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ORIGINAL ARTICLE

# Feasibility and Safety of Taxane-PIPAC in Patients with Peritoneal Malignancies—a Retrospective Bi-institutional Study

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**Abstract**
Taxanes have a favorable pharmacokinetic profile for intraperitoneal application. We report our initial experience with taxane-PIPAC (pressurized intraperitoneal chemotherapy) for unresectable peritoneal metastases from different primary sites in terms of safety, feasibility, response rate, and conversion to resectability. In this retrospective study, PIPAC was performed alone or in combination with systemic chemotherapy. Paclitaxel was used as a single agent, whereas docetaxel was used in combination with cisplatin-adriamycin or oxaliplatin-adriamycin. From December 2019 to December 2021, 47 patients underwent 82 PIPAC procedures (1 PIPAC in 55.3%, 2 in 29.7%, 3 in 14.8%). The most common primary sites were ovarian cancer (31.9%), gastric cancer (23.4%), and colorectal cancer (21.2%). Docetaxel-cisplatin-adriamycin was used in 33 (70.2%) patients, docetaxel-oxaliplatin-adriamycin in 12 (25.5%), and paclitaxel alone in 2 (4.2%) patients. Grade 1–2 complications were observed in 24 (51%) and grade 3–4 complications in 6 (12.7%) patients (8.5% of 82 PIPACs). 16/47 (34.0%) patients had a clinical response to PIPAC. The mean PCI was 25.9 ± 9.2 for the first PIPACs and 22.4 ± 9 for the subsequent PIPACs with an average reduction of 3.6 points [change in PCI ranged from − 14 to + 8]. The PRGS was 1/2 in 4/47 (8.5%) patients (19.0% patients with > 1 PIPAC). A reduction in ascites was observed in 35.4% presenting with ascites. Nine (19.1%) patients had conversion to operability leading to a subsequent cytoreductive surgery in 8 (17%) patients. PIPAC with docetaxel is feasible and safe. The role of PIPAC with both docetaxel and paclitaxel either alone or in combination with other drugs should be investigated in prospective studies.

**Keywords** PIPAC · Taxanes · Paclitaxel · Docetaxel · Peritoneal metastases · Peritoneal surface malignancy

## Introduction

Pressurized intraperitoneal aerosolized chemotherapy (PIPAC) is used in selected patients with unresectable peritoneal metastases (PM) as a palliative therapy alone or in combination with systemic chemotherapy (SC) [1]. It has been used for both newly diagnosed unresectable PM and after multiple lines of SC. The reported response rates ranging from 20 to 50% in different primary tumors are encouraging [2, 3]. Two regimens were initially developed by the pioneers of this drug delivery system—the combination of cisplatin and doxorubicin and single agent oxaliplatin [4, 5]. The drug doses were set arbitrarily. A fraction (usually 1/10) of the dose used for performing HIPEC was used initially, and this was widely adopted by centers that started offering this treatment [4, 6]. Preclinical studies on PIPAC have largely focused on the distribution of the drug in the peritoneal cavity, characteristics of the aerosol, and drug penetration into normal and tumor-bearing peritoneum [7–10]. There are no head-to-head comparisons between different drugs and/or regimens. Phase 1 dose escalation studies in published literature are few in number. There is one dose escalation study for the combination of cisplatin and doxorubicin and three for oxaliplatin all showing dose limiting toxicity at different doses [11–13]. A phase 1 dose escalation study on the combination of mitomycin C PIPAC

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and FOLFIRI is currently underway to determine ceiling dose and safety of this treatment combination [14].

Taxanes have a favorable pharmacokinetic profile for intraperitoneal (IP) use [15]. The large molecular size, prolonged retention in the peritoneal cavity, and cell cycle-specific cytotoxicity make them ideal for repeated intraperitoneal application [16, 17]. Their use for performing HIPEC is limited by conflicting data on the thermal enhancement properties and cell cycle specific cytotoxicity [18, 19]. Both paclitaxel and docetaxel have been used in normothermic intraperitoneal chemotherapy (NIPEC) protocols as adjuvant, neoadjuvant, and palliative therapy for peritoneal malignancies [20–22].

