

HOW I DO IT

Semi-Closed^{Q1} Hyperthermic-Antiblastic Peritoneal Perfusion (HAPP) in the Treatment of Peritoneal Carcinosis

MICHELE DE SIMONE, MD,^{1*} RICCARDO BARONE, MD,² MARCO VAIRA, MD,¹ BARTOLOMEO AGHEMO, MD,³ PIERROBERTO MIOLI, MD,³ CARLO FRANCO, MD,⁴ STEFANO SCUDERI, MD,¹ DANIELA COSTAMAGNA, MD,¹ AND MARCELLO DEI POLI, PhD²

¹Advanced Surgical Oncology Center, Ospedale S. Giovanni Battista, University of Turin, Turin, Italy

²III University Division of Surgery, Azienda Ospedaliera S. Giovanni Battista, Turin, Italy

³Department of Emergency Surgery, Azienda Ospedaliera S. Giovanni Battista, Turin, Italy

⁴VII Anesthesia Service, Azienda Ospedaliera S. Giovanni Battista, Turin, Italy

INTRODUCTION

Peritoneal carcinosis represents an extremely negative prognostic factor and, in a large number of cases, is rapidly lethal [1,2]. In the literature, a method that appears to be particularly effective in the treatment of this pathology consists of the cytoreduction of all visceral and peritoneal (peritonectomy) macroscopic lesions associated with hyperthermic-antiblastic peritoneal perfusion (HAPP) [3–18].

The first perfusion technique was executed making use of a closed method, which includes the suture of the entire laparotomy before starting perfusion. It has the advantage of being quick to perform, but there are several disadvantages:

1. The abdominal distribution of the perfusate and the uniformity of the temperature in the cavity are not optimal, even with the use of different tricks [5,12,19,20].
2. It is not possible to intervene immediately on tubes when an obstruction occurs, making impossible to maintain continuous and high perfusion flows.
3. During chemohyperthermic treatment, there is no visual control of the intestinal loops and of the whole abdominal cavity.

In an effort to overcome these drawbacks, first Sugarbaker, and then other investigators, introduced the open technique [21], suspending the skin of the abdominal incision by a self-retaining retractor, in order to obtain a virtual cavity.

However, this system presents a number of drawbacks as well:

1. The wide abdominal breach results in marked heat dispersion.
2. The high risk that cytostatic drugs may leak out of the patient's abdomen increases the risk of professional exposition.

We attempted to identify a perfusion technique designed to overcome the drawbacks of the methods used to date, setting the following goals:

1. To reduce heat dispersion
2. To ensure an uniform distribution of the temperature
3. To create a better cavity effect with more efficient intraabdominal flows
4. To control the peritoneal cavity visually during the entire treatment process reducing the risk that chemotherapeutic agents might leak out of the abdomen
5. To develop a system that is rapid and simple to perform

To achieve these aims and thereby create the ideal peritoneal perfusion, we developed a semi-closed method.

Grant sponsor: Compagnia di San Paolo of Turin; Grant sponsor: Regional Government of Piedmont.

*Correspondence to: Michele De Simone, MD, Centro di Chirurgia Oncologica Avanzata UOA Chirurgia d'Urgenza e P.S. Azienda Ospedaliera S. Giovanni Battista C.so Bramante, 88, Turin 10126, Italy. Fax: +39-011-6960170. E-mail: michele.desimone@unito.it

Accepted 18 September 2002

DOI 10.1002/jso.10190

Published online in Wiley InterScience (www.interscience.wiley.com).

MATERIALS AND METHODS

The semi-closed method, performed in the last 88 patients, leaves an opening in the abdominal wall allowing the surgeon to insert one hand, thus reducing heat dispersion and the leakage of cytostatic fluid from the abdominal cavity. For this purpose, a running suture is made along the upper and lower ends of the surgical wound, leaving a central gap of ~20 cm; the abdominal wall is suspended by a self-retaining retractor (Thompson Surgical Instruments, Traverse City, MI); and the central opening is covered by a polyvinylchloride (PCV) membrane. In the last 45 cases, this procedure was further simplified and accelerated using Backhaus skin holders to close the upper and lower portion of the abdominal wound and disposable self-locking bands to suspend the skin from the retractor (Fig. 1) and, to improve the flows, we created sealed circuits capable of allowing a better diffusion of the perfusate with more inflow and outflow points and two-part inflow catheters with progressive holes (Fig. 2). The perfusion technique is performed making use of a Roller inflow pump and a second outflow pump, which returns to the patient's abdominal cavity after being heated by passing through a heat exchanger (Performer RanD, Medolla (MO), Italy) (Fig. 3).

