Evaluation of Quality of Life of Patients Submitted to Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Carcinosis of Gastrointestinal and Ovarian Origin and Identification of Factors Influencing Outcome

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Abstract. Background: The prognosis of patients with peritoneal tumors has been improved by the association of cytoreductive surgery with hyperthermic intraperitoneal chemotherapy, though still with an unclear impact on patients’ quality of life. The purpose of our study was to evaluate the quality of life in 18 cases submitted to cytoreductive surgery and hyperthermic intraperitoneal chemotherapy and particularly to identify the factors that influence it. Patients and Methods: Quality of life was evaluated using the functional assessment of cancer therapy; the results were correlated with 25 parameters. Results: The study demonstrated that the patients’ quality of life was not modified by treatment with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy; the dose of mitomycin C, the site of the primary tumor, gastrointestinal, renal and neurological toxicity, adjuvant chemotherapy, the patients’ age and leukopenia were factors that influenced the quality of life. Conclusion: Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy allows conservation of preoperative quality of life.

The introduction into clinical practice of a combined treatment of cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) has had a major impact on the prognosis of peritoneal carcinosis. Such an approach has improved the prognosis of patients with peritoneal tumors, not only of secondary but also of primary (1). Being an extremely complex procedure, HIPEC causes some morbility – in the series with more than 50 patients, it ranged from 12 to 35% (2), and its impact on the quality of life (QOL) is still not completely clear. The purpose of our study was to evaluate the QOL in a group of patients submitted to CRS plus HIPEC and particularly to identify the factors that have statistical influence on it.

Patients and Methods

In the period of September 2003 to November 2007, 17 patients (4 males, 13 females), with a mean age of 56 years (range, 30-77) were enrolled. Seven had colon carcinoma, 5 gastric cancer and 5 ovarian cancer. In one patient with colon cancer, owing to a local recurrence, the treatment was repeated after 15 months, so that the study is based on 18 cases.

All the patients were submitted to CRS + HIPEC for the presence of peritoneal carcinomatosis, except for four patients affected by gastric cancer, in two of whom the indication for HIPEC was made on the basis of a positive peritoneal cytology, while in the other two the intent was prophylactic since intraoperative staging documented a T3 and a T4 tumor, both histologically of diffuse type.

Four patients, affected by ovarian cancer, were subjected to neoadjuvant chemotherapy with carboplatin and taxol. All the patients were submitted to adjuvant chemotherapy.

Intraoperative staging of the peritoneal carcinomatosis was carried out according to the peritoneal cancer index (PCI) (3). CRS was performed according to the technique described by Sugarbaker (3). All the patients were subjected to HIPEC with the closed-abdomen technique, which foresees the positioning of five abdominal drainages, two inflows on the right (subhepatic sheath and pelvic pouch) and three outflows on the left (subhepatic, left subdiaphragmatic, shallow pelvis) and of two thermometric probes...
(upper and lower abdomen), temporary suture of the skin and perfusion with a preheated solution for peritoneal dialysis. Once a peritoneal temperature of 41-43°C is reached, the drugs are administered according to the following schedule: i) cisplatin (CDDP) at 25 mg/m²/l, plus mitomycin C (MMC) at 3.3 mg/m²/l, for 60 min for the treatment of gastric and colon carcinomatosis; ii) CDDP at 43 mg/l, and doxorubicin at 15.25 mg/l, for 90 min for ovarian carcinomatosis.

The QOL was evaluated in the preoperative period and at 3 and 6 months after surgery using the functional assessment of cancer therapy (FACT) (4-6). It comprises four subscales: physical well-being (PWB), social/family well-being (SWB), emotional well-being (EWB), and functional well-being (FWB). Patients are given a questionnaire composed of 27 questions attributing a variable score to the answers from 0 to 4. The PWB, SWB, EWB, and FWB subscales and the FACT-G total have a lowest possible score of 0. The highest possible score is 28 for the PWB, SWB, and FWB subscales; 24 for the EWB subscale. The higher the value of the SWB and PWB SCORE the better the QOL; the QOL will be better with lower values of the PWB and EWB scores. The results of the evaluation were correlated statistically with the following parameters: site of the primary tumour; sex; age; previous surgical operations; preoperative chemotherapy; PCI; number of surgical procedures; completeness of cytoreduction (CC) score; MMC, CDDP and doxorubicin dose; duration of the surgery; postoperative anemia, leukopenia, and fever; intestinal fistulas; anastomotic dehiscence; infections; postoperative hospitalization period; adjuvant chemotherapy; and gastrointestinal, renal, pulmonary, cardiac and neurological toxicity.

Statistical analysis was carried out by calculating the non-parametric correlation coefficient. P-values <0.05 were considered statistically significant.

**Results**

The mean duration of the CRS+HIPEC was 562 min (range, 430-720 min). The mean PCI value, considering that the cases without gross disease were assigned a score of 0, was 9.66 (range, 0-27). The mean CC score was 0.22 (range, 0-1). Morbidity was 27.7% (4 of grade 1 and 1 of grade 2). There were no severe complications and no perioperative mortality.

