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V7
PIPAC: 8 KEY POINTS FOR A GOOD PRACTICE

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Pressurized intraperitoneal aerosol chemotherapy (PIPAC) is an innovative treatment allowing to increase locoregional drug delivery for non resectable peritoneal carcinomatosis. Drastic compliance to safety protocol with careful surgery is mandatory to ensure his safe implementation. The goal of our video is to report the key points of the technique.

CO44
PRESSURIZED INTRAPERITONEAL AEROSOL CHEMOTHERAPY (PIPAC) ASSOCIATED WITH SYSTEMIC CHEMOTHERAPY WITH VEGF-A, EVALUATION OF SAFETY AND FEASIBILITY

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Objectives

Pressurized intraperitoneal aerosol chemotherapy (PIPAC) is a promising technic for non-resectable peritoneal metastasis (PM). Target therapies such as VEGF-A have demonstrated their efficiencies in colorectal and ovarian cancer. The objective of this study is to evaluate the safety and the feasibility of the association of these two treatments.

Methods

This is a retrospective analysis of prospective maintained PIPAC database of Lyon Sud university hospital of all patients diagnosed with non-resectable PM. All patients who underwent PIPAC in association with systemic chemotherapy and VEGF-A were compared with all patients who underwent PIPAC in association with systemic chemotherapy alone regarding postoperative complications according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

Results

From December 2015 to December 2017, 134 patients underwent 406 PIPAC in Lyon Sud University Hospital. Twenty six and 108 patients were included in VEGF-A group and No-VEGF-A group respectively. The two groups were comparable in term of gender, age, body mass index (BMI) and Peritoneal cancer index (PCI). Median age was 59.3 years (P = 0.106), Median BMI was 22.1 (P = 0.638) and median PCI was 19 (P = 0.234). Bevacizumab and Aflibercept were used in 24 and 2 patients respectively in VEGF-A group. Major complications (CTCAE - III, IV) occurred in 4 (15.4%) and 9 (8.3%) patients (P = 0.278) for VEGF-A group and No-VEGF-A group respectively. In multivariate analysis, for patients of VEGF-A group, the PM from colon cancer was the only independent factor associated with increased morbidity (odds ratio 13.886; 95 % CI 3.286–58.687, P = 0.0098). This could be explained by the majority of patient (69%) in VEGF-A group were from PM of colon cancer.

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Conclusion

PIPAC associated with VEGF-A is feasible, safe and well tolerated. The potential oncologic benefits of the concomitant use of VEGF-A and PIPAC remains to be evaluated by further prospective trials.

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CO45

IS A SINGLE LAPAROSCOPIC BIOPSY ENOUGH TO DETERMINE THE REGRESSION GRADING SCORE OF PERITONEAL METASTASES AFTER PALLIATIVE CHEMOTHERAPY?

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Objectives

Laparoscopic peritoneal biopsies are increasingly used to evaluate therapy response of peritoneal metastases (PM) after systemic chemotherapy (SC). So far, influence of methodological aspects such as quality and number of biopsies on assessment remain unclear. Aim is to determine variability of the regression grading score between multiple peritoneal biopsies.

Methods

Prospective cohort of 126 laparoscopies in 49 patients with histologically proven PM: Gastric (n = 22); colorectal/appendiceal (n = 17); hepatobiliary/pancreatic (n = 8); ovarian/tubal (n = 5); Pseudomyxoma peritonei (n = 3), malignant mesothelioma (n = 2); others (n = 2) treated with various regimen of SC. 4 biopsies taken routinely from all abdominal quadrants. Analysis by an independent pathologist. Determination of the regression grading score based on the 4-tied Peritoneal Regression Grading Score (PRGS).

Results

Out of 126 histological examinations, 120 (95,2%) showed agreement in ≥2 biopsies, 37 (29,3%) in ≥3 biopsies and only 18 (14.2%) in all 4 biopsies. In 6 cases (4,8%), PRGS was different in each biopsy.

Conclusion

A single biopsy is not enough to determine safely the regression grading score of PM under palliative therapy. Little additional information is provided by a 2nd biopsy but there is a significant increase of the informational content between the 2nd and the 3rd biopsy. Thus, at least 3 peritoneal biopsies should be taken in order to determine accurately regression grading score of PM under palliative therapy.

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CO46

ADJUVANT PRESSURIZED INTRAPERITONEAL AEROSOL CHEMOTHERAPY (PIPAC) IN RESECTED HIGH-RISK COLON CANCER PATIENTS

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Objectives

Peritoneal metastasis (PM) is the second most common site of recurrence in colon cancer patients, and accounts for approximately one-third of all recurrences. Patients with T4 or intraperitoneal perforated colon cancers have an increased risk of developing PM, and since manifest PM is difficult to treat, high-risk patients should be offered prophylactic treatment. The present study will evaluate the effect of Pressurized IntraPeritoneal Aerosol Chemotherapy (PIPAC) directed adjuvant therapy in these patients.

