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Pressurized IntraPeritoneal Aerosol Chemotherapy – Practical aspects

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Abstract

Introduction: Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) has been introduced as novel treatment for peritoneal carcinomatosis. Only proper patient selection, stringent safety protocol and careful surgery allow for a secure procedure. We hereby report the essentials for safe implementation.

Methods: All consecutive procedures within 20 months after PIPAC implementation were analyzed with regards to practical and surgical aspects. Special emphasis was laid on modifications of technique and safety measures during the implementation process with systematic use of a dedicated checklist. Further, surgical difficulty was documented by use of a visual analogue scale (VAS).

Results: 127 PIPAC procedures were performed in 58 patients from January 2015 until October 2016. 81% of patients had at least one previous laparotomy. Median operation time was 91 min (87–103) for the first 20 cases, 93 min (IQR 88–107) for PIPAC21-50, and 103 min (IQR 91–121) for the following 77 procedures. Primary and secondary non-access occurred in 3 patients (2%), all of them having prior hyperthermic intraperitoneal chemotherapy (HIPEC). Using open Hasson technique, one single bowel lesion occurred, which was the only intraoperative complication. One 5 mm and another 10/12 mm trocar were used in 88% of procedures while additional trocars were needed in 12%. No leak of cytostatics was observed and no procedure needed to be stopped. VAS for overall difficulty of the procedure was 3 ± 2.4, and 3 ± 2.9 and 3 ± 2.5, respectively, for abdominal access and intraoperative staging.

Conclusions: With standardized surgical approach and dedicated safety checklist, PIPAC can be safely introduced in clinical routine with minimal learning curve.

Keywords: Intraperitoneal chemotherapy; PIPAC; Peritoneal carcinomatosis; Surgical technique; Learning curve

Introduction

Pressurized IntraPeritoneal Aerosol Chemotherapy (PIPAC) has been suggested as novel treatment modality for patients with refractory peritoneal cancer.[1–4] PIPAC combines the benefits of intraperitoneal administration (increased intra-tumoral concentrations,[5,6] low systemic toxicity[4,7]), pressurized vaporization (homogenous distribution,[2] deep penetration[4,5,8]) and minimal-invasive approach (repetitive application possible, low morbidity, better quality of life[9–13]). Most scientific studies on PIPAC were published by the pioneer team in Germany which elaborated also safety rules in order to minimize occupational health risks.[1] Encouraging clinical results and lack of therapeutic alternatives in patients with advanced peritoneal cancer are stimuli for clinical implementation.[9,10,12,13] Therefore, PIPAC is nowadays offered as treatment option in over 50 mostly European centers with about the same number of trained teams which are about to implement this novel approach in their respective institutions. This fast development entails also risks and calls for formal training, standardization and a safe implementation procedure.

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The aim of the present study was to assess practical aspects and difficulties in a non-selected consecutive series of PIPAC procedures in order to provide guidance and facilitate safe implementation of PIPAC program.

Patients and methods

PIPAC was introduced at the University Hospital of Lausanne (CHUV) in January 2015 for patients with isolated peritoneal disease that was persistent or progressive after prior standard surgical and/or medical treatment. Of note, cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) was preferred treatment choice for eligible patients. PIPAC was delivered in most patients as isolated treatment. Exceptionally, patients with predominating symptomatic PC and very limited systemic disease were considered for PIPAC which was then combined with concomitant systemic chemotherapy. Exclusion criteria for PIPAC were intestinal occlusion, portal vein thrombosis and medical contra-indications impeding therapeutic capnoperitoneum. Indication was confirmed by the multidisciplinary tumor board. All patients entered a prospectively maintained coded online data base (secuTrial®, interactive Systems GmbH, Berlin, Germany). This analysis included all consecutive procedures until October 2016; excluded were only patients who refused to provide informed consent for participation. The study was approved by the Institutional Review Board (N°2016-00274) and online-registered under www.researchregistry.com (UIN: 1916). STROBE criteria (http://strobe-statement.org) were applied for the reporting of the study.

PIPAC procedure and safety considerations (Figs. 1 and 2)

Methodology and surgical approach of PIPAC procedure have been reported elsewhere[4,14,15] and are explained in detail with the provided illustrations and photo documentation. Briefly, pneumoperitoneum was established by open placement of one 10 mm and one 5 mm balloon trocar, preferentially using existing scars from previous surgeries. Ascites was quantified, aspirated and sent for cytology. The peritoneal cancer index (PCI)[16] was documented and representative peritoneal nodules were biopsied. Local peritonectomy of a non-diseased area was performed to assess effects (e.g. fibrosis) of PIPAC on the healthy peritoneum.

Cytostatic solutions were prepared by clinical pharmacology on prescription by the medical oncologist and delivered to the operation room as liquid solution in securely closed plastic covers. Oxaliplatin was applied at a dose of 92 mg/m^2 for carcinosis of colorectal origin, while Cisplatin (7.5 mg/m^2) in combination with Doxorubicin (1.5 mg/m^2) was used for ovarian, gastric and other malignancies.[9,10,13]

Liquid chemotherapy was aerosolized by use of a pressure injector (Accutron HP-D, Medtron®, Saarbrücken, Germany) and a specific nebulizer (MicroPump®, CapnoPen®, Reger, Villingendorf, Germany; CE-certified: class 2A) at 37 °C for 30 min and under standard laparoscopic pressure of 12 mm Hg. At the end of the procedure, pneumoperitoneum was evacuated in a closed aerosol evacuation system (CAWS) with two microparticle filters to capture residual molecules. PIPAC was administered repetitively (3× at least) at an interval of about 6 weeks.

The safety protocol included the 3 levels of containment as recommended[1,15] (Fig. 2). Further, a tailored checklist containing all safety aspects (team time out, staff and procedure-related safety aspects) was systematically double-checked before administration of cytostatics. For this purpose, the original checklist from the German pioneer group was translated into French and adapted according to the experience of the first 50 PIPAC applications. The English version of the current checklist is provided as Online Appendix 1.

A standardized clinical pathway (care map) was used to support implementation and standardize and optimize perioperative care with regards to medications, nutrition, nursing and blood drawings. The initial version was adapted after careful analysis of the first 100 procedures. The current PIPAC care map is attached as Online Appendix 2.

Outcome measures

Prospectively collected data included surgical details and intraoperative findings with information on feasibility, trocar placement, biopsies, and additional procedures as detailed in Table 1. Detailed information on demographics, clinical outcomes and quality of life under PIPAC has been previously reported by our group (submitted data).

Assessment of surgical difficulty

Subjective assessment was performed by the operating surgeon (MH, FG, HT) at the end of the procedure by use of a visual analogue scale (0–10: very difficult) rating abdominal access, intraoperative staging (PCI) and overall difficulty.

Statistical analysis

Categorical variables are given as frequencies with percentages and compared with chi-square test. Continuous variables are presented as mean with standard deviation (SD) or median value with range or interquartile range (IQR) as appropriate. Depending on the normality of distribution, Student's t test and Mann–Whitney U test were used. A p value <0.05 was considered to be statistically significant in all tests. Data analyses were generated using SPSS v20 statistical software (Chicago, IL, USA) and GraphPad Prism 7 (GraphPad Software, Inc. La Jolla, CA, USA).

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