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HYPERTHERMAL INTRAPERITONEAL PERFUSION

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Introduction

Cytoreduction surgery, associated to hyperthermal intraperitoneal chemotherapy (HIPC), it constitutes a new modality for treating patients with carcinoma dissemination in the peritoneal region[(1)]. Its principles are based in the assumption that surgery enables peritoneal disease reduction and enables to reduce adherences, creating conditions for better effectiveness of the chemotherapeutics. Studies published in international scientific publications showed an increase in the patient's survival of colon, stomach and ovary cancer subjected to HIPC[(2-4)].

Spratt *et al*. were the first to use chemotherapy with hyperthermia in experimental studies, with the objective of optimizing the cytotoxic effects of chemotherapeutics, and in 1979 the first HIPC[(5)] was performed. In hyperthermal chemotherapy, the chemotherapeutic effects are enhanced by the action of heat due to the increase in cellular permeability, the alteration of the active drug transport and alteration of metabolism. Hyperthermia increases the release of macromolecules from the chemical agents in neoplasic cells[(6)].

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Intraperitoneal perfusion can be performed by the open technique, also known as the Coliseum Technique, or by the closed technique[7]. In both of them, the catheters are connected to an extracorporeal circulation machine, whose thruster roller enables perfusion. The circuit is also composed by a heater, a heat exchanger and a temperature monitor. The heat exchanger maintains the solution to be infused between 43 and 44°C, so that in the peritoneal cavity, when the temperature of 41-42°C is reached, the perfusion is initiated and then maintained for 90 minutes[8] (Figure 1).

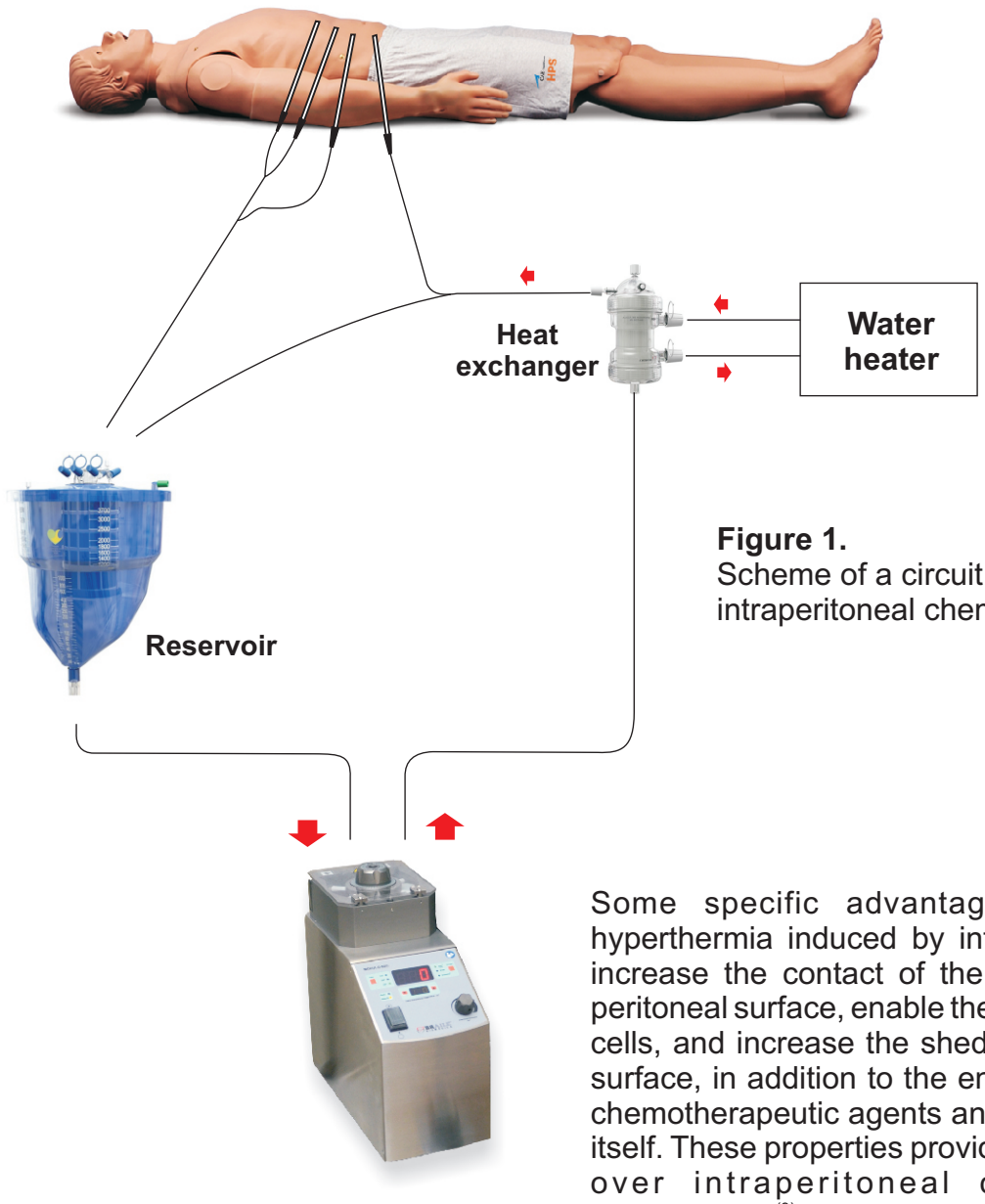

Figure 1.
Scheme of a circuit of hyperthermal intraperitoneal chemotherapy (HIPC).