RESULTS

Between October 1995 and March 2002, we carried out 110 HAPPs. The first 7 procedures were carried out with the closed technique and the next 15 with the open technique, until we perfected the new system of semi-closed perfusion, which was used to treat 88 patients. The results were satisfactory: with the semi-closed system,

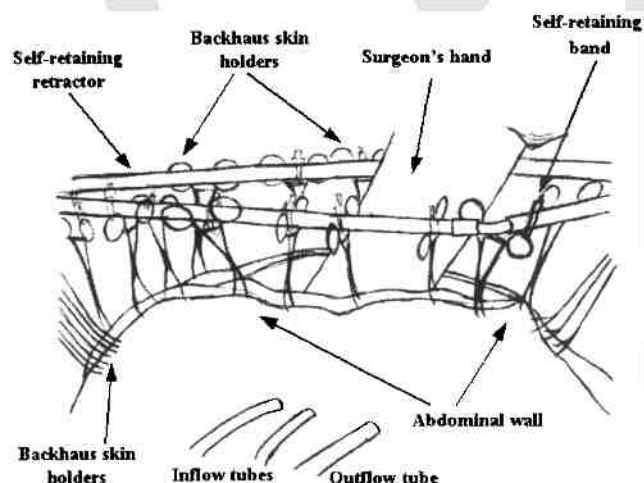


Fig. 1. Suspension system used in the semi-closed perfusion technique. The upper and lower portions of the incision are closed using Backhaus skin holders, which are placed along the free edges of the laparotomy. Self-retaining bands allow the skin to be suspended from the self-retaining retractor.

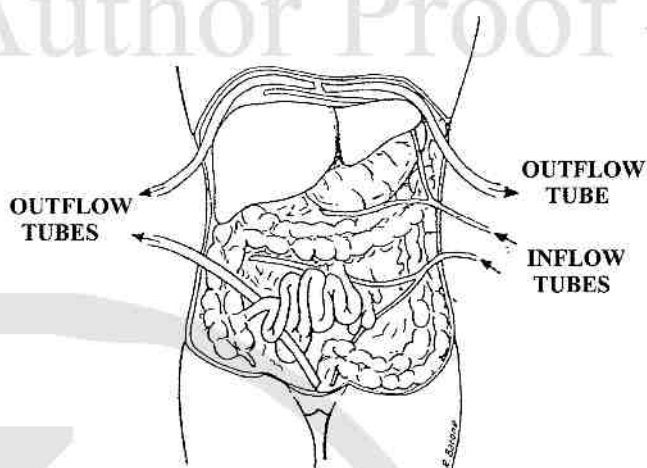
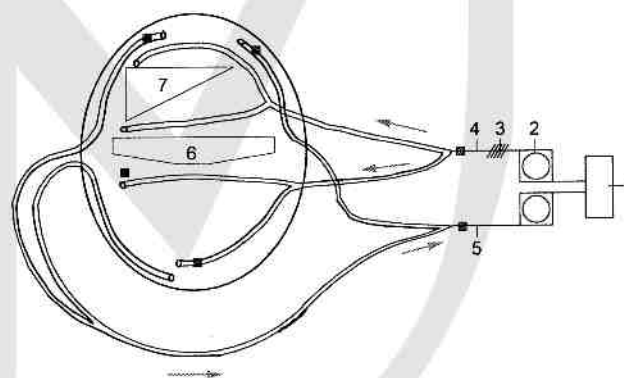


Fig. 2. Position of inflow and outflow catheters inside the abdominal cavity (see description in text).

it is possible to ensure visual control of the peritoneal cavity throughout treatment, with a low risk of leaking chemotherapeutic substances from the patient's abdomen. The temperatures inside the abdomen were uniformly and quickly distributed, with minimal heat dispersion. The intraperitoneal temperature of 41.7°C, which is required to start administering chemotherapy, is achieved 10 min after circulation has started with an inflow temperature of 42.8–43.5°C.



- 1) Reservoir
- 2) Double heads pump
- 3) Heat exchanger
- 4) Inflow
- 5) Outflow
- 6) Transverse colon
- 7) Liver

- Temperature sensors
- Temperature sensor that is shifted manually from one zone of the pseudo-cavity to another

Fig. 3. Diagram showing the abdominal cavity and the perfusion circuit, the pump system and the heat exchanger (see description in text).

CONCLUSIONS

The semi-closed technique is more advanced than the traditional perfusion systems using the closed or open system. In fact, the semi-closed technique permits homogeneous distribution of the temperatures and of the cytostatic fluids into the peritoneal cavity, reducing heat dispersion and rendering minimizing leakage of chemotherapeutic drugs from the patient's abdomen. A marginal level of perfusate is preserved at the edges of the abdominal cavity, as well as high flows of ~1,200 ml/min.

Using this system, we have succeeded in moving closer to an ideal perfusion technique. The improvements that we shall continue to introduce will make perfusion increasingly effective, rapid, and safe.

