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Letter to the editors

Inefficiency of early prophylactic hemodialysis in *cis*-platinum overdose

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Sir,

Platinum complexes can induce nephrotoxicity, as other heavy metals do [4]. Following a cisplatin (CDDP) overdose (200 mg/m^2 or 6.4 mg/kg in 8 h), we performed hemodialysis 4 h after the end of the CDDP infusion, with the aim of limiting nephrotoxicity and bone marrow depression [1].

The patient, a 41-year-old nurse suffering from stage III [6] primary ovarian carcinoma, was transferred to our Intensive Care Unit (ICU) for CDDP overdose administered on day 5 of the first course of polychemotherapy. On day 1 she had received doxorubicin (25 mg/m^2) and teniposide (35 mg/m^2). On days 2–4 the treatment consisted in cyclophosphamide (200 mg/m^2) and 5-fluorouracil (350 mg/m^2). On day 5 (19. 10. 84) a 100-mg/m^2 CDDP infusion was started. During the next 5 h 1000 ml 5% dextrose was administered. Six hours after the beginning of this CDDP infusion the patient inadvertently received a new dose of CDDP (100 mg/m^2). The onset of nausea, vomiting, and diarrhea 1 h after the end of this second dose led to discovery of the error. Thus, i.v. treatment with 25% mannitol and 5% dextrose was immediately initiated, and the patient was transferred to the ICU. She complained of nausea, thirst, a metallic taste in her mouth, and headache. Four hours after the end of the second CDDP dose hemodialysis was initiated. Despite this treatment, which was associated with osmotic polyuria (mannitol), acute renal failure (ARF), metabolic acidosis, and febrile bone marrow aplasia (Table 1) occurred 5 days after CDDP toxification. The patient was treated with three sessions of hemodialysis, amikacin, cefotaxin, and platelet transfusions. On 4. 11. 1984, ARF and pancytopenia had resolved; the patient was discharged from the ICU in good condition. Two months later, during the second course of chemotherapy (CDDP: 50 mg/m^2), asymptomatic myelosuppression was observed without ARF.

Since platinum nephrotoxicity is dose-dependent [4], and in view of the high risks of ARF [1] and bone marrow aplasia [1] and of the biphasic plasma clearance of CDDP [4, 5], we decided to perform 'early prophylactic' hemodialysis. A further reason for this treatment was the poor prognosis of patients suffering from multiple organ system failure [2]. The inability of hemodialysis to prevent ARF in our patient is clearly explained by its failure to remove CDDP (Table 1). The kinetics demonstrate that CDDP plasma clearance is biphasic: there is a rapid initial phase (half-life: 45 min) followed by a slow decay period with a half-life of 65 h. This second phase is due to the high binding (65%–90%) of CDDP to plasma proteins [4, 5]. Despite the fact the plasma protein binding increases with time, the

Table 1. Partial laboratory data and plasma platinum concentrations

	18. 10. 84	*	19. 10. 84	21. 10. 84	24. 10. 84	4. 11. 84
Hours after second dose of CDDP		4	8 After HD[a]			
BUN (mmol/l)	1.9	2.3	3	21.5	41.75	5.2
Creatinine (μmol/l)	72	100		172	390	108
Carbon dioxide (mmol/l)	23	23	20	25	9	26
Hb (g/100 ml)	13.3	13.3		11.5	9.9	9.6
WBC X 10^9/l	7.2	8.9		7.6	0.4	7.8
Platelets X 10^9/l	242	278		170	45	143
Total platinum (ugPt/ml) [3]		4.21	4.08	1.91		

* Cisplatin overdose
[a] HD, hemodialysis

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ineffectiveness of hemodialysis in our patient suggests that CDDP was completely protein-bound as little as 4 h after the second infusion.

We confirm that hemodialysis is not effective in removing CDDP administered 4 h sooner. This technique cannot be recommended in acute CDDP toxification, considering the delay between diagnosis and the beginning of extracorporeal circulation; therefore plasma exchange, which removes plasma proteins, might be considered.

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