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Research Article

Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC), Report of the First Series of Cases in Ecuador

Gordillo Villamar Rene[1*], Medina Donoso Gabriel[2], Angos Mediavilla Veronica[3], Gordillo Aldas Daniela[3]

[1]Department of the General Surgery Service, General Hospital Ibarra of the Social Security, Ecuador; [2]Department of General and Laparoscopic Surgery, Central University, Ecuador; [3]Department of Medicine, International University, Ecuador

ABSTRACT

Cyto-Reductive Surgery (CRS) + intraperitoneal hyperthermic chemotherapy (HIPEC) has a survival rate at 10 and 15 years of 63% and 59% respectively in patients with peritoneal neoplasms; severe morbidity is described in older adult patients from 17 to 56% in experienced centers, with a hospital mortality of up to 8%, there is some resistance to its implementation due to complications related to 56%, but the expectation of potential benefit is always attractive.

Keywords: HIPEC; Cytoreductive surgery; Advanced cancer; Hyperthermal intraperitoneal chemotherapy

INTRODUCTION

CRS with hyperthermic intra peritoneal chemotherapy (HIPEC) has a survival rate at 10 and 15 years of 63% and 59% respectively [1,2] in patients with peritoneal neoplasms; severe morbidity is described in older adult patients from 17 to 56% in experienced centres, with a hospital mortality of up to 8% [3], one of the first prospective randomised studies on the treatment of carcinomatosis secondary to colorectal cancer with a potential benefit of HIPEC compared to systemic chemotherapy was published in 2003 [4,5]. CRS + HIPEC together has gained ground in recent years, for instance in ovarian cancer [6] , and has even been described as effective up to 75% compared to surgery alone without intraperitoneal chemotherapy (18%) at 3 years of follow-up [7-10]; several studies show an acceptable range of morbidity-mortality [8,9]. Some authors do not take age into account as criteria for exclusion, instead considering risk-benefit in relation to a good quality of life in the terminal stage [2]. Due to the greater cytotoxicity evidenced and the lesser number of adverse effects compared to systemic therapy [11], the administration of chemotherapy agents is attractive. Studies with 10 years of follow-up show a 12% reduction in the risk of death with each cycle of intraperitoneal chemotherapy and with an upward trend in the number of cycles, an increase in life of 3.9 months is obtained by a 10% rise in each cycle [12,13]. Currently there is some resistance to its implementation due to related complications and less than half of the patients reach the planned sessions [14].In fact, the direct cytotoxic benefit lies in the increased susceptibility of the tumoral tissue when exposed to the agent at high temperature [15]. Indigestive and gynecological malignancies, HIPEC has been shown to be effective in gastric cancer [16,17], colorectal cancer and epithelial carcinoma of the ovary [5]. In our country it is an unattractive technique with undetermined results due to its poor implementation, in addition to that, the advanced stage of the patients who consult in search of a curative treatment, which makes the options limited, in consideration of that we have implemented this therapy as an option in those patients with unfavorable prognosis, many of them have abandoned their treatment by their own or by decision of their doctor; this being the reason why our case series include patients in advanced stages, which undoubtedly determines a discouraging result in any therapy to be implemented but the expectation of a potential benefit is always attractive and has been taken as the last therapeutic option in most cases.

METHOD

Cytoreductive surgery added to hyperthermic intraperitoneal chemotherapy differs from the approach, since after an accurate and complete inspection, peritonectomy is initiated by quadrants from the edge of the incision starting from the umbilical level in a centrifugal way towards the angles of the abdomen, progressively removing the parietal peritoneum.Resection continues with the margins established by the technique according to the type and origin of the tumor, then total omentectomy is performed in all cases, almost all like omental cake.Total parietal peritonectomy was performed in 4 patients due to the extension of the lesion (melanoma, ovarian cancer, biliary carcinomatosis and gastric adenocarcinoma) Table 1, when tumor implants were small and multiple (0,25 mm) electro fulguration with high voltage was

