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Laparoscopic intraperitoneal hyperthermic chemotherapy for palliation of debilitating malignant ascites

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Abstract

Aim: To report the use of laparoscopic Intraperitoneal Hyperthermic Chemotherapy (LIPHC) in the treatment of malignant ascites.
Methods: From September 2001 to December 2003, 14 patients between the age of 56 and 78 years were treated. Ascites was from gastric cancer (5 cases), colorectal cancer (3 cases), ovarian cancer (3 cases), breast cancer (2 cases) and peritoneal mesothelioma (1 case). The LIPHC was carried out at 42 °C for 90 min with 1.5% dextrose solution as a carrier. Chemotherapy was cisplatin and doxorubicin or mitomycin depending on the type of primary tumor. The drains were left in situ after surgery and removed when perfuse drainage ceased.
Results: Ascites was controlled in all the treated cases. A CT scan performed in follow-up showed a small, clinically undetectable, fluid accumulation in the pelvis of one patient.
Conclusions: This method resulted in benefit for those peritoneal carcinomatosis patients with debilitating malignant ascites who were excluded from cytoreductive surgery. Proficiency in laparoscopic staging procedures and experience in the management of carcinomatosis and intraperitoneal hyperthermic chemotherapy (IPHC) are required for the success of the procedure.

Keywords: Carcinomatosis; Laparoscopy; Hyperthermia; Cisplatin; Doxorubicin; Intraperitoneal chemotherapy

Introduction

Laparoscopy is now regarded as an effective tool for diagnosing and staging malignancy.[1] Benefits for patients include less pain and shorter hospitalization as compared to exploratory laparotomy. Studies have shown that the use of laparoscopy significantly decreases the incidence of unnecessary laparotomy for unresectable diseases in up to 67% of patients with abdominal malignancy.[2] By minimizing surgical trauma and time for postoperative recovery, the procedure facilitates postoperative therapy for unresectable intra-abdominal malignancies. The cumulative benefits laparoscopy offers necessitates the call for new studies in order to expand the indications for its safe and effective treatment of patients suffering from intra-abdominal malignancies.

Peritoneal carcinomatosis of colorectal origin has a dismal prognosis with a median survival of less than 6 months.[3] Recently, a potentially curative treatment has been proposed using cytoreductive surgery combined with intraperitoneal hyperthermic chemotherapy (IPHC). Although this treatment modality has been viewed with much skepticism for many years, approximately one-third of treated patients have been shown to be long-term survivors. Several phase II studies and one phase III study of cytoreductive surgery combined with IPHC for carcinomatosis of a colorectal origin have shown improved median survival.[4,5] The patients who survive longer than 5 years are probably cured. The procedure is associated with a high morbidity and mortality so the potential improvement in survival has to be balanced. The resection of all tumor deposits greater than 1–2 mm diameter is mandatory before using IPHC with curative content. Appropriate selection of suitable patients for definitive treatment is necessary.

Although some patients may benefit from cytoreductive surgery plus IPHC with long-term survival, others are not candidates for extensive combined interventions. Patients

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with debilitating ascites may have profound need for symptom relief but cannot be considered for major surgery. Laparoscopy may be used not only to exclude these patients from a curative approach but also to definitively palliate the malignant ascites.[6] The purpose of this report is to review a personal experience in the use of laparoscopic surgery to assist in the delivery of IPHC and definitively palliate the symptoms of malignant ascites.

Methods

A Hasson trocar was placed in the right or left pararectal area through a 1-cm incision taking care not to contaminate the wall with the ascitic fluid. The ascites was completely suctioned out of the peritoneal cavity through the trocar prior to insufflating with CO_2. After placing the 30° 5-mm scope under direct vision, a second 5-mm trocar was placed in the iliac fossa contralateral to the scope. If necessary, viscerolysis was performed to free the abdominal cavity of cancerous adhesions. If extended viscerolysis was considered dangerous, it was only pursued to ensure communication between all abdominal quadrants so that the hyperthermic chemotherapy agent could flow through the inflow tubes and drains to reach all the peritoneal surfaces. Then, three additional 5-mm trocars were sequentially placed on the right and left side into the free iliac fossa (Fig. 1).