Some specific advantages of HIPC are: avoid hyperthermia induced by intraperitoneal chemotherapy, increase the contact of the chemotherapeutic with the peritoneal surface, enable the removal of fluctuating tumor cells, and increase the shedding of cells adhered to the surface, in addition to the enhancement of the effects of chemotherapeutic agents and the cytotoxic effect of heat itself. These properties provide HIPC with the advantages over intraperitoneal chemotherapy without hyperthermia[9]. **Braile Biomédica's Intraperitoneal Perfusion System** is fully manufactured in compatible and atoxic polymeric material, resistant to pressure, to impact, to temperature variations and to the action of chemical and biological agents. It is composed by a reservoir for solution storage, a high-performance heat exchanger and multiperforated cannula for infusion and drainage (Figure 2).

(a) Reservoir

(b) Heat exchanger

(c) Multiperfurated cannula

Figure 2. Intraperitoneal Perfusion System.

Results of Using the Intraperitoneal Perfusion System

Due to the variability of the cytoreduction technique combined with HIPC, there is no consensus regarding perfusion time and temperature, the use of the open or closed technique and the chemotherapeutic dosage[10]. Thus, we will present some results obtained during the HIPC procedures with the use of **Braile Biomédica's Intraperitoneum Perfusion System** (Table 1), in order to show its safety and effectiveness.

Table 1. Results of procedures in patients subjected to chemotherapy with **Braile Biomédica's Hyperthermal Intraperitoneum Perfusion System.**

Patient	Pathology	Chemotherapeutic (dose)	Age (years)	Weight (kg)	T_i - T_f (ºC)	$T_{máx}$ Abd (ºC)
1	Ovary cancer	Cisplatin (125 mg)	78	67	35.3 - 37.8	42.2
2	Kidney cancer	Mitomycin (64 mg)	45	74	36.2 - 39.2	42.0
3	Ovary cancer	Mitomycin (51 mg)	61	60	35.9 - 38.1	42.2
4	Pseudomyxoma	Mitomycin (60 mg)	26	70	36.4 - 38.5	43.0
5	Vesicle cancer	Mitomycin (66 mg)	46	70	36.3 - 38.1	44.9
6	Appendicitis cancer	Mitomycin (65 mg)	56	75	36.4 - 38.0	42.3
7	Ovary and colon cancer	Mitomycin (36 mg)	37	91	35.3 - 37.4	42.0
8	Appendix cancer and adenocarcinoma	Mitomycin (12 mg)	54	60	36.3 - 38.4	42.0
9	Colon cancer	Mitomycin (67 mg)	57	78	36.0 - 38.8	43.0
10	Ovary cancer	Paclitaxel (288 mg)	60	50	36.2 - 38.5	42.6
11	Appendix cancer and pseudomyxoma	Mitomycin (60 mg)	68	83	37.0 - 40.4	43.0
12	Colon and appendix cancer	Cisplatin (130 mg) and Mitomycin (28 mg)	68	65	36.0 - 39.7	42.5
13	Adenocarcinoma	Mitomycin (60 mg)	40	65	36.3 - 38.4	42.3
14	Ovary cancer and pseudomyxoma	Mitomycin (53 mg)	59	52	33.7 - 37.9	42.3
15	Mesotelioma	Cisplatin (81 mg) and Doxorrubicin (24 mg)	24	53	35.4 - 39.3	43.0
16	Ovary cancer	Plastistin (68 mg) and Adriblastin (20 mg)	60	48	34.7 - 38.0	43.3
17	Tumor colorretal	Mitomycin (70 mg)	50	112	36.0 - 37.2	40.7
18	Stomach cancer	Mitomycin (60 mg) and Cisplatin (240 mg)	50	82	36.5 - 38.2	43.0
19	Rectal colon cancer	Mitomycin (61 mg)	44	80	35.5 - 38.3	42.2
20	Peritonium cancer	Mitomycin (52 mg)	59	54	35.8 - 37.8	41.1
Mean ± Standard Deviation			52.1±13.6	69.4±15.8	35.9±0.7 - 38.4±0.8	42.4±0.8

T_i = initial temperature; T_f = final temperature; $T_{máx\ Abd.}$ = max abdominal temperature.

Considerations

The use of intraperitoneal perfusion associated to cytoreduction surgery was shown to be a viable procedure, offering benefits for patients with disease dissemination restricted to the peritoneum. For the tumors with invasive characteristics, in general, the prognosis essentially depends on the possibility of complete cytoreduction, the extension of peritoneal dissemination and the absence of lymph node compromise or metastasis. For non-invasive tumors, this therapeutic approach has been adopted as standard conduct[1].

The results observed during the use of **Braile Biomédica's Intraperitoneal Perfusion System** confirmed its quality and showed, in the short-term, its safety and effectiveness. Clinical trials with follow-up are required for the better judgment of the real benefits of cytoreduction associated to HIPC, both with preventive and therapeutic purposes, and the **Intraperitoneal Perfusion System** itself.

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