***Correspondence to:** Gordillo Villamar Rene, *Surgeon of the General Surgery Service of the General Hospital Ibarra of the Social Security of Ecuador*, Ecuador, Tel: +593992778775; E-mail: rygordillo@hotmail.com

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performed mainly in the hepatic capsule (seat of most lesions), with electro fulguration in cut mode at 100W which allows its thermal disintegration; in this way the reduction of macroscopic tumor load is obtained. When it was evident that the seeds were firmly attached to vital structures with a residual tumor greater than 2.5 cm, it was decided to abort the chemotherapy procedure (the objective is a complete cytoreduction CC=0 or CC=1), since if there are remaining lesions greater than 0.25 mm (CC=2), the subsequent application of intraperitoneal chemotherapy does not offer the desired benefits and with CC=3 or lesions greater than 2.5 cm the prognosis with HIPEC does not increase.

If there are other highly compromised organs, they must be resected. In any case, the decision on the extension of the resections and the organs involved is trans operative and taken at the discretion of the surgical team (information that the patient and his or her family must know beforehand and must be stated in the informed consent). After resective surgery, intraperitoneal chemotherapy is applied with a perfusion machine. Our group uses the ThermoChem HT-1000 from the company ThermaSolutions®, a closed or open technique also called coliseumcan be used, we prefer to perform it after closing the cavity, with circulation of the chemotherapyagent at 1500 ml/min, and with temperatures between 42 - 43 degrees centigrade, the agent we use is mitomycin C, with a dosage of 20-30 mg/m^2 of body surface, our perfusion time is always 90 minutes. After the chemotherapy is removed, the cavity is opened again for a second check, verifying the absence of thermal damage to the intra-abdominal organs and/or perforations; it is at this point where the pending anastomosis are performed to avoid potential residual tumor activity at the edges of the resected segments, we always place at least two drains for subsequent monitoring.

RESULT

A total of 37 patients with a diagnosis of peritoneal carcinomatosis with no evidence of extraperitoneal tumour activity were assessed in consultation, 14 were excluded because they presented a high Tomographic peritoneal carcinomatosis index PCI (Sugarbaker), 15 did not decide to have any type of procedure due to the basic diagnosis and poor prognosis, negative experiences, prolonged hospitalizations, aggressive surgeries and morbidity related to oncological treatments. Moreover a total of eight patients of those selected accepted the treatment, with a SugarbakerPCI<20, the diagnoses were: pseudomyxoma peritonei(2 patients) 62 and 51 years old, gastric cancer with seal ring cells and plastic linitis 31 years old, intraperitoneal melanoma 61 years old, epithelial carcinoma of the ovary 57 years old, carcinomatosis of biliary origin 40 years old, gastric adenocarcinoma 65 years old and a synchronic adenocarcinoma of the colon + colonic polyposis 53 years old in whom the procedure was performed totally by laparoscopy; mean age of 52.5 +/- 10.95 years Table 1 and 2; mean stay of 12 days +/- 4 Table 2 with at least 1 day in intensive therapy 6/8, 75%, support with total parenteral nutrition post-surgery in7/8, 87,5%, anastomosis leakage in 3 of 8 patients (37.5%), start of diet at 5.75 days +/- 1.29 , re-interventions in 3 patients (37.5%) and readmissions in 4 patients (50%) Table 3. Survival time for peritoneal pseudomyxoma was 4 years, gastric cancer with ring seal cells 3 years, melanoma died in the immediate post-surgical period, epithelial cancer of the ovary survived 2.5 months, carcinomatosis

Table 1. Distribution of the total number of patients (8) by diagnosis, age, type of surgery and survival. Age in years, HIPEC includes cytoreductive surgery plus intraperitoneal chemotherapy, RADICAL refers to complete exeresis of the peritoneum and more than 2 organs, Survival in months (m).

