

Tubular Dysfunction after Peritonectomy and Chemohyperthermic Treatment with Cisplatin

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Abstract. Peritoneal carcinomatosis has always been regarded as a contraindication in traditional cancer surgery treatment; however, good results have been reported by using new combined medical-surgical loco-regional techniques. Peritonectomy and chemohyperthermic perfusion with cisplatin (CIIP) seem to play a central role in obtaining a better survival rate than with the traditional procedures, even though there is a cisplatin nephrotoxic effect. The aim of this study was to investigate entity and type of renal injury after CIIP. Forty-two patients (12 males and 30 females) with recurrent or primary peritoneal carcinomatosis who underwent peritonectomy and cytoreductive surgery with hyperthermic intraperitoneal chemotherapy with cisplatin were enrolled. A significant worsening in renal function was observed on the third post-operative day and this condition then persisted for three months. A reduction in estimated-Glomerular Filtration Rate (e-GFR) and an alteration in the albumin:creatinine ratio proved tubular injury. On the third post-operative day after cisplatin administration, a high toxicity peak was found following platinum free fraction excretion. Proximal tubular injury was confirmed even at the three month analysis. A significant correlation between the total protein reduction rate and the decrease in renal function was established. In relation to that, the platinum free fraction could increase because of a binding protein shortage and the nephrotoxic effect could be enhanced due to platinum accumulation within the post-operative period. This finding suggests that the higher the protein reduction is, the lower the e-GFR determination is at three months.

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It is quite well-established that peritoneal carcinomatosis occurrence represents a contraindication in surgical malignancy treatment. Most authors have observed a survival rate of lower than three months in patients affected by peritoneal carcinomatosis, and rarely a response to chemotherapy or a one-year survival rate has been reported (1-3). Anyway, in this severe condition, where peritoneal metastatic involvement is the only expression of neoplastic disease, a loco-regional therapy should be considered (4). Peritonectomy and hyperthermic antineoplastic perfusion represent an association of a surgical procedure and a nephrotoxic drug administration of cis-Diamminodichloroplatinum (CDDP) during intra-abdominal hyperthermic continuous perfusion (5-6). CDDP has demonstrated good antineoplastic activity against colo-rectal, stomach, ovarian, endometrial and testicular cancer (7-8). Once cisplatin enters a cell, its chloride ligands are replaced by water molecules generating a positively charged aquated species that can react with nucleophilic sites on intracellular macromolecules to form protein, RNA and DNA adducts. The reaction with DNA yields monofunctional adducts, intra- and inter-strand crosslinks with the platinum atom (8-9).

Patients and Methods

In 2005, 42 patients (12 males and 30 females) who underwent a peritonectomy in association with hyperthermic CDDP antineoplastic perfusion were enrolled in this study. The population baseline characteristics are described as follows: mean age of 59.8±9.9, peritoneal carcinomatosis due to appendix cancer in five cases, colorectal cancer in 16 patients, ovarian cancer in 13, gastric in four, three patients had an endometrial cancer and one mesothelioma. After surgical removal of the carcinomatosis, a solution of antineoplastic agents including CDDP at 25 mg/m²/l in gastrointestinal cancer or at 43 mg/m²/l in ovarian and endometrial cancer in association with mitomycin/doxorubicine, 3.3 mg/m² and of 15 mg/l, respectively, was injected into the abdomen. A stable temperature of 42-43°C was maintained by the Performer LRT® (RAND, Medolla [MO], Italy) acting as an extracorporeal circulating pump, draining and aspirating the injected solution