REFERENCES

1. Chu DZ, Lang NP, Thompson C, et al.: Peritoneal carcinomatosis in nongynecologic malignancies: A prospective study of prognosis factors. *Cancer* 1989;2:364–337^{Q3}.
2. De Simone M, Aimone M, Izzo G, et al.: Hyperthermic antitumor perfusion of the extremities, the pelvic cavity and the peritoneum. Surgical techniques and methods. Initial clinical experience. *Panminerva Med* 1996;38(suppl 1):28–34.
3. Pestieau SR, Sugarbaker PH: Treatment of primary colon cancer with peritoneal carcinomatosis: Comparison of concomitant vs. delayed management. *Dis Colon Rectum* 2000;43:1341–1346.
4. Loggie BW, Fleming RA, Mequellon RP, et al.: Cytoreductive surgery with intraperitoneal hyperthermic chemotherapy for disseminated peritoneal cancer of gastrointestinal origin. *Am Surg* 2000;66:561–568.
5. Elias D, Antoun S, Raynard B, et al.: Traitement des carcinomes péritonéaux par exérèse complète et chimiohyperthermie intrapéritonéale. Etude de phase I-II permettant de définir la meilleure procédure technique. *Chirurgie* 1999;124:380–389.
6. Cavaliere F, Perri P, Di Filippo F, et al.: Treatment of peritoneal carcinomatosis with intent to cure. *J Surg Oncol* 2000;74:41–44.
7. Bartlett DL, Buell JF, Libutti SK, et al.: A phase I trial of continuous hyperthermic peritoneal perfusion with tumor necrosis factor and cisplatin in treatment of peritoneal carcinomatosis. *Cancer* 1998;83:1251–1261.
8. Yonemura Y, Fujimura T, Fushida S, et al.: Hyperthermochemotherapy for treatment of peritoneal carcinomatosis. In^{Q4} "Peritoneal Dissemination: Molecular Mechanisms and the Latest Therapy." Kanazawa, Japan: Maeda Shoten, 1998:237–260.
9. Kobayashi K, Fujimoto S, Takahashi M, et al.: Clinical result of intraperitoneal hyperthermic chemoperfusion for gastric cancer with serosal invasion to prevent peritoneal recurrence. *Gan To Kagaku Ryoko* 1998;25:1436–1438.
10. Hirose K, Katayama K, Lida A, et al.: Efficacy of continuous hyperthermic peritoneal perfusion for the prophylaxis and treatment of peritoneal metastasis of advanced gastric cancer: Evaluation by multivariate regression analysis. *Oncology* 1999; 57:106–114.
11. Hamazoe R, Macta M, Kaibara N: Intraperitoneal thermochemotherapy for prevention of peritoneal recurrence of gastric cancer. Final results of a randomized controlled study. *Cancer* 1994;73:2048–2052.
12. François Y, Grandclément E, Sayag-Beaujard AC, et al.: Chimiohyperthermie intrapéritonéale avec mitomycine C dans les cancers de l'estomac avec carcinose péritonéale. *Chirurgie* 1997; 134:237–242.
13. Steller MA, Egorin MJ, Trimble EL, et al.: A pilot phase I trial of continuous hyperthermic peritoneal perfusion with high-dose Carboplatin as primary treatment of patients with small-volume residual ovarian cancer. *Cancer Chemother Pharmacol* 1999;43: 106–114.
14. Nicoletto MO, Padrini R, Galeotti F, et al.: Pharmacokinetics of intraperitoneal hyperthermic perfusion with mitoxantrone in ovarian cancer. *Cancer Chemother Pharmacol* 2000;45:457–462.
15. Rossi CR, Pilati P, Mocellin S, et al.: Carcinoma dell'ovaio: Studio pilota sulla perfusione ipertermico-antitumorale intrapéritonéale intraoperatoria. *Tumori* 1999;85(suppl 1):S43–45.
16. Sebbag G, Yan H, Shmookler BM, et al.: Results of treatment of 33 patients with peritoneal mesothelioma. *Br J Surg* 2000;87: 1587–1593.
17. Park BJ, Alexander HR, Libutti SK, et al.: Treatment of primary peritoneal mesothelioma by continuous hyperthermic peritoneal perfusion (CHPP). *Ann Surg Oncol* 1999;6:582–590.
18. Falk MH, Issels RD: Hyperthermia. *Oncol Int J Hyperthermia* 2001;17:1–18.
19. Gilly F, Carry PY, Sayag AC, et al.: Regional chemotherapy (with Mitomycin C) and intra-operative hyperthermia for digestive cancer with peritoneal carcinomatosis. *Hepatogastroenterology* 1994;41:124–129.
20. Fujimura T, Katayama K, Fushida S, et al.: Effect of hyperthermochemotherapy on miscellaneous diseases. In^{Q5} "Peritoneal Dissemination: Molecular Mechanisms and the Latest Therapy." Kanazawa, Japan: Maeda Shoten, 1998:267–274.
21. Auerbach AM, Sugarbaker PH^{Q6}: Methodologic considerations in treatment using intraperitoneal chemotherapy. In^{Q7} "Peritoneal Carcinomatosis: Principles of Management." Boston: Kluwer Academic, 1996:289–309.

Q1: Please note: quotation marks not necessary for semi, closed, and open.

Q2: Please check or revise running head copy.

Q3: Please check page range.

Q4: Name(s) of editor(s)?

Q5: Name(s) of editor(s)?

Q6: Please double-check names as spelled in ref. 21 on list and in text.

Q7: Name(s) of editor(s)?