in tissue cellulitis, fibrosis, necrosis, pain, edema, and erythema.