Annals of Surgical Oncology, **7**(4):296–300

Hemodynamic and Cardiac Function Parameters During Heated Intraoperative Intraperitoneal Chemotherapy Using the Open "Coliseum Technique"

Jesus Esquivel, MD, Francisco Angulo, MD, Rebecca K. Bland, CRNA, Arvil D. Stephens, BS, and Paul H. Sugarbaker, MD

Background: Heated intraoperative intraperitoneal chemotherapy achieves high peritoneal concentrations with limited systemic absorption and has become an important tool in the management of patients with peritoneal carcinomatosis from low-grade malignancies such as pseudomyxoma peritonei and in selected cases of high-grade tumors such as colon adenocarcinoma. When the closed abdomen technique is used, its perioperative toxicity seems to be related to the hemodynamic and cardiac function changes associated with increased body temperature and increased intra-abdominal pressure.

Methods: Hemodynamic and cardiac function variables during heated intraoperative intraperitoneal chemotherapy, using an open abdomen "coliseum technique," were measured in 15 patients with the use of a noninvasive esophageal Doppler monitor.

Results: The hemodynamic and cardiac function changes were characterized by an increased heart rate, increased cardiac output and decreased systemic vascular resistance associated with an increased body temperature, and decreased effective circulating volume with the urinary output tending to decrease as the therapy progressed.

Conclusion: Heated intraoperative intraperitoneal chemotherapy with the open abdomen coliseum technique induces a hyperdynamic circulatory state with an increased intravenous fluid requirement and avoids changes because of increased intra-abdominal pressure. Hemodynamic and cardiac stability, as documented by normal blood pressure and adequate urinary output, can be achieved by liberal intravenous fluids, titrated to frequent urinary output determination.

Key Words: Heated intraoperative intraperitoneal chemotherapy—Operative monitoring.

Peritoneal carcinomatosis is a well-recognized entity that affects a large number of patients worldwide every year. Recently, the treatment has undergone significant changes that have had a measurable impact on the outcome of patients with peritoneal carcinomatosis from both high- and low-grade malignancies. Traditionally, the treatment would consist of surgical exploration, extensive biopsies, and an extensive debulking of the tumor.[1] Subsequently, the patient would be referred to a medical oncologist for systemic chemotherapy. Most of these patients suffered terribly, and in a median time of approximately 9 months for patients with carcinomatosis from a high-grade tumor and 2½ years for those with carcinomatosis from a low-grade tumor such as pseudomyxoma peritonei, the patients died of intestinal obstruction and terminal starvation.

Recent advances in surgical technique, with the introduction of peritonectomy procedures, have allowed surgeons to completely remove all visible tumor.[2] Also, innovative strategies for the delivery of intraperitoneal chemotherapy have changed the treatment of patients with peritoneal carcinomatosis from a low-grade malignancy and in selective patients with high-grade tumors from a palliative approach to a curative one.[3] Five-year survival rates of approximately 80% for patients with pseudomyxoma peritonei, and to 40% for patients with peritoneal carcinomatosis from a high-grade malignancy such as colon cancer, have been achieved.[1] It has been previously reported that the effects of regional (intraperi-

Received June 29, 1999; accepted January 21, 2000.
From The Washington Cancer Institute, Washington, DC.
Address correspondence and reprint requests to: Paul H. Sugarbaker, MD, FACS, FRCS, The Washington Cancer Institute, 110 Irving Street, NW, Washington, DC 20010; Fax: 1-202-877-8602.

toneal chemotherapy) can be maximized by delivering the chemotherapy at 42°C to 43°C. Heated intraoperative intraperitoneal chemotherapy achieves high peritoneal concentrations with limited systemic absorption.[4] Previously, the techniques, pharmacokinetics, and safety considerations of the closed abdominal heated intraoperative intraperitoneal chemotherapy have been reported.[5] Deficiencies in the distribution of heat and chemotherapy with the closed technique prompted the development of the open "coliseum technique" to improve the distribution of heat and drugs to all the abdominopelvic regions.

The purpose of this study was to report the changes in hemodynamic and cardiac function variables by using a noninvasive measurement during heated intraoperative intraperitoneal chemotherapy with an open technique and to outline a strategy to prevent intraoperative complications.

