Biliary Excretion of Platinum in a Patient Treated with *cis*-Dichlorodiammineplatinum (II)

M. D. SHELLEY, R. G. FISH,* AND M. ADAMS
South Wales Radiotherapy and Oncology Service, Velindre Hospital, Cardiff, Great Britain
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Biliary excretion of platinum was measured in a patient receiving an intravenous infusion of *cis*-dichlorodiammineplatinum (II). Over a 3-day period, less than 1% of the administered platinum was detected in the bile, and 47% appeared in the urine, indicating that biliary excretion is a minor route of elimination.

It has been proposed that in humans the anticancer drug *cis*-dichlorodiammineplatinum (II) (CDDP) undergoes enterohepatic recycling and that this accounts for the secondary platinum peaks often observed in plasma after drug therapy (6). In animals, less than 2% of the administered platinum is eliminated via the biliary system over a 24-h period (2). Information on the biliary excretion of platinum in humans is limited to a report on one patient who had a permanent T-tube inserted (1). Intermittent sampling of bile from this patient showed that the platinum concentration reached 8% of the highest level in plasma but was not detectable 4 h after termination of the CDDP infusion. We report on the biliary excretion of platinum in a patient from whom it was possible to collect bile continuously via a cholecystostomy.

Biliary excretion was examined in a 56-year-old female who had a history of abdominal pain and recent jaundice. Laparotomy and histological examination confirmed a papillary adenocarcinoma of the ovary which was infiltrating the gallbladder and right lobe of the liver. The common bile duct and hepatic duct were also infiltrated, with extension into the intrahepatic radicles. An internal bypass of the biliary tract was not feasible, and external drainage of the gallbladder was accomplished. At 4 weeks after the operation, a 6-h intravenous infusion of CDDP (80 mg/m²) was administered. Before drug therapy, serum urea, creatinine, and electrolyte levels were within the normal range, but bilirubin (45 μmol/liter) and γ-glutamyl transferase (205 IU/liter) levels were elevated. Twenty-four hours before and after CDDP infusion, 2 liters of 5% dextrose–normal saline and normal saline, respectively, were administered intravenously. A bolus of mannitol (12.5 g) was given immediately before CDDP. The cytotoxic drug was administered in 2 liters of normal saline containing 25 g of mannitol. Plasma samples and all urine and bile samples were collected for 3 days and stored at −20°C.

All samples were analyzed for platinum by atomic absorption spectrophotometry (3). The absorbance was linearly related to the platinum concentration in the range of 0.05 to 1 μg/ml. The assay precision (standard error of the mean) was 4.6% at a concentration of 0.05 μg/ml, 1.9% at 0.1 μg/ml, and 0.6% at 1 μg/ml. Bile samples were evaluated with preinfusion bile to overcome any matrix interference.

The maximum bile flow (12 ml/h) coincided with the peak concentration of platinum in the bile (0.6 μg/ml) which reached 30% of the corresponding platinum level in plasma (1.9 μg/ml) at the end of the drug infusion (Fig. 1). After 3 days, platinum levels in bile were below detection, and the total volume of bile collected was 0.5 liters. The cumulative amounts of platinum excreted over 72 h via the renal and biliary systems were 47.0 and 0.21% of the administered platinum, respectively (Fig. 1). These results suggest that biliary excretion is a minor route of elimination in this patient, although subjects with normal biliary function (5) may excrete greater amounts of platinum in bile.

In this patient, insufficient platinum was excreted in the bile (40 μg in the first 9 h) to account for any secondary increases in the platinum concentration in plasma. Whether enterohepatic recycling or other mechanisms, such as a rapid release from tissue compartments (4) or hemodynamic changes, or both account for this phenomenon remains to be established.

LITERATURE CITED


* Corresponding author.