A 5-mm grasper was passed from the peritoneal cavity out through the 5-mm trocar in order to place closed-suction drains into the pelvic cavity and into the right and left subdiaphragmatic space. These three suctioning drains are connected together to provide a single outflow. The 5-mm trocars were removed and an infusion trocar was placed directly through the 10-mm trocar site where the camera had been inserted. To make the peritoneal space watertight, all drains were secured with a purse-string suture to the skin and connected to the perfusion machine which should be set at an inflow temperature of 43–44 °C (Fig. 2). An average temperature of 42 °C in the whole peritoneal cavity was sought.

The temperature was measured by means of two probes. One was at the inflow site and the other at the junction between the three outflow drains. The patient's body temperature was monitored by means of three probes: at the skin, in the external ear canal, and in the rectum or bladder. The mean duration of laparoscopic preparation was 45 min, with a range of 30–120 min depending on the extent of viscerolysis.

To allow the chemotherapy solution to distribute itself to the whole peritoneal surface, the operating table tilt is changed at 15-min intervals during perfusion as follows: (1) level, (2) Trendelenburg + left tilt, (3) Trendelenburg + right tilt, (4) level, (5) reverse Trendelenburg + left tilt, (6) reverse Trendelenburg + right tilt.

Perfusion lasted 90 min after which the chemotherapy agent was recovered and a lavage of 2000 cc of 1.5% dextrose was performed to remove residual chemotherapy. The drains were connected to gravity bags and were removed postoperatively after copious drainage ceased. After removing all drains, the patient was discharged from the hospital.

Chemotherapy

The hyperthermic intraperitoneal chemotherapy was cisplatin 50 mg/m^2 and doxorubicin 15 mg/m^2 for ascites from ovarian cancer, peritoneal mesothelioma or breast cancer. In ascites from rectal colon and stomach cancer mitomycin

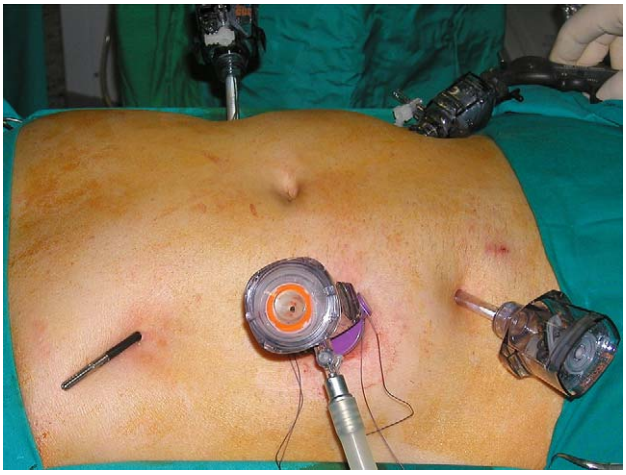

Figure 1. Five 5-mm trocars for viscerolysis and placement of three intraperitoneal drains.

Figure 2. Inflow catheter and drains secured with a purse-string suture at the skin.

12.5 mg/m^2 was used.[7] The volume of perfusate used was 2000 cc; it consisted of a peritoneal dialysis solution containing 1.5% dextrose. Fresh frozen plasma (1200 cc) was infused during perfusion. Furosemide was administered along with intravenous fluids to maintain a 400 cc/h diuresis.

Results

All the patients accepted and signed an informed consent prior to undergoing the procedure and were counseled about possible complications. From September 2001 to December 2003, 14 patients between the age of 56 and 78 years were treated with neoplastic ascites. The primary tumor was gastric cancer in 5 cases, colorectal cancer in 3 cases, ovarian cancer in 3 cases, breast cancer in 2 cases, and peritoneal mesothelioma in 1 case. The mean perfusion temperature, measured at the outflow site, was 40 °C. The patients' body temperature, measured by means of three thermometer probes, never exceeded 39.5 °C.

Neither mortality nor morbidity was observed in connection with the procedure. In all cases we observed a complete disappearance of the ascites. In one case a CT scan 1 year later showed a small, clinically undetectable, ascitic accumulation in the pelvis.

Four patients were lost to follow-up. Six patients are alive at this time and are included in the follow-up with the following survival times: 83, 673, 400, 66, 667, and 100 days. Four patients died of disease free from ascites. The average survival of the 10 patients available for follow-up is 203 days (range 21–667).

The longest survival times (673 and 667 days) were observed in the two breast cancer patients, whereas the shortest survival times (21, 67, 40, and 83 days) were observed in the cases of ascites from gastric cancer.