MATERIALS AND METHODS

From September 24, 1997, to January 7, 1998, fifteen consecutive patients (5 females and 10 males), between the ages of 31 and 70 years, and weighing between 54 and 133 kg, underwent cytoreductive surgery and heated intraoperative intraperitoneal chemotherapy. None of these patients had known cardiac disease, hypertension, or pulmonary disease. A single patient had previous doxorubicin chemotherapy but no ECG abnormalities or signs of cardiomyopathy. The diagnosis on these patients included pseudomyxoma peritonei (12 patients), peritoneal mesothelioma (2 patients), and gastrointestinal stromal tumor (1 patient). A standard technique for the delivery of heated chemotherapy was used. By using the open coliseum technique, the abdominopelvic lavage was performed for 90 minutes with a heat exchanger, a cardiopulmonary bypass pump, and a heater/cooler unit (3M Cardiovascular Inc., Ann Arbor, MI). Three liters of 1.5% dextrose peritoneal dialysis solution containing 12.5 mg/m^2 of mitomycin C for males (maximum dose, 25 mg) or 10.0 mg/m^2 for females (maximum dose, 20 mg) was heated and then infused into the abdomen via a Tenckhoff (Quinton, Inc., Seattle, WA) catheter at a rate of approximately 1 liter per minute. The fluid was returned from the abdomen via four Jakson-Pratt drains by an outflow pump, which established the inflow-outflow circuit.

Temperatures were measured with a Labcraft digital thermometer (Curtin Matheson Scientific, Jessup, MD). The temperature at the inflow line was approximately 44°C. The Tenckhoff temperature probe was maintained between 43°C and 44°C, and a distant intra-abdominal site averaged 39.6°C. An esophageal temperature probe was used to check the patient's body temperature. External cooling was provided with a cooling blanket to avoid systemic hyperthermia.

Throughout the perfusion, the surgeon continuously manipulated the intra-abdominal viscera to disperse both heat and chemotherapy throughout all abdominopelvic regions. All reconstructive procedures were performed after the heated intraoperative intraperitoneal chemotherapy was completed. Cardiac function and volume status were measured beat by beat during the 90-minute therapy by using an esophageal Doppler monitor (EDM).[6] The central venous pressure was measured via a double-lumen central venous catheter. Continuous blood pressure monitoring was provided by an arterial radial line. Esophageal Doppler monitoring was performed with a 6-mm noninvasive esophageal probe that was introduced through the nose and advanced into the esophagus at the level of the descending aorta. This stationary probe directs a continuous 4-MHz beam of ultrasound waves at blood flowing in the descending aorta. Alterations in the frequency of the reflected ultrasound waves caused by the moving blood cells are translated by the EDM into a waveform, recording the velocity of the blood against time and producing real-time information about left ventricular flow. Analysis of this waveform provides measurements of a range of cardiac variables. Once an adequate signal was obtained, the probe was secured to the nose with tape.

A baseline recording is performed 10 minutes before the heated chemotherapy lavage is started. Measurements included the following: heart rate, systolic and diastolic blood pressure, central venous pressure, estimated cardiac output, estimated stroke volume, flow time, peak velocity, cardiac index, and systemic vascular resistance. In addition, end-tidal CO_2, urinary output, esophageal temperature, and Tenckhoff catheter temperature are also recorded. After the baseline reading, measurements are repeated every 10 minutes during the 90-minute therapy and once again at 10 minutes after completion of the therapy. The urinary output is recorded every 15 minutes. A renal dose of dopamine (1.5 μg/kg/min), liberal intravenous fluids (1500 ml/hour), and low-dose furosemide (20 mg) are used to keep urinary output at more than 100 ml every 15 minutes. All urinary output patients tolerated the procedure well.

Once the therapy is finished, the remaining fluid is aspirated from the abdomen with two Yankawer suctions and disposed of properly. The EDM is removed, and gastrointestinal anastomoses are performed as indicated. The patients are subsequently transferred to the postanesthesia care unit.

RESULTS

The mean heart rate 10 minutes before the heated intraoperative intraperitoneal chemotherapy was 89.7 (SD, 17.6) beats per minute and had a steady increase to 100 (SD, 15) beats per minute at 80 minutes, which approaches statistical significance ($P = .09$). Ten minutes after stopping the lavage, the heart rate continued to be elevated, at 98.7 (SD, 14) beats per minute (Table 1).

Both systolic and diastolic blood pressures did not show any significant variation throughout the 90-minute therapy, although both tended to decrease as the body temperature increased (Table 1). The mean central venous pressure before the chemotherapy was started was 18 (SD, 05.8) mm Hg and remained without any significant change throughout the course (Table 1).

