First PIPAC Treatment in a Spanish Public Hospital: A Novel Technique for the Treatment of Carcinomatosis☆

Primer tratamiento PIPAC en un hospital público español. Una novedosa técnica para el tratamiento de la carcinomatosis

Peritoneal carcinomatosis is a metastatic state consisting of tumor dissemination affecting the peritoneal serosa and neighboring structures. The origin is usually gastrointestinal or gynecological tumors, and less frequently sarcomas, stromal and peritoneal tumors.

Considered a terminal situation, it was not until Sugarbaker developed the cytoreduction surgical technique associated with hyperthermic intraperitoneal chemotherapy (HIPEC)[1] that its treatment with curative intent became possible. This procedure demonstrated reproducible results that far outperformed those obtained with classic management, consisting of systemic chemotherapy and palliative measures.[1,2]

However, many patients present with advanced peritoneal carcinomatosis, which impedes curative surgery and is relegated to palliative management. During the remainder of their lives, these patients experience progressive clinical deterioration (pain, distension, dyspnea, ascites and intestinal obstruction), resulting in declining quality of life.

Recently, a new surgical technique has been developed for the palliative treatment of these patients. It involves the use of aerosolized chemotherapy at an elevated intra-abdominal pressure, which causes the destruction of, or at least a decrease in, tumor implants in the abdominal cavity, achieving significant improvement in patient quality of life.[3]

Known as pressurized intraperitoneal aerosol chemotherapy (PIPAC), it consists of 3 key elements: relative safety, minimum duration and proven patient benefits.[4]

It was developed in 2011 by Professor Reymond for palliative use in patients with unresectable carcinomatosis. Since then, several articles have appeared, first about the application in animals and later regarding clinical practice in humans. To date, the published studies are based on 3 types of tumors, mainly ovarian, gastric and colorectal.[4]

Despite its palliative intent, it has been shown that up to 5% of patients have tumor remission, which allows for re-evaluation for curative surgery.[4,5]

The procedure is performed laparoscopically with 2 balloon trocars, 10 and 5 mm, through which a nebulizer (Capnopen®) and a 5 mm optical system are inserted. PIPAC is minimally invasive, and recovery is fast (in some European hospitals, it is conducted as day surgery), so treatment with systemic chemotherapy can be resumed. Therefore, it is a coadjuvant procedure to systemic chemotherapy, which does not lose its fundamental role.

The technique involves administering aerosol chemotherapy in the abdominal cavity at a high pressure (12 mmHg), which achieves greater penetration of the cytostatic agent and a more homogeneous distribution using lower doses than usual in HIPEC, causing minor side effects.[6–9]

This fact should not be confused with the overall result of cytoreductive surgery associated with HIPEC, since PIPAC is administered on unresected tumor tissue and HIPEC on the tumor bed or, in the worst case scenario, on few residual tumors. In fact, any surgical procedure associated with PIPAC is contraindicated due to the weakness that its application causes to healthy tissue when greater tissue depth is reached, resulting in a risk of complications.[4]

The results of this treatment are evident from the beginning (even though the average number of procedures performed was 3), with improved quality of life due to a decrease in pain, ascites, abdominal distension and gastrointestinal symptoms. In addition, in all procedures, peritoneal biopsies were taken to analyze the histological response of the tumor to successive treatments, which demonstrated significant tumor regression.[4,8–10]

Despite the relative innocuity of the procedure, Alyami et al., in their multicenter study on the implementation of a PIPAC treatment program, point out that the highest rates of morbidity and mortality occurred during the treatment of the first 20 patients, highlighting the importance of a correct learning curve in the selection of patients, even at hospitals with extensive experience in the management of peritoneal carcinomatosis.[8]

On May 8, the Carcinomatosis Unit of the General and Digestive Surgery Service at the Hospital Universitario de Gran Canaria Dr. Negrín conducted the first PIPAC at a public hospital in Spain.

Following the established protocol,[10] doxorubicin and cisplatin were administered at doses of 1.5 and 7.5 mg/m^2, respectively, instilled by a high-pressure pump at a maximum of 20 bar, with a flow of 30 mL/m for 30 min, at a constant intra-abdominal pressure of 12 mmHg. The treatment was applied to a 63-year-old patient with ovarian carcinomatosis previously considered by our group as unresectable due to massive involvement of the small intestine and a peritoneal cancer index (PCI) of 29. At the time of the intervention, the patient had a PCI of 31. During the procedure, 450 cc of ascitic liquid were extracted and peritoneal biopsies were taken to

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compare with biopsies from the following procedures. The patient was discharged on the second postoperative day without incident.

In conclusion, PIPAC is a new, relatively innocuous and beneficial technique for patients with unresectable carcinomatosis. More studies are needed to accurately determine its efficacy and range of application.

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