Methods

PIPAC-OPC3 is a prospective phase 2 cohort study designed to treat high-risk colon cancer patients with adjuvant PIPAC directed therapy (ClinicalTrials.gov Identifier NCT03280511, European Clinical Trials Database (EudraCT) 2017-002637-37). Based on an estimated absolute risk reduction of 15% (25% to 10%) regarding the development of PM in high-risk colon cancer patients, 60 patients will be included (two-sided, α: 0.05, power: 0.8). Eligible patients will receive two PIPAC treatments with oxaliplatin (92 mg/m2) at 4–6 weeks interval. During laparoscopy the peritoneum is biopsied at two locations, and peritoneal lavage with 500 milliliters of saline and laparoscopic ultrasound is performed. The patients are screened for adverse medical events, and surgery related complications after each PIPAC procedure. After the second PIPAC procedure, the patients will be examined in the outpatient clinic and followed with CT scans 12, 24 and 36 months after resection. The primary outcome of the PIPAC-OPC3 trial is the rate of peritoneal recurrence on the 36 months CT scan. Secondary outcomes include the number of conversions from positive to negative peritoneal lavage cytology after one PIPAC procedure, completion rate of two adjuvant PIPAC treatments, toxicity and complication rate, and recurrence free and overall survival rates after 1-, 3- and 5 years.

Results

PIPAC-OPC3 is the first prospective study on PIPAC directed therapy in the adjuvant setting. The study just opened and so far, two patients have completed the planned treatment. The expected accrual is two years. At the PSOGI 2018 conference, we expect to present data from several patients.

Conclusion

We present our preliminary experience with PIPAC directed adjuvant treatment of high-risk colon cancer patients. With this presentation, we wish to establish scientific discussions on patient selection, chemotherapy type/dose and follow-up strategy in adjuvant PIPAC directed therapy.

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CO47

ANESTHESIA IN TOXIC SPACES: PIPAC PRESSURIZED INTRAPERITONEAL AEROSOL CHEMOTHERAPY

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Objectives

Pressurized Intraperitoneal Vaporized Chemotherapy (PIPAC) is a new technique of chemotherapy application for peritoneal carcinosis. Specificity of this technique is the transient chemo-toxic environment created in the theatre, requesting anticipation from the anaesthesiologist who will not be able to enter the room for 30 minutes.

Methods

From January 2015 until February 2018, all patients undergoing PIPAC procedure in the department of visceral surgery were included in the study. Due to the chemo-toxic environment, anaesthesia was conducted in order to monitor the patient out of the theatre room during the vaporization of the chemotherapy. Safety check list and anaesthesia recommendation were elaborated. All per-operative anaesthetic complications were recorded, including monitoring or equipment dysfunction. Postoperative nausea and vomiting (PONV) and pain were assessed at 24, 48, and 72 hours in a quality control database for the first 74 procedures. Postoperative surgical complications were graded using the Clavien-Dindo classification.

Results

196 PIPAC were performed on 89 patients. Per-operative anaesthesiologic complications were 9(4.6%) patients with mild hypothermia, leading to 4 delayed recovery. 7(3.6%) patients suffered delayed recovery due to excessive sedation or curarization. 31(16%) patients suffered moderate to severe pain in recovery room, requiring iv morphine with median doses of 13 mg. Pain score using VAS (0–10) showed an average score between 1 and 2 at rest until 72 h and, between 1 and 3 at mobilization. PONV were present in less than 10% of the patient at 12 h and in 40% of cases at 72 h. The surgical complications were 37 (19%) patients experiencing postoperative morbidity. Severe complications per patient (Clavien-Dindo grade ≥ IIIa) occurred in 6 (6.7%) patients, 3 (3.3%) wall hematomas with need of drainage and 2 iatrogenic small bowel lesions. One patient developed cardiogenic shock and arrhythmia 4 days after the 3rd PIPAC procedure with fatal outcome. Autopsy did not find any intraabdominal complication.

Conclusion

Anaesthetic management of PIPAC patient can be safely performed with safety check list and anaesthetics protocols.

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CO48

DESCRIPTION OF ATM 220® TECHNOLOGY AND GRANULOMETRIC CHARACTERIZATION OF THE AEROSOL APPLIED FOR HYPERTHERMIC INTRACAVITARY NANOAEROSOL THERAPY (HINAT)

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Objectives

Hyperthermic Intracavitary NanoAerosol Therapy (HINAT) is a novel drug delivery technique for intraperitoneal chemotherapy. HINAT is based on extracorporeal generation and heating of an aerosol using a pneumatic atomizing device (modified ATM 220®, Topas, Germany) and electro-precipitation (Ultravision®, UK). Claimed advantages of HINAT are a smaller, homogeneous droplet size and generation of hyperthermia.

Methods

Industry-standard ATM220®, operated as described previously (Pabst et al. 2018). Determination of droplet size as well as influence of tubing by laser diffraction. Determination of time needed for transferring therapeutic drug doses on the basis of published data. Evaluation of HINAT technology for generating intraperitoneal hyperthermia using thermodynamic laws.

Results

Median aerodynamic diameter Dv(50) is 1.130 ± 0.057 µm (Glc 5%), and log-normally distributed. During HINAT, aerosol is transported through tubing of >150 cm and droplet size distribution is altered. No visible staining (pure blue ink) of a blotting paper placed at the exit of tubing. Assuming the published mass transfer of 4.25 g/h, time for delivering a dose of 3 mg DOX is 20 min; 15 mg CIS 3 h 25 min; 184 mg oxaliplatin (OX) 8 h 26 min. Due to the continuous gas leak, operating CO2 flow is 200–250 l/h. Even assuming a CO2 flow of 10 l/min, heat required to evaporate water to saturate the initially dry CO2 stream from 25°C to 37°C is 16 J/s, which cannot be provided by the system tested.

Conclusion

ATM220® provides an outstanding droplet size and repartition at the exit of the device. However, transport over tubing impacts the aerosol characteristics negatively. Only DOX, but not CIS or OX can be aerosolized within a reasonable timeframe. The continuous gas flow complicates proof of tightness. Without applying clinically unacceptable upstream temperatures, HINAT technology cannot generate hyperthermia of 41–43°C.