The mean estimated cardiac output before starting was 8.2 (01.5) liters/min and increased steadily, reaching a maximum at 70 minutes of 9.9 (03.0) liters/min and remaining elevated even 10 minutes after the therapy was terminated. This increment in the cardiac output was statistically significant ($P = .04$) (Table 1). As expected, the mean estimated cardiac index also had a steady increment and also peaked at 70 minutes; however, this increment was not statistically significant ($P = .06$). In a similar manner, the peak velocity, which reflects cardiac contractility, increased from a pretherapy value of 89.0 (SD, 18.7) cm/sec to a maximum of 97.8 (SD, 24.7) cm/sec at 90 minutes and remained elevated 10 minutes after therapy with a mean of 94.0 (SD, 28.4) cm/sec.

Both stroke volume and flow time decreased during the first 20 minutes of therapy and then increased gradually, attaining the highest values at 70 minutes, and then decreased again during the last 20 minutes of therapy. None of these changes was statistically significant (Table 1). Systemic vascular resistance decreased as patient temperature increased,and it began to increase after the therapy was finished but was still below the baseline level 10 minutes after therapy was concluded. Its lowest point correlated with the highest cardiac output.

The end-tidal CO_2 had a mean baseline of 31.6 (SD, 1.99) torr and increased constantly to a maximum of 34.6 (SD, 2.35) torr at 70 minutes; it then had a small decline but 10 minutes after therapy was still above the baseline. As shown in Table 1, these changes were statistically significant ($P = .002$).

Patient temperature, which was recorded with an esophageal probe, had a pretreatment mean value of 35.9°C (SD, 0.95°C) and increased constantly as the heated intraperitoneal chemotherapy was given. It reached its maximum value at 80 minutes, at 38.3°C (SD, 0.97°C), and started decreasing as soon as the therapy

TABLE 1. *Noninvasive hemodynamic measurements during heated intraoperative intraperitoneal chemotherapy (HIIC)*

Variable	Pre	10	20	30	40	50	60	70	80	90	Post	*P*
HR	89.7 (17.6)	91.1 (16.9)	96.6 (18.2)	95.7 (17.5)	95.8 (16.9)	97.9 (14.7)	96.8 (14.2)	98.8 (13.6)	100 (15.0)	99.0 (15.0)	98.7 (14.0)	.094
Syst BP	118 (12.2)	116 (12.9)	114 (12.4)	114 (12.4)	114 (12.9)	119 (16.0)	117 (13.0)	111 (11.5)	113 (16.5)	112 (12.9)	113 (16.4)	.116
Diast BP	65 (12.1)	65 (10.7)	64 (09.0)	64 (12.6)	64 (11.2)	63 (09.9)	63 (12.2)	60 (11.3)	62 (13.0)	61 (11.5)	60 (13.1)	.360
CVP	18 (05.8)	19 (05.8)	18 (06.2)	18 (06.6)	19 (06.8)	19 (06.9)	19 (06.9)	19 (07.0)	19 (06.2)	19 (06.3)	18 (06.5)	.656
COe	8.2 (01.5)	8.3 (02.2)	8.4 (02.4)	8.6 (02.4)	8.7 (02.5)	9.5 (02.8)	9.3 (02.9)	9.9 (03.0)	9.7 (03.1)	9.8 (02.6)	9.6 (02.5)	**.048**
CIe	4.2 (0.72)	4.2 (0.95)	4.2 (1.06)	4.4 (1.08)	4.4 (1.08)	4.8 (1.17)	4.7 (1.31)	5.0 (1.35)	4.8 (1.34)	4.9 (1.20)	4.8 (1.28)	.062
SVe	97.6 (26.4)	96.9 (31.7)	94.5 (33.7)	96.4 (33.2)	100 (39.8)	106 (38.6)	98.4 (32.0)	107 (40.3)	102 (36.6)	102 (34.0)	99.8 (34.3)	.692
FTc	0.42 (0.04)	0.40 (0.04)	0.39 (0.05)	0.40 (0.06)	0.40 (0.05)	0.43 (0.06)	0.42 (0.05)	0.43 (0.09)	0.42 (0.08)	0.41 (0.04)	0.41 (0.05)	.502
PV	89.0 (18.7)	92.0 (15.4)	92.4 (16.3)	92.8 (17.1)	93.6 (20.9)	94.5 (19.9)	92.2 (16.6)	95.7 (17.5)	96.9 (19.0)	97.8 (24.7)	94.0 (28.4)	.280
SVR	661 (211)	662 (267)	655 (294)	654 (337)	646 (296)	565 (180)	596 (296)	520 (227)	570 (263)	527 (234)	552 (249)	.110
ET_{CO_2}	31.6 (1.99)	32.2 (2.31)	32.6 (2.77)	33.2 (2.79)	33.4 (2.06)	34.0 (2.05)	34.3 (2.05)	34.6 (2.35)	34.6 (2.10)	34.1 (2.17)	34.4 (2.64)	**.002**
ET	35.9 (0.95)	36.6 (1.03)	37.2 (1.04)	37.6 (1.04)	37.8 (1.01)	38.0 (1.01)	38.1 (1.02)	38.2 (1.00)	38.3 (0.97)	38.3 (0.98)	38.0 (0.78)	**.000**
DT	N/A	39.9 (2.85)	40.2 (2.48)	40.6 (2.29)	40.3 (2.05)	40.1 (1.77)	41.0 (2.44)	41.3 (2.34)	41.5 (2.68)	40.7 (1.57)	N/A	.183
TT	N/A	43.7 (1.42)	44.1 (1.68)	43.9 (1.57)	43.6 (1.53)	44.1 (1.21)	44.2 (1.28)	44.5 (1.59)	43.9 (1.48)	43.6 (1.40)	N/A	.850
UO		430 (233)		261 (130)	240 (121)		209 (118)		169 (103)	169 (77)		**.003**