Aerosolized chemotherapy is expected to have a greater depth of penetration that is further augmented by the use of a therapeutic capnoperitoneum, and the distribution of drug is expected to be more homogeneous compared to other forms of IPC [7, 23]. Repeated application is possible; it can be combined with SC, and the response can be assessed both visually and pathologically after each procedure [23]. PIPAC, thus, has several theoretic advantages over other forms of IP chemotherapy (IPC). Given their favorable pharmacokinetic profile and antitumor activity, taxanes could be useful drugs for PIPAC and used either alone or in combination with the current PIPAC regimens.

There is no published literature on the use of taxane-PIPAC in humans. A phase 1 dose-escalation study on nano-particle albumin bound (NAB) paclitaxel is underway to determine the maximum-tolerated dose of NAB-paclitaxel-PIPAC [24]. In this retrospective cohort study from two Indian centers, we present our initial experience with taxane-PIPAC in terms of safety and feasibility. Our second aim was to look at the response rate and conversion to resectability.

## Methods

This is a retrospective analysis of prospectively collected data. All patients who received PIPAC with a taxane (paclitaxel or docetaxel) alone or in combination with one or more other drugs were included in this study. The demographic, clinical, surgical, and systemic therapy details were retrieved for all patients. Institutional review board permission was obtained at both centers for this study.

### Patient Selection and Surgical Details

PIPAC was performed for patients who had progressive disease after one or more lines of systemic chemotherapy for unresectable isolated PM. From 2021 onwards, selected patients with newly diagnosed isolated PM were treated with PIPAC and SC to achieve a better response or symptom control. For few patients with pleural involvement, PIPAC was performed with pressurized intrathoracic aerosolized chemotherapy (PITAC). Patients with visceral metastases and other distant metastases (extraperitoneal metastases) in addition to PM were not offered PIPAC. Patients with a poor performance status (ECOG > 2) or with subacute intestinal obstruction were not offered PIPAC. Blood counts and liver and renal function test had to be within the normal range for performing PIPAC. All patients had radiological and/or histopathological evidence of primary or secondary peritoneal surface malignancy.

### PIPAC Technique

PIPAC was performed as described previously [25]. After insufflation of a 12 mmHg $CO_2$ pneumoperitoneum (with open access or a Veres needle), two balloon trocars measuring 12 mm were inserted into the abdominal cavity. We used either the open technique or optical ports to ensure safe entry. The port sites depended on previous scars and disease distribution—e.g., adherence of bowel loops to the midline scar visible on imaging precluded port insertion in the midline.

An evaluation of the peritoneal cancer index (PCI) was performed [26]. Biopsies were performed from at least two different regions and if possible 4, of the peritoneal cavity, and ascitic fluid was completely drained and sent for cytological examination. The safety checklist was adhered to during all procedures [25].

The different drug regimens for PIPAC used are listed in Table 1.

We used stat dosing instead of the conventional body surface area-based dosing. The dose of paclitaxel was 20 mg which would work out to less than one-third of the dose used in HIPEC [27]. Docetaxel was used in combination with cisplatin and adriamycin or oxaliplatin and adriamycin. The dose of docetaxel was 20 mg which is less than half the dose used for NIPEC (30 mg/m$^2$) [21]. We used stat doses of adriamycin (4 mg), cisplatin (15 mg), and oxaliplatin (90 mg) contrary to the practices followed at many other centers [27]. This dose usually works out to be the same as the body surface area-based dosing considering that majority of the Indian patients have a BSA of 1.5–1.7 m$^2$. For oxaliplatin we used a dose of 90 mg as in our experience with oxaliplatin 92 mg/m$^2$ as a single agent; patients experience post-operative pain (unpublished experience).

To administer the drugs, we had to deviate from the current recommendations for performing PIPAC [28]. The platinum agents and taxanes were not combined in the same syringe. For the cisplatin regimen, cisplatin and adriamycin were diluted in 150 ml 0.9% NaCl as previously described, and docetaxel was administered separately in another 150 ml of 0.9% NaCl. For the oxaliplatin regimen, oxaliplatin was