In two cases of concomitant neoplastic intestinal occlusion, a laparoscopic ileostomy was created prior to beginning the hyperthermic intraperitoneal chemotherapy.

Discussion

Generally accepted indications to perform laparoscopy in cancer patients is for staging.[8] However, laparoscopic intraperitoneal hyperthermic chemotherapy (LIPHC) may provide treatment benefits greater than conventional methods for treatment of malignant ascites which include diuretics, repeated paracenteses, and systemic chemotherapy. Although sometimes initially successful, these methods lose their efficacy over time.

The palliative treatment of ascites with intraperitoneal instillations of mitoxantrone has been successful but may only achieve an average decrease of ascites of $\geq$50%.[9] In a prior publication, Chang et al. treated seven patients with intra-abdominal malignancy by LIPHC.[10] Only two of these seven had debilitating malignant ascites, one from mesothelioma and the other from breast cancer. In both cases the ascites disappeared. Our experience differed from that of Chang for several reasons. First, all of our cases were accompanied by debilitating malignant ascites from carcinomatosis. The hyperthermic chemotherapy we used was cisplatin and doxorubicin or mitomycin at the same dosages used in IPHC after complete cytoreduction. Also, we did not perfuse chemotherapy through the trocars, but used videolaparoscopy to place three out-flow drains and a single in-flow catheter through the laparoscopic ports. In so doing we achieved a closed-loop irrigation enabling full contact between chemotherapy and cancer nodules. Finally, we left the drains in situ in the postoperative period. We believe that in the days following treatment reactive fluid is produced in the peritoneal cavity which, if not drained, could jeopardize the outcome of therapy or lead to the formation of fluid collections and infected ascites.

The role of laparoscopy in patients with carcinomatosis is not limited to the systematic placement of drains and treatment with hyperthermic chemotherapy. A second prominent role of laparoscopy is to evaluate patients for definitive and potentially curative interventions with cytoreductive surgery and peritoneal carcinomatosis.[11] Radiologic studies are well known to be inadequate in assessing the extent of carcinomatosis.[12] Pomel and colleagues judged by laparoscopic criteria that 8 of 11 patients who were studied had criteria for resectability and were thereby scheduled for combined treatment using cytoreductive surgery and perioperative intraperitoneal chemotherapy.[13] Three patients who were assessed as having unresectable disease were confirmed at the time of exploration to have cancer deposits that could not be completely removed by cytoreductive surgery. The definitive criteria by which patients with carcinomatosis are selected for definitive treatment with cytoreduction versus a palliative approach have yet to be clearly defined.

The mechanism whereby ascites is resolved through the use of intraperitoneal chemohyperthermia has not been fully explained. In theory, the heated chemotherapy may eradicate viable cancer several cell layers deep on all the peritoneal surfaces. Then, a thin layer of fibrosis may develop on the exposed surfaces. The fibrous layer may direct the cancerous fluid into the capillary bed and thereby into the systemic circulation, causing a resolution of the problematic reaccumulation of ascites.

One group of patients who may not profit from this laparoscopic application of intraperitoneal chemohyperthermia are those who have pseudomyxoma peritonei and a thick mucoid ascites. It is unlikely that this gelatinous ascites can be suctioned through the port sites completely enough to resolve the ascites problem. Rather, in these patients a small laparotomy is advised and under direct vision mucoid debris removed using liposuction equipment. Care to avoid suction damage to the surfaces of the small bowel is necessary. Following complete removal of ascites along with some manual lysis of adhesions, the IPCH can then be utilized.

Unfortunately, as the use of laparoscopy in diagnosing and treating abdominal malignancy has become more common, published reports regarding the occurrence of port site metastases have appeared.[14–16] The mechanism whereby cancer cells are forced into the subcutaneous tissue along the trocar sites as a result of increased intra-abdominal pressures seems straightforward. In patients who will be candidates for potentially curative management of carcinomatosis, it has been recommended that all port sites be in the midline and that the open laparoscopic procedure be performed to prevent bowel perforation.[17] In this instance the trocar sites can be excised as part of the midline abdominal incision. In other instances, intraperitoneal chemohyperthermia can be recommended after biopsy of a cancerous mass in the presence of malignant ascites in order to minimize cancer fluid escape through laparoscopy port sites. Again, the combination of laparoscopic surgery and intraperitoneal chemohyperthermia seems to be appropriate.

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