Data are expressed in mean and standard deviation (SD) values; boldfaced *P* values reflect statistical significance.

Pre, before HIIC; Post, after HIIC; HR, heart rate; Syst BP, systolic blood pressure; Diast BP, diastolic blood pressure; CVP, central venous pressure; COe, cardiac output estimate; CIe, cardiac index estimate; SVe, stroke volume estimate; FTc, flow time (preload); PV, peak velocity (contractility); SVR, systemic vascular resistance; ET_{CO_2}, end-tidal CO_2; ET, esophageal temperature; DT, distant catheter temperature; TT, Tenckhoff catheter temperature; UO, urinary output.

was finished. This increment was statistically significant with $P < .0001$. Meanwhile, the temperature at the Tenckhoff catheter fluctuated between 43.6°C (SD, 1.53°C) and 44.5°C (SD, 1.59°C) (Table 1).

Urinary output was measured every 15 minutes and was kept at more than 100 ml by giving a renal dose of dopamine (1.5 μg/kg/min) throughout the heated therapy, along with intravenous fluids at 1500 ml/hour of crystalloid and forced diuresis with furosemide as needed.

DISCUSSION

Heated intraoperative intraperitoneal chemotherapy has become one of the techniques of the surgical oncologist and it is being used with increasing frequency worldwide as the safety, morbidity rate, and therapeutic considerations are better understood and recognized. The indications for this particular method of treatment continue to increase in number, and it is now accepted as part of the treatment of gastrointestinal and ovarian malignancies that have disseminated throughout the peritoneal cavity and that have been adequately cytoreduced. Also, to prevent peritoneal seeding and resection site recurrence, it is being used as an adjuvant treatment for malignancies that have perforated a hollow viscus. On occasion, this regimen is used in patients with intractable ascites from peritoneal surface malignancies such as peritoneal mesothelioma.

Patients developed a hyperdynamic circulatory state that was characterized by a steady increase in heart rate and cardiac output that reached its maximum at between 70 and 80 minutes. These changes correlated with the patients' maximum increase in venous capacitance and maximal esophageal temperature. In addition, the highest end-tidal CO_2 was also reached during this period. As the body temperature decreased after completion of the heated therapy, the hyperdynamic circulatory state began to normalize, although it was still above baseline 10 minutes after the chemotherapeutic lavage was concluded.

Perioperative management of patients who undergo cytoreductive surgery for peritoneal carcinomatosis is a challenge to the anesthesiologist. These patients have a large abdominal incision with great insensible fluid losses, are in the operating room for many hours, and most of them have had a large volume of ascites drained. Therefore, it is imperative that if a new method of treatment is to be instituted, special attention should be given to its potential perioperative complications. Safety considerations and postoperative morbidity rates with these techniques have been reported previously.[5] Kanakoudis et al.[7] reported that most of the perioperative complications and changes in cardiac and hemodynamic functions during the heated intraoperative intraperitoneal chemotherapy were related not only to the acute changes of the body temperature but also to the increased intra-abdominal pressure secondary to the increased intra-abdominal fluid and a closed abdominal wall. They strongly advised extensive hemodynamic monitoring in patients who underwent heated intraoperative intraperitoneal chemotherapy.

