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Case Report

Introducing Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) in Peritoneal Surface Malignancy: First experience from Nepal

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ABSTRACT

Introducing Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) in Peritoneal Surface Malignancy: First experience from Nepal

Introduction: Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) has emerged as a novel approach to deliver intraperitoneal chemotherapy effectively and safely, in patients with peritoneal metastases from various primary. Gastric cancer with peritoneal metastases carries a poor prognosis, and treatment is often palliative. This report describes the first Nepalese experience with the use of PIPAC combined with systemic chemotherapy in the management of peritoneal disease from gastric carcinoma.

Methods: The treatment was undertaken at Bhaktapur Cancer Hospital, a comprehensive cancer hospital in Kathmandu.

Case History: A 29-year-old male diagnosed with carcinoma of the stomach was found to have peritoneal metastases with a low Peritoneal Cancer Index (PCI) of 3 on staging laparoscopy. He received neoadjuvant systemic chemotherapy with the FLOT regimen (5-fluorouracil, leucovorin, oxaliplatin, and docetaxel) along with PIPAC using cisplatin and doxorubicin. Treatment response was assessed clinically and radiologically after completion of neoadjuvant therapy.

The patient demonstrated a favourable response clinically and radiologically. He subsequently underwent complete cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) using cisplatin and

doxorubicin. The postoperative period was uneventful, and the patient successfully completed the remaining cycles of systemic FLOT chemotherapy. However, the long-term survival benefit is yet to be determined.

Conclusion: This case highlights the feasibility and safety of incorporating PIPAC as part of a multimodal treatment approach for gastric cancer with limited peritoneal metastases. Although the overall treatment duration was long and complex, this approach represents a ray of hope for carefully selected patients, offering the potential for disease control and improved long-term outcomes even in resource-limited settings.

Keywords: Carcinoma stomach; Peritoneal surface malignancy; Pressurized intraperitoneal aerosol chemotherapy

INTRODUCTION

Pressurized intraperitoneal aerosol chemotherapy (PIPAC) is a minimally invasive technique in which cytotoxic drugs are aerosolized using special aerosol generator and administered into the peritoneal cavity under pressure. PIPAC has increasingly been investigated for unresectable peritoneal metastases (PM) from gastrointestinal and gynecological malignancies.

Gastric cancer remains a major health problem around the globe. PM from gastric cancer occurs in 15-30% of patients at initial diagnosis and additionally 40-60% patients experience PM as the sole site of recurrence after curative intent treatment.[1,2] The presence of PM is traditionally associated with a poor prognosis and has generally been managed with systemic chemotherapy with palliative intent. The limited penetration of intravenously administered chemotherapy into PM and thereby poor response, has led to the development of regional treatment strategies like normothermic intraperitoneal chemotherapy (NIPC), hyperthermic intraperitoneal chemotherapy (HIPEC), early post-operative intraperitoneal chemotherapy (EPIC) and PIPAC, each has its own indication, advantages and disadvantages.[3]

Although PIPAC has mainly been used with palliative intent, its potential role as a neoadjuvant or conversion strategy before CRS and HIPEC has generated increasing interest.[4] PIPAC may allow repeated treatment of peritoneal disease while systemic chemotherapy controls extra-peritoneal disease and may provide an opportunity to assess tumor biology before definitive surgery. Current evidence in gastric cancer is encouraging but remains based predominantly on retrospective studies and small prospective series.[5,6]

We report a first documented use of PIPAC in Nepal in a young patient with gastric adenocarcinoma and limited peritoneal disease, in whom PIPAC was incorporated between systemic chemotherapy and he underwent subsequent CRS and HIPEC and completed the intended treatment.

CASE REPORT

A 29-year-old man presented with abdominal discomfort and was diagnosed with locally advanced carcinoma of the stomach on imaging. His case was discussed in a multidisciplinary tumor board, and staging laparoscopy was performed to determine the extent of peritoneal disease as per unit protocol.

Laparoscopy revealed peritoneal deposits predominantly in the upper abdomen. The PCI was 3. Peritoneal biopsy confirmed adenocarcinoma consistent with gastric primary. In view of biopsy-proven peritoneal metastasis, upfront curative gastrectomy was not considered appropriate, and systemic chemotherapy with FLOT was initiated.
After completion of three cycles of FLOT, the patient was reassessed by the multidisciplinary team. Considering his young age, limited initial peritoneal tumor burden, and potential for subsequent complete cytoreduction, PIPAC was incorporated into the treatment strategy.

PIPAC was performed on 17th April 2025 according to standard protocol. This represented the first documented PIPAC procedure performed in Nepal. