PHARMACOKINETICS OF CISPLATIN DURING INTRAPERITONEAL HYPERTHERMIC CHEMOTHERAPY PERFUSION (IHCP) IN PATIENTS WITH PERITONEAL CARCINOMATOSIS

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Background. Intraperitoneal chemotherapy, mainly when performed after cytoreductive surgery, is considered potentially curative for the treatment of solid tumors with spread to the peritoneal surface. Intraperitoneal treatment can be intraoperatively performed just after a complete surgical resection of peritoneal tumor. However, little is known regarding the pharmacokinetics of cisplatin during intraperitoneal hypertermic perfusion (IHCP). The objective of this study was to determine the pharmacokinetics profile of cisplatin, administered by IHCP technique to patients with peritoneal carcinomatosis. **Methods**. After surgical cytoreduction, 12 patients were given cisplatin 100 mg/m^2 (CDDP) in saline solution during 50 min of perfusion (inflow temperature, 41.5°C; flow rate, 800 ml/min; use of a closed circuit). We determined total cisplatin concentration in perfusate, plasma and urine samples obtained during / after perfusion with Atomic Absorption Spectrometer. The pharmacokinetic parameters ($t_{1/2}$, AUC, C_{max}, T_{max},) of CDDP were computed using a standard non-compartmental, method. **Results.** Large interindividual variability of the pharmacokinetic parameters occurred. The maximum CDDP concentration in plasma was reached after 46.5±10.50 min (T_{max}) the beginning of administration; it was 2.8±0.92 µg/ml (C_{max}) and a mean half-life of the elimination phase ($t_{1/2}$) was of 15.1.± 9.68 hours. The mean areas under the curve (AUC $_{0\text{-}60}$) for perfusate and plasma were, respectively, 1848.3±315.96 and 110.3 ±30.29 µg.min/ml; the mean areas under the curve (AUC $_{0\text{-}360}$) for plasma was 637.6±265.62 µg.min/ml. The mean AUC peritoneal fluid / plasma ratio was 16.7±5.10. At 24 hours, the urinary CDDP recovery was 5.30 ± 4.6 % of administered dose and 62.2±19.20 % of cisplatin remaining in the body after the peritoneum was emptied. **Conclusion**. When selecting antiblastic agents to be administered intraperitoneally, it is important to bear in mind that a low lipoliphility and a high molecular weight are the ideal drug characteristics. Drugs with these features, such as cisplatin, allow a favourable ratio to be achieved between peritoneal and plasma concentrations, due to the reduced tendency to diffuse through the plasma-peritoneal barrier, even after extensive removal of the peritoneum. The results of this study showed that a high proportion of the cisplatin dose remaining in the peritoneal cavity and was absorbed by target tumor cells with evidenced pharmacological advantages: higher and direct drug exposure of the tumor, limited systemic absorption and mild toxicity. Controlled studies to evaluate clearly the benefit of this therapeutic approach, and standardized criteria will be necessary.