Our data suggest that the hemodynamic and cardiac function alterations, observed during heated intraoperative intraperitoneal chemotherapy using the coliseum technique, seem to be determined by the thermal stress induced in the patient with its subsequent hyperdynamic circulatory state. Incremental increases of patient core temperature were associated with (1) increased cardiac output, (2) decreased systemic vascular resistance, (3) increased heart rate, and (4) increased end-tidal CO_2.

Use of constant noninvasive monitoring provided by the EDM caused administration of sufficient intravenous fluids to keep preload relatively constant during the hyperthermic therapy. The mean infusion rate per hour of intravenous fluids, as measured in 10 patients before the EDM was used, was 1220 ml/hour. When measured in 10 patients in whom the EDM was used, the mean infusion rate per hour increased to 1781 ml/hour. This fluid administration enabled the anesthesiologist to maintain an adequate effective circulating volume despite the decrease in systemic vascular resistance associated with the patient's vasodilation as a consequence of the increasing temperature. There were no significant changes in the patient systolic or diastolic blood pressures, and the central venous pressure remained relatively unchanged. It seems that the most physiological maneuver, to minimize intraoperative complications, is to maintain an adequate effective circulating volume by giving liberal intravenous fluids, which counteracts the increased venous capacitance.

In two patients, a Swan-Ganz catheter was placed at the same time as the EDM, and there seemed to be an adequate correlation between cardiac output determined by the thermodilution method using the Swan-Ganz catheter and cardiac output determined by use of the EDM. Before this study, patients with compromised cardiopulmonary function had been monitored by using a Swan-Ganz catheter during cytoreductive surgery and heated intraoperative intraperitoneal chemotherapy. At present, however, the EDM is used when more precise and minute-to-minute cardiac output monitoring is thought to be necessary, and Swan-Ganz monitoring has been discontinued altogether. To detect trends in cardiac function, we believe that the EDM is a useful tool to generate valuable information in an easy, noninvasive, and reproducible way that permits rapid intervention by the anesthesiologist during the operation.

The EDM was easily inserted and provided immediate and constant information on cardiac function and volume status. It was not associated with any complications that may have occurred with a pulmonary artery catheter, such as sepsis, arrythmias, or formation of thrombi. Since analysis of these 15 patients, we have performed more than 100 heated intraoperative intraperitoneal chemotherapy treatments without having to prematurely terminate any of them. Our monitoring equipment consists of a central venous pressure line, a radial arterial line, an ECG monitor, and a Foley catheter. In addition, in selected patients with a significant cardiac history, we use the noninvasive EDM during heated intraoperative intraperitoneal chemotherapy. A renal dose of dopamine, furosemide, and liberal intravenous fluids, to keep the urinary output at more than 100 ml every 15 minutes, are given routinely.

REFERENCES

1. Sugarbaker PH, Ronnett BM, Archer A, et al. *Pseudomyxoma Peritonei* Syndrome In: *Advances in Surgery, Vol. 30.* St. Louis: Mosby-Year Book Inc., 1997:233–80.
2. Sugarbaker PH. Peritonectomy procedures. *Ann Surg* 1995;221: 29–42.
3. Sugarbaker PH, Averbach AM, Jacquet P, et al. A simplified approach to hyperthermic intraoperative intraperitoneal chemotherapy using a self retaining retractor. In: *Sugarbaker PH, ed. Peritoneal Carcinomatosis: Principles of Management.* Norwell, MA: Kluwer, 1996:415–21.
4. Jacquet P, Averbach AM, Stephens AD, Stuart OA, Chang D, Sugarbaker PH. Heated intraoperative intraperitoneal mitomycin C and early postoperative intraperitoneal 5-fluorouracil: pharmacokinetics studies. *Oncology* 1998;55:130–8.
5. White SK, Stephens AD, Sugarbaker PH. Hyperthermic intraoperative intraperitoneal chemotherapy: safety considerations. *AORN J* 1996;63:716–24.
6. Singer M. Esophageal Doppler monitoring of aortic blood flow: beat by beat cardiac output monitoring. *Int Anesthesiol Clin* 1993; 31:99–125.
7. Kanakoudis F, Petrou A, Michaloudis D, Chortaria G, Konstantinidou A. Anaesthesia for intra-peritoneal perfusion of hyperthermic chemotherapy: haemodynamic changes, oxygen consumption and delivery. *Anaesthesia* 1996;51:1033–6.