**Table 1** Various drug regimens used for performing taxane-PIPAC

| Regimen | Carrier solution | Drug combination and sequence of aerosolization | Duration of PIPAC | Main indications |
|---|---|---|---|---|
| Paclitaxel 20 mg | 0.9% NaCl | 1st syringe – paclitaxel | 30 min | Ovarian cancer, gastric cancer |
| Cisplatin 15 mg + adriamycin 4 mg + docetaxel 20 mg | 0.9% NaCl | 1st syringe – cisplatin + adriamycin<br>2nd syringe – docetaxel | 30 min | Ovarian cancer, gastric cancer, colorectal cancer, peritoneal mesothelioma |
| Docetaxel 20 mg + oxaliplatin 90 mg + adriamycin 4 mg | 0.9% NaCl for docetaxel and adriamycin<br>5% dextrose for oxaliplatin | 1st syringe – docetaxel + adriamycin<br>2nd syringe – oxaliplatin | 30 min | Ovarian cancer, gastric cancer, colorectal cancer, peritoneal mesothelioma, appendix cancer/PMP |

diluted in 150 ml of 5% dextrose, while docetaxel and adriamycin were diluted with 150 ml 0.9% NaCl. The total volume in each syringe was 150 ml. The chemotherapy solution was aerosolized using a microinjection pump at a flow rate of 0.6 ml/s at 200 psi. The drugs in each syringe were aerosolized in sequence that required two team members to remain in the operating room when drug is aerosolized and released in the abdominal cavity. Personal protective equipment was used to minimize exposure to the chemotherapeutic agents. The application time of 30 min was counted after all the drugs were aerosolized. The intraabdominal pressure was maintained at 12 mm of hg throughout the application time.

At the end of the procedure, the chemotherapy aerosol was exsufflated via a closed line into a closed suction system that solidifies the aerosol as we have described previously [25].

### Additional Surgical Procedures

Additional surgical procedures like omentectomy, oophorectomy, adhesiolysis, hernia repair, and PITAC were performed in selected patients along with PIPAC.

### Perioperative Management

Post-operative management was in the ward, and routine intensive care admission was not done. All patients were observed overnight in the hospital and for longer if required depending on the general condition and the patients' residence (often in a different city or town). Adverse events were recorded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4 [29].

### Assessment of Response

Imaging was not performed before each PIPAC procedure. Resolution of symptoms, tumor markers, and the overall clinical picture were considered. During the second PIPAC onwards, the difference in surgical PCI was calculated for each subsequent procedure. Biopsies were performed from 2 to 4 regions to assess the pathological response. The pathological regression grade score (PRGS) was used to assess the pathological response [30]. The highest score of all regions biopsied was considered and not the average score.

### Systemic Chemotherapy

SC was administered as deemed necessary by the treating team of physicians. If SC was administered, the interval between two PIPACs was 6–8 weeks, while it was 4–6 weeks for PIPAC monotherapy. No patient received SC during the PIPAC procedure itself.

### Statistical Methods

Categorical data are presented as number (%) of the entire cohort. Non-normally distributed continuous data are expressed as the median and range. For some parameters of the continuous data like PCI, the mean and standard deviation have been calculated.

## Results

From December 2019 to December 2021, 47 patients treated with 82 PIPAC procedures using taxanes were included in this study. The median age was 53 years. The most common primary site was ovarian cancer ($N = 15$; 31.9%) followed by gastric cancer ($N = 11$; 23.4%) and then colorectal cancer ($N = 10$; 21.2%) (Table 2). 59.5% patients received prior SC, and one-third of all patients had received 2 or more lines before undergoing PIPAC. Prior surgery had been performed in 48.9% of which 17 (36.1%) had surgery for resection of the primary tumor,

**Table 2** Clinical details of patients treated with PIPAC using taxanes

| Variable | | No of patients $N=47$ $N$ (%) |
|---|---|---|
| Age (years) | Median [range] | 53 [18–87] |
| Sex | Male | 20 (42.5) |
| | Female | 27 (57.5) |
| Primary tumor site | Colorectal | 10 (21.2) |
| | Ovary | 15 (31.9) |
| | Stomach | 11 (23.4) |
| | Mesothelioma | 6 (12.7) |
| | Others | 5 (10.6) |
| Previous systemic chemotherapy | Yes | 28 (59.5) |
| | No | 19 (40.) |
| No of previous lines of systemic chemotherapy | 1 | 9 (19.1) |
| | 2 | 10 (21.2) |
| | > 2 | 5 (10.6) |
| | Missing | 3 (6.3) |
| Prior surgery | Yes | 23 (48.9) |
| | No | 24 (51.1) |
| ECOG performance status | 0 | 13 (27.6) |
| | 1 | 16 (34.0) |
| | 2 | 18 (38.2) |
| Clinical symptoms of PM | Yes | 33 (70.2) |
| | No | 14 (28.8) |
| No of PIPAC procedures | 1 | 26 (55.3) |
| | 2 | 14 (29.7) |
| | 3 or more | 7 (14.8) |
| Drug used for PIPAC | Paclitaxel | 2 (4.2) |
| | Docetaxel + cisplatin + adriamycin | 33 (70.2) |
| | Docetaxel + oxaliplatin + adriamycin | 12 (25.5) |
| Concurrent systemic chemotherapy | | 40 (85.1) |
| Reason's for discontinuation of PIPAC | Conversion to operable disease | 9 (19.1) |
| | Logistic concerns | 14(29.7) |
| | Disease progression/lack of benefit | 21(44.6) |
| | Complication of the procedure | 3 (6.3) |
| Complications | Major (grades 3–4) | 6 (12.8) |
| | Minor (grades 1–2) | 24 (51.0) |
| Type of major complication | Bowel injury during access | 1 (2.1) |
| | Bowel perforation | 1 (2.1) |
| | Neutropenia | 2 (4.2) |
| | Bowel obstruction | 1 (2.1) |
| | Systemic sepsis | 1 (2.1) |
| | Respiratory distress | 1 (2.1) |
| Post-operative mortality | | 0 (0.0) |

Abbreviations: *ECOG* Eastern Cooperative Oncology Group, *PM* peritoneal metastases

3 (6.3%) had a prior CRS (2 with HIPEC), and 7 (14.8%) patients had debulking surgery for peritoneal disease. The ECOG performance status was 0 in 13 (27.6) patients, 1 in 16 (34%), and 2 in 18 (38.2%) patients. Clinical symptoms due to PM like ascites, loss of appetite, and abdominal pain were reported in 33 (70.2%) patients. Ascites was present in 31 (65.9%) patients of which 17 (36.1%) patients had ascites more than 1 l and 7 (14.8%) had more than 5 l of ascites during the first procedure. None of the patients had subacute bowel obstruction.

## PIPAC Procedures

Twenty-six (55.3%) patients had a single PIPAC procedure, 14 (29.7%) had two, and 7 (14.8%) patients underwent 3 or more procedures. The maximum number of procedures performed in a single patient was 6. The combination of docetaxel, cisplatin, and adriamycin was used in 33 (70.2%) patients; docetaxel, oxaliplatin, and adriamycin in 12 (25.5%); and paclitaxel alone in 2 (4.2%) patients. Non-access was not observed in any patient though 1 patient required laparotomy due to bowel injury during trocar entry.

The reasons for discontinuing PIPAC were surgical complications in 3 (6.3%) patients, disease progression in 21 (44.6%), conversion to CRS in 9 (19.1%), and logistic issues in 14 (29.7%) patients. The logistic issues included inability to travel due to lockdown imposed for control of the COVID-19 pandemic ($N=5$), cost constraints ($N=4$), and patient refusal for further treatment ($N=5$) (Fig. 1).

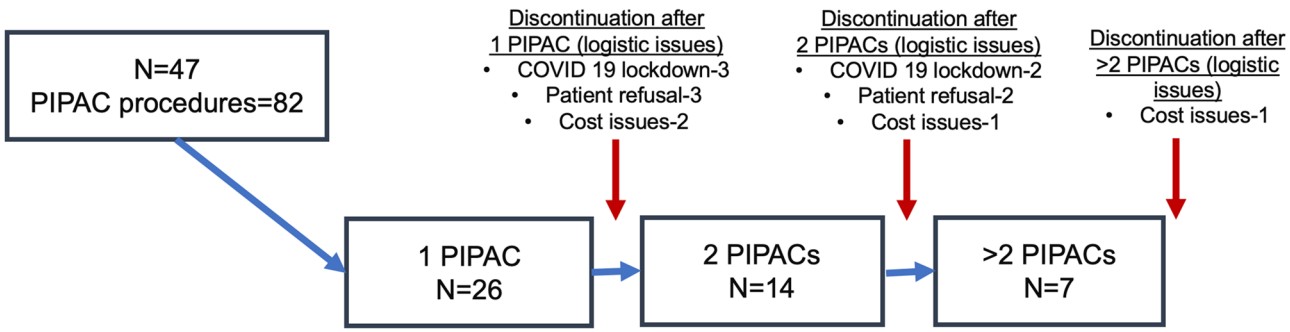
## Morbidity

Grade 1–2 complications were observed in 24 (51%) and grade 3–4 complications in 6 (12.7%) patients (7/82 (8.5%) PIPACs). There were no post-operative deaths. There was one access injury that was surgical repaired and the patient recovered. Another patient with a bowel perforation that occurred 8 days post the second PIPAC with paclitaxel recovered with percutaneous drainage and supportive treatment and was able to resume systemic treatment. One patient developed bowel obstruction 10 days after PIPAC and was not able to take further treatment. One patient had respiratory distress that was managed with non-invasive ventilation in the intensive care unit, and the patient recovered.

## Treatment Response

16/47 (34.0%) patients had some clinical response to PIPAC. Of the 26 patients who received only one PIPAC, 5 (19.2%) had a very good response and were able to undergo CRS and HIPEC. There were 21 patients that had two or more PIPACs, and surgical and pathological evaluation of response was possible in these patients. The median PCI for the first PIPAC procedure was 24 [range 12–39] and for the last one was 19 [range 10–37]. The mean PCI for the first PIPAC procedures was $25.9 \pm 9.2$ and $22.4 \pm 9$ for the subsequent PIPACs. Thus, an average reduction of 3.6 points [change in PCI ranged from $-14$ to $+8$] was observed overall in patients who had more than one procedure. The PRGS was 1 or 2 in 4/47 (8.5%) patients (4/21 (19.0%) patients who had more than 1 PIPAC) (Table 3).

In 31 patients with ascites, a reduction in ascites was observed in 11 (35.4%) patients. Nine (19.1%) patients had conversion to operability leading to a subsequent CRS ± HIPEC in 8 patients: 5 had 1 PIPAC, 2 had 2 PIPACs, and 2 patients had 3 PIPACs (Fig. 1). One patient who had operable disease after PIPAC refused CRS and preferred to continue with SC alone. In one patient, PIPAC was used as a bridge to a planned CRS. There were two patients with epithelial ovarian cancer, three with gastric and one each with peritoneal mesothelioma, colorectal cancer, and PMP that had conversion from inoperable to operable disease. Regarding the two patients with ovarian cancer, one had extensive disease at presentation that poorly responded to NACT. After the addition of PIPAC, she was able to undergo a complete CRS. The second patient had a first recurrence that was partially platinum sensitive, and the disease responded well to the combination of PIPAC and SC. PIPAC was added as SC alone did not produce a good response.




| | | | |
|---|---|---|---|
| Major complications | 2 (9.5%) | 2 (14.2%) | 2 (28.5%) |
| Conversion to CRS | 5 (23.8%) | 2 (14.2%) | 2 (28.5%) |
| Decrease in ascites | 5 (23.8%) | 4 (28.5%) | 2 (28.5%) |
| Disease progression* | 13 (61.9%) | 6 (42.8%) | 2 (28.5%) |
| PRGS 1/2 | 0 | 1 (7.1%) | 3 (42.8%) |

**Fig. 1** Major clinical outcomes after one, two, and more than two PIPAC procedures. Abbreviations: CRS, cytoreductive surgery; PRGS, peritoneal regression grade score. *Based on clinical and/or radiological evaluation

**Table 3** Clinical details of 82 PIPAC procedures using taxanes performed in 47 patients

| Variable | | No of procedures $N=82$ $N$ (%) |
|---|---|---|
| Sex | Male | 35 (40.2) |
| | Female | 47 (59.8) |
| Primary tumor site | Colorectal | 22 (25.2) |
| | Ovary | 27 (31.0) |
| | Stomach | 17 (19.5) |
| | Mesothelioma | 10 (11.4) |
| | Others | 6 (6.8) |
| Ascites^ | Present | 45 (54.8) |
| | Absent | 37 (45.2) |
| Difficult access | Yes | 14 (17.0) |
| | No | 68 (83.0) |
| PCI | < 10 | 5 (6.0) |
| | 11–20 | 14 (17.0) |
| | 21–30 | 31 (39.0) |
| | 31–39 | 22 (25.2) |
| Mean PCI when more than one PIPAC procedure was performed ($N=56$) | During the first procedure | 25.9 ± 9.2 |
| | During subsequent PIPACs | 22.4 ± 9.0 |
| PIPAC regimen | Paclitaxel | 5 |
| | Docetaxel + cisplatin + adriamycin | 57 |
| | Docetaxel + oxaliplatin + adriamycin | 20 |
| Duration of PIPAC (application time | 30 min | 82 (100.0) |
| | Any other | 0 (0.0) |
| Additional surgical procedure | Adhesiolysis | 2 (2.4) |
| | Hernia repair | 1 (1.2) |
| | Omentectomy | 0 (0.0) |
| | Oophorectomy | 0 (0.0) |
| | CRS | 0 (0.0) |
| | Bowel anastomosis | 0 (0.0) |
| | Thoracic CRS | 2 (2.4) |
| | PITAC | 2 (2.4) |
| PRGS | 4 | 17 (20.7) |
| | 3 | 13 (15.8) |
| | 2 | 5 (6.0) |
| | 1 | 2 (2.4) |
| | Not assessed | 47 (59.8) |
| Median hospital stay (days) | | 2 [1–15] |

^All the PIPACs in which ascites was present are considered

Abbreviations: *PCI* peritoneal cancer index, *CRS* cytoreductive surgery, *PITAC* pressurized intrathoracic chemotherapy, *PRGS* peritoneal regression grade score

## Discussion

This preliminary experience of performing PIPAC with taxanes in addition to drugs commonly used for performing PIPAC shows that it is feasible and safe. The major morbidity of 8.5% in all PIPAC procedures is similar to that reported for PIPAC with oxaliplatin and cisplatin-adriamycin [31–33]. Paclitaxel as a single agent was discontinued because of a perforation in 1 patient but its role as should be explored in future studies. The cumulative toxicity needs to be studied in a larger series with patients undergoing 3 PIPACs. Though the superiority of the combination of PIPAC and systemic therapy over PIPAC has not been proven, both centers preferred to perform PIPAC in combination with SC; as a result of which, 85% of the patients received concurrent SC [34]. The response rate of nearly 35% and conversion to resectability in nearly 20% are encouraging since only 15% patients had 3 or more PIPACs.

There is no preclinical data on taxane-PIPAC, but both drugs have been used extensively for IPC either alone or in combination with other drugs in case of docetaxel. We had to modify the technique of PIPAC to administer docetaxel and platinum agents in different syringes. Though docetaxel is "Y compatible" with cisplatin, adriamycin, and oxaliplatin, we preferred not to mix the taxane and the platinum. "Y" compatibility refers to the administration of a single drug simultaneously at a Y-site connection with another drug. Each drug is in a different solution.

