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Oxaliplatin Pharmacokinetics on Hemodialysis in a Patient with Diffuse Large B Cell Lymphoma

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Introduction

- Oxaliplatin is widely used in diverse anticancer regimens. Elimination occurs mainly by the kidneys, clearance strongly correlates with GFR.
- CKD and ESRD patients are especially prone to accumulation and drug-related toxicity.
- The role of extra-corporal RRT in oxaliplatin clearance is not clear. Pharmacokinetic data is limited to single HD cycles. No data is available on the absolute clearance of oxaliplatin by HD.
- HD dose as a parameter of oxaliplatin clearance has not been studied so far.

Methods

- Sample collection included spent dialysate, ultrafiltrate, serum before and after HD as well as pre- and post-dialyzer after 15, 0, 120, 180 and 240 min of HD.
- Total serum platinum concentrations were quantified by inductively coupled plasma mass spectrometry.
- HD was performed as high-flux bicarbonate dialysis (GENIUS® dialysis system, F60S polysulfone high-flux dialyzer, both Fresenius Medical Care, Bad Homburg, Germany; blood flow (Q_b) and dialysate flow (Q_d) rates 250 mL/min).
- Dialyzer clearance (CL_{dial}) was calculated from pre- (C_a) and postfilter (C_v) serum drug concentrations: CL_{dial} = plasma perfusion rate (Q_b × (1–hematocrit)) × extraction ratio ((C_a–C_v)/C_a).

Case report

- A 61-year-old anuric HD patient was referred to our tertiary care hospital in April 2014 with cervical, supraclavicular, and retroperitoneal lymphadenopathy.
- Histology revealed follicular lymphoma grade 3A, stage IIIA.
- Due to additional cardiovascular comorbidity, the patient received six courses of rituximab and bendamustine, which led to partial remission as best response.
- Despite rituximab maintenance, clinical relapse with recurrence in the known localisations plus splenic infiltration and histopathological transformation to diffuse large B cell lymphoma occurred in September 2015.
- Second-line treatment with rituximab, gemcitabine, and oxaliplatin was chosen.
- Because of ESRD secondary to polycystic kidney disease requiring regular home HD since 2002 and lack of evidence for long-term oxaliplatin clearance, dosage of oxaliplatin was reduced to 50 mg/m² (50% reduction, Fig. 1).

Disclaimer

- Informed consent was obtained from the patient.
- This work has meanwhile been published in Annals of Hematology: *Ann Hematol* 2016;95: 649-650.

Results

1 CXT course protocol

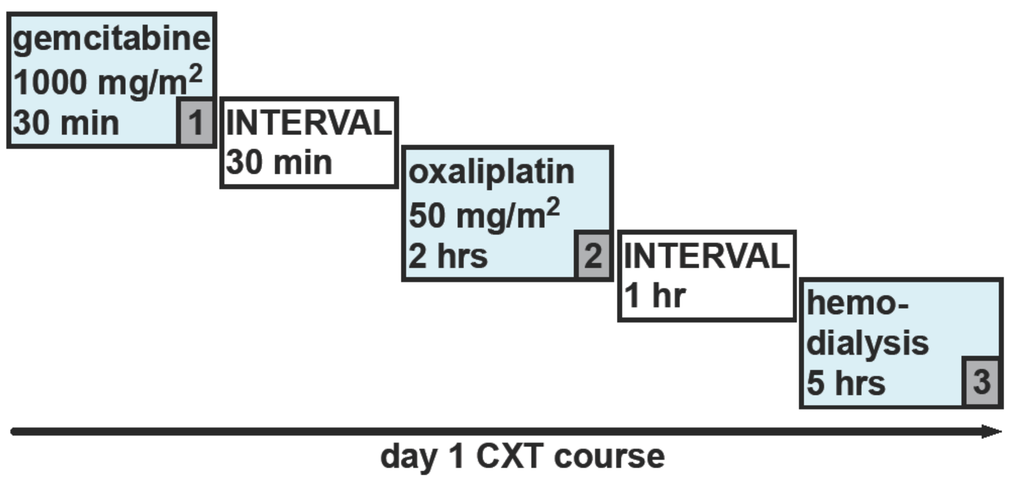

Fig. 1 CXT course protocol with 50% dose reduction.