DIAGNOSIS	NUMBER OF PATIENTS	AGE	SURGERY	RADICAL	SURGERY SURVIVAL
Peritoneal Pseudomyxoma	2	62	HIPEC	NO	48 m
		51	HIPEC	NO	4 m
Gstric cancer	2	31	HIPEC	NO	36 m
		65	HIPEC	YES	1 m
Melanoma	1	61	HIPEC	YES	1 m
Ovarian cancer	1	57	HIPEC	YES	2 m
Biliary Carcinomatosis	1	40	HIPEC	YES	24 m
Colon cancer	1	53	HIPEC LAP	NO	2m

Table 2. Average of general variables, age, stay, survival and standard deviation (SD). Non-radical: surgery with exceresis of the entire peritoneum, Radical: surgery with exceresis of the entire parietal peritoneum and more than 2 organs.

	VALUE	DS
Average age	52,5 años	10,95
Hospital stay	12 días	4
Global Survival	16,5 meses	18
Non radical	22,2 meses	19,9
Radical	7 meses	9,8

Table 3. Percentage of complications and post-surgical variables. Immediate post-surgical intensive therapy, 2 readmissions did not require reintervention, 1 patient was readmitted twice; parenteral nutrition was administered to all patients in the immediate post-surgical period.

	PATIENTS	PERCENTAGE
24-hour intensive care	6	75%
Parenteral Nutrition	7	87,5%
Anastomosis leakage	3	37,50%
Reinterventions	3	37,50%
Re-entry	4	50%

of bile origin 2 years, second peritoneal pseudomyxoma 5 months, gastric adenocarcinoma 1 month and colon adenocarcinoma until now is in his second post-surgical month with excellent evolution; average of 16.5 months +/- 18 of total survival Table 1.The highest rate of complications was in cases where a total peritonectomy and major resections wereperformed due to very advanced disease and where several organs were resected, so that the average survival rate of patients without a total peritonectomy was 22.2 months +/- 19.9; and in those where it was performed 7 +/- 9.8 months Table 2.

DISCUSSION

Many patients have been included for HIPEC procedures, considering the appropriate inclusion criteria [2], which include age, as shown by the WHO data; the increase in life expectancy forces to include increasingly patients over 60 years [18], as well as almost 60 and 70% of new cases and cancer-related morbidity occurs in people over 65 years [19], data compatible with the age range of our patients; In addition, older patients with advanced stages like those in the study have few therapeutic options [20,21] , so HIPEC procedure becomes a very attractive treatment, taking into account those characteristics that patients should have and that also indicate their current stage and a possible evolution after the proposed treatment [22,23]. Despite the promising results of this therapy, there are complications of 12 to 57% in specialized centers [24,25] and a mortality of 0.9 to 12% [26,27], data similar to those obtained in our series directly relating the results and morbi-mortality according to the stage, characteristics of the patient and the aggression of the surgery with respect to the exeresis of compromised structures, without neglecting the learning curve [28,29]; although some authors do not directly relate certain specific characteristics of the patients with adverse results [30,31], it is clear that the greater the extraction of organs and structures that are compromised, the greater the results and morbidity, data that are consistent with our study [32,33].The survival of patients with colorectal cancer varies from 12 to 32 months with a maximum survival of 5 years in extreme cases [34]. In ovarian cancer submitted to HIPEC, survival is reported up to 22 to 64 months [35]. Our series shows cases with a survival rate of over 2 years; and in young patients with good general condition, promising results are shown with an improvement in their quality of life [36,37] after the procedure, so it should be considered in this group of people.

CONCLUSION

Cytoreductive surgery with intra peritoneal hyperthermic chemotherapy is an option to be considered in patients with advanced stages of cancer, obtaining an increase in survival compared to surgery or systemic chemotherapy alone when it is performed on selected patients; it is not exempt from complications, which are more frequent the more advanced the stage or the more radical the procedure. While our series is still very short and the tumor index differs in them so the comparison is not precise, more cases are needed to provide more accurate data. The procedure through a totally laparoscopic approach is feasible, promising and because of its low rate of carcinomatosis, its postoperative prognosis and clinical evolution is considerably better.

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