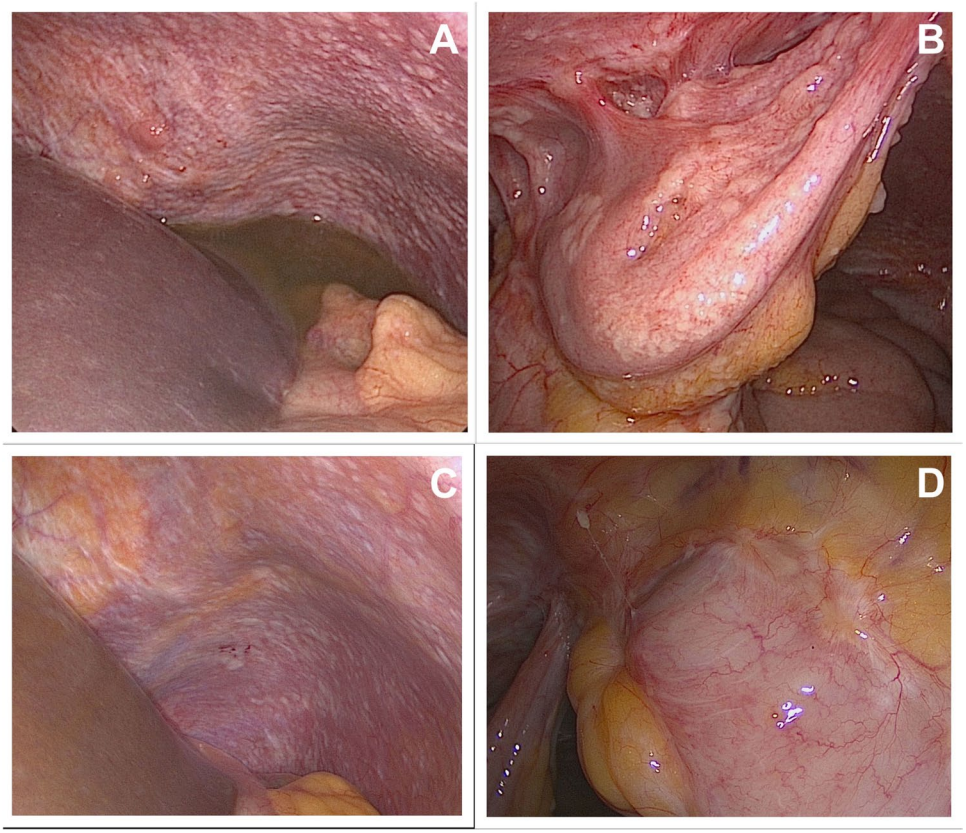



**Fig. 2** The peritoneal disease in a patient with advanced ovarian cancer who had a poor response to 3 cycles of systemic chemotherapy and was treated with systemic chemotherapy and PIPAC subsequently. **A** and **B** Peritoneal deposits before the first PIPAC. **C** and **D** Peritoneal deposits after the first PIPAC

There is a theoretical risk of exposure to aerosolized chemotherapy to individuals present inside the operating room during PIPAC. Studies performed on the distribution of aerosol in the operating in which extensive sampling of the surrounding surfaces for the presence of cisplatin after PIPAC was performed have shown very low levels of cisplatin around the operating table and in the air if the recommended measures like laminar flow ventilation and balloon trocars are used [35].

Only 45% of the patients underwent more than one PIPAC. In a third of the patients, this was due to logistic regions like lockdowns during the pandemic that prevented them for coming for the scheduled treatment or financial constraints. Our patient selection was at times not very ideal as we had to perform this treatment as a last ditch in patients who had exhausted all other therapeutic options and were symptomatic from the PM. Forty-five percent of the patients had disease progression due to which PIPAC was discontinued.

One patient developed bowel injury during port placement, and another patient developed an ileal perforation 8 days following the PIPAC procedure. In our experience, even in the absence of signs of subacute obstruction, patients who have abdominal pain confined to one region or have clumping of bowel loops in one region (e.g., along the scar of a previous surgery) are the ones who could develop a perforation, and though access may not be a problem, PIPAC seems to be of limited use in these patients. So far no predictive factors for a response to PIPAC have been identified for any of the primary tumors. In our experience, patients with miliary disease respond better compared to those with large deposits (lesion score 2/3 versus 1) though we have not investigated this formally [26].

The unexpected finding was the conversion to operability in 9 (19.1%) patients considering that < 50% of the patients had more than 1 PIPAC. Some patients had a very good response to 1 PIPAC alone (Fig. 2). When the disease became resectable after 1 PIPAC, we chose not to perform the second PIPAC due to cost constraints. The procedure was terminated after an evaluation of the disease extent, and biopsies had been performed. The intensification of the PIPAC regimen could be responsible for this. In two recent publications, 14.3% of the patients with gastric cancer and 54% patients with peritoneal mesothelioma had conversion to resectable disease [2, 36]. However, nearly 50% of the patients in both series had 3 or more PIPACs. The best method of assessing a response to PIPAC is still uncertain [37]. Nearly 35% of the patients had a reduction in ascites, and another 20% were able to undergo CRS. A grade 1 or 2 PRGS score was observed in < 10% of the total PIPAC and in 18.9% (7/37 PIPACs) of the procedures for which it was

evaluated (Table 3). Several patients experienced symptomatic relief though the PRGS was grade 3 or 4.

This study has several limitations like the retrospective nature and a small sample size with the inclusion of different primary tumors. The selection criteria and indications were not uniform, and more than half the patients had only one PIPAC. Due to the heterogeneity of the patient population, it is not possible to study the response for different primary tumors separately or present the survival data. Thus, the impact of molecular profile, systemic chemotherapy, and other factors on the response cannot be elucidated. Quality-of-life scores that would more accurately capture the benefit of PIPAC are not available. The drugs were aerosolized separately leading to doubling of the time for aerosolization, but it may be possible to combine all the drugs except oxaliplatin in the same syringe. Despite these limitations, this is the first report on the use of taxane-PIPAC showing its feasibility and safety, and the response rates are encouraging. It is unclear whether systemic antitumor activity and IP activity of drugs are similar. The role of PIPAC with paclitaxel and docetaxel should be evaluated in well-designed studies for different primary tumors.

## Conclusions

PIPAC with docetaxel in combination with other drugs commonly used for performing PIPAC is feasible and safe. The best methodology for using these drug combinations for PIPAC needs further evaluation. The role of PIPAC with both docetaxel and paclitaxel for different primary tumors should be investigated.

## Declarations

**Conflict of Interest** The authors declare no competing interests.

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