2 Myelotoxic reaction in response to CXT & HD

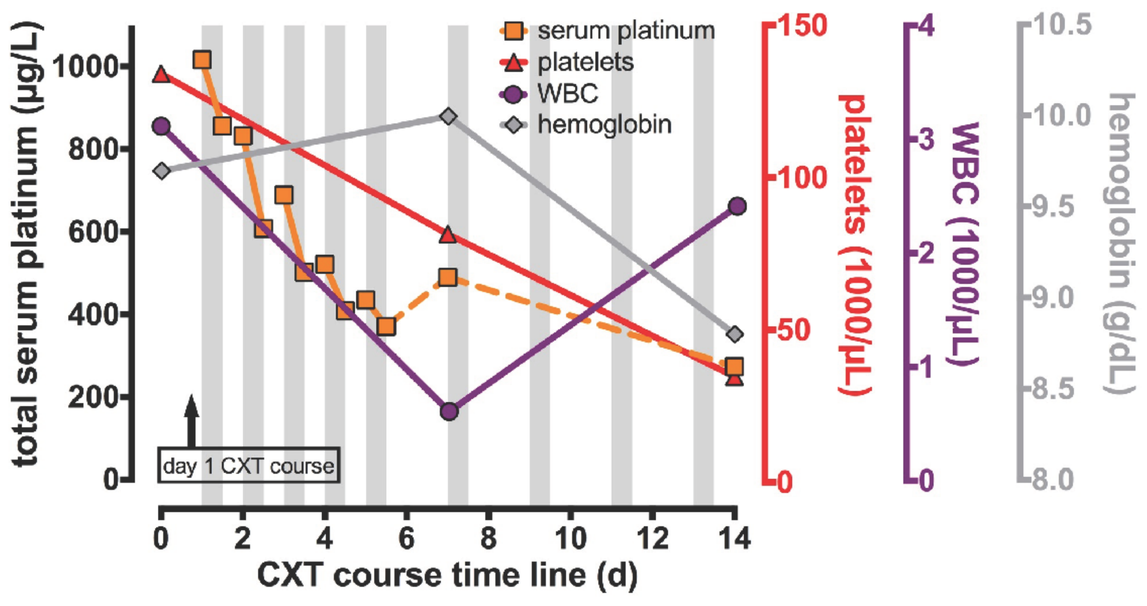

Fig. 2 Adequate myelotoxic reaction (platelets, WBC, and hemoglobin) in response to dosage-reduced oxaliplatin administration and timing of HD treatment (depicted by gray areas).

3 Serum platinum kinetics in two HD cycles

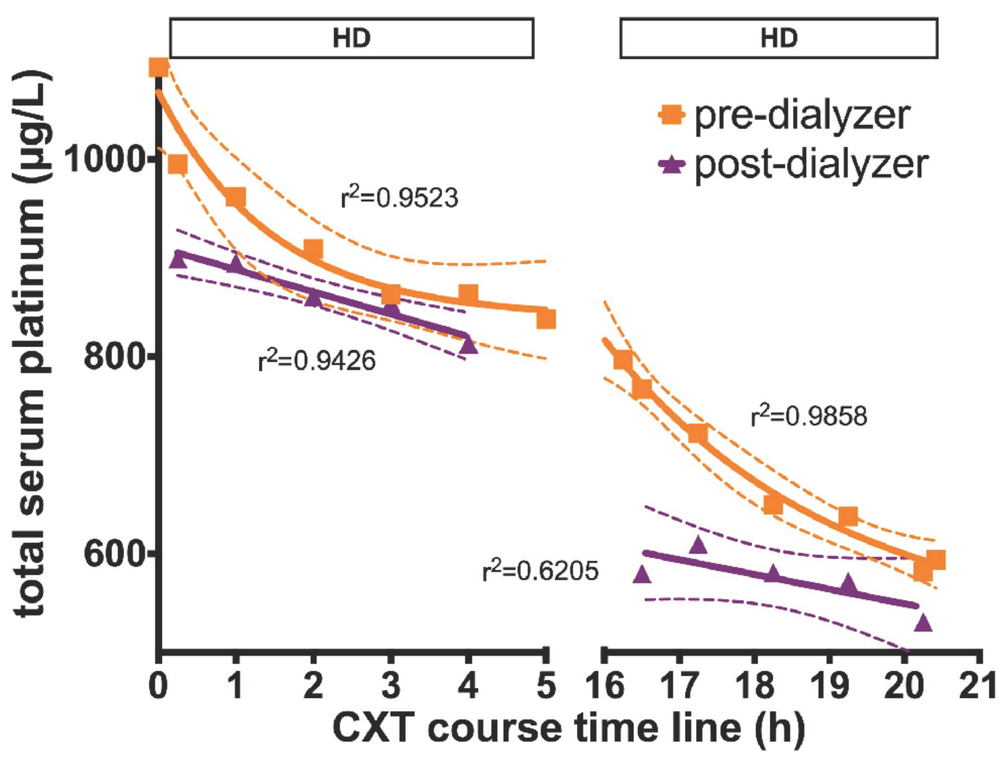

Fig. 3 Clearance of pre-dialyzer serum platinum on days 1 and 2 after oxaliplatin administration (50 mg/m²) follows an exponential decay relationship. Post-dialyzer serum platinum is best described linearly. Total amount of platinum eliminated by 5 h of HD: 153 µg (ultrafiltrate) + 4815 µg (spent dialysate) = 4968 µg. Calculated dialyzer clearance Cl_{dial} = 28.43 mL/min.

Conclusion

- Similarly to patients with normal GFR, daily dialysis over five consecutive days was able to reduce serum platinum below 50% of C_{max}.
- Oxaliplatin clearance by daily HD efficiently reduces platinum levels to non-toxic levels (C_{min} 435 µg/L after 5 days and 273 µg/L after 14 days), which should be incorporated into dose adjustment concepts.
- Showing a partial response after 3 cycles, we can also conclude antitumoral therapeutic effectiveness.

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