The mean FACT scores preoperatively and at 3 and 6 months were: PWB: 7.56, 12.62 and 8.43, respectively; EWB: 11.31, 12.37 and 11.87, respectively; SWB: 15.50, 16.25 and 16.06, respectively; and FWB: 17.12, 10.50 and 16.37, respectively. Statistical evaluation showed that the PWB (p<0.02) and FWB (p<0.05) assessment gave basal values indicative of a good QOL which worsened at 3 months from the surgery, to return at 6 months from the therapy to preoperative values. There are no statistically significant variations in EWB score (p<0.04). SWB was not influenced by the treatment (p<0.05).

Moreover, statistical analysis demonstrated an inversely proportional correlation between MMC dose and PWB score at 3 months (p<0.05); between primary tumor site and EWB score at 3 months (p<0.05); between FWB score, MMC dose (p<0.01) and adjuvant chemotherapy (p<0.001) at 3 months; and between EWB score, gastrointestinal toxicity (p<0.05) and adjuvant chemotherapy (p<0.001) at 6 months (Table I). In contrast, there was a directly proportional correlation between CC score and PWB score at 6 months (p<0.001), between basal SWB score, patient age (p<0.01) and neurological toxicity (p<0.001); between FACT-familial score, patient age (p<0.001), leukopenia (p<0.01) and adjuvant chemotherapy (p<0.01) at 3 months; between SWB score, patient age (p<0.001), MMC dose (p<0.01), leukopenia (p<0.01) and renal toxicity (p<0.01) at 6 months; and between CC score and SWB score (p<0.01) at 6 months (Table II).
Discussion

The association of CRS with HIPEC, as clearly shown by scientific literature, improves the survival of patients affected by peritoneal carcinomatosis of gastrointestinal (7-10) and, perhaps, of ovarian origin (11), with an acceptable incidence of morbidity and mortality (12-16). Among the various aspects still debated is that the impact on the QOL of patients submitted to such treatment has not been dealt with in a satisfactory manner. However, it has been demonstrated that the QOL varies particularly in the first 6 months, without further modifications in the first year (17). In light of such considerations, we wanted to evaluate the behavior of the QOL in a group of patients submitted to such treatment and particularly to evaluate what factors significantly interfere.

With this aim, we used the FACT, a questionnaire already applied in the evaluation of QOL in numerous pathologies (6). Our study demonstrated that the QOL of patients submitted to CRS plus HIPEC, certainly satisfactory before the intervention, was not significantly modified by the treatment. In fact, after a brief period (3 months from the surgery), the patients were able to lead a life similar to that they had had before the intervention. Statistical evaluation demonstrated good basal values for PWB (p<0.02) and FWB (p<0.05) that worsened at 3 months and then returned to initial values at 6 months from the surgery. The EWB score did not undergo significant variations (p<0.4), and SWB score was not affected by the treatment (p<0.05).

The second endpoint of the study was to evaluate the factors that influence the QOL of the patient in a positive or negative manner. Statistical analysis demonstrated that the MMC dose negatively influenced PWB score at 3 months (p<0.05), an effect probably linked to the toxicity of the drug. Gastric and colonic sites of the primary tumor, probably due to the greater aggressiveness of the disease and the higher PCI value (which necessitates a more demolitive surgery), worsened the EWB score at 3 months (p<0.05); the EWB score at 6 months was impaired by gastrointestinal toxicity (p<0.05) and particularly by adjuvant chemotherapy (p<0.001), probably in relation to the need to subject the patient to further medical therapy. MMC dose (p<0.01) and adjuvant chemotherapy (p<0.001) were worse for FWB score at 3 months, probably in relation to the side-effects of the antineoplastic therapy.

In contrast, low CC values corresponded to an improvement in PWB score at 6 months (p<0.001). The CC score being the parameter that evaluated the radicality of the cytoreduction, it seems clear that less residual disease corresponds with a better QOL of the patient. Administration of adjuvant chemotherapy (p<0.01) and the appearance of postoperative leukopenia (p<0.01) resulted in an improvement in the SWB score at 3 months, whereas age (p<0.001), high MMC doses (p<0.01), renal toxicity (p<0.01) and postoperative leukopenia (p<0.01) were correlated with an improvement in the SWB score at 6 months. Such positive variations determined by factors that should negatively influence the QOL, together with evidence that the FACT-familial score did not undergo statistically significant variations throughout the study could, in our opinion, be explained by the fact that providing the patient and family with good information allows them to accept an aggressive treatment with the eventual correlated complications, thereby inducing an improvement in familial relations.

In conclusion, we affirm that our study, also in accord with the few data of the literature (18, 19), has demonstrated that CRS and HIPEC, burdened by a morbidity of 27.7%, after 6 months from the surgery allows the same QOL levels of the preoperative period to be maintained, which, to enroll a patient for such an invasive treatment, must, by necessity, be rather high.

References


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