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LETTER TO THE EDITOR

Oxaliplatin overdosage successfully recovered with mild toxicities

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To the Editor

A 64-year-old woman diagnosed of metastatic colorectal cancer was being treated in our department with oxaliplatin 130 mg/m^2 on Day 1 and capecitabine 1000 mg/m^2 bid on Days 1 to 14 every three weeks. Oxaliplatin infusion has been prolonged up to six hours after the first cycle due to pharyngolaryngeal dysesthesia. At the third cycle, a typographic error occurred, and mistakenly 636 mg of oxaliplatin were prescribed, instead of the correct dose (236 mg). This medical error was not identified by the oncology nurses responsible for preparing and administering the treatment. After 240 minutes of infusion she complained of mild pharyngolaryngeal dysesthesia and the mistake was identified in the medical file. Oxaliplatin infusion was immediately stopped and it was calculated that 500 mg had been administered (275 mg/m^2 approximately). Inpatient hyperhydration, with normal saline and furosemide to obtain a diuresis rate of 100 mL/h, and preventive measures for mucositis and diarrhoea were started, and capecitabine schedule was not begun. Vital constants were closely monitored and blood and urinary samples were obtained daily, to assess toxicities. She experienced grade 2 peripheral neurotoxicity for five days, grade 2 diarrhoea resolved in 36 hours, grade 2 thrombocytopenia (72 000/μL), grade 1 neutropenia (1900/μL) and grade 2 asthenia. Eight days later the patient was discharged asymptomatic and ambulatory follow-up was planned. Twenty-three days after the overdose, and fully recovered from any previous side effect, she received the fourth cycle of oxaliplatin and capecitabine without unexpected consequences.

Oxaliplatin is a third generation platinum compound approved for the treatment of colorectal carcinoma in combination with fluoropyrimidines [1]. In the early phase I trials, 135 mg/m^2 was the recommended dose in monotherapy [2]. Sensory neuropathy was the dose-limiting toxicity and no haematologic toxicities were seen at doses up to 200 mg/m^2. Oxaliplatin has a very short elimination half-life (16–27 min), when its concentration in the plasma ultrafiltrate is measured [3]. There is no known antidote and only monitoring and supportive care are recommended in case of overdoses [1]. Another five unpublished cases of oxaliplatin overdoses (doses between 360 and 700 mg) are registered in the last updated information page of the FDA [1]. One patient (500 mg) died of acute respiratory failure and bradycardia probably due to an anaphylactic reaction, but the other four completely recovered without severe toxicities, except for one case with uncomplicated grade 4 thrombocytopenia.

Several oxaliplatin-based combination regimens have been explored, most of them with oxaliplatin doses ranging from 85 to 130 mg/m^2 every two or three weeks. In recent years proofs of activity of oxaliplatin in curable tumours, such as high grade lymphomas and germ cell tumours, have been reported [4,5]. Today, we know that prolongation of infusion time for oxaliplatin may mitigate acute toxicities, and it has been suggested that acute and cumulative neuropathy and other toxicities may be prevented using calcium and magnesium supplementations [6]. Based on our observation and other overdose cases described, we think that there may be

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a role for a prospective evaluation of higher doses of oxaliplatin with all these preventive measures, for the treatment of curable tumours with a well known dose-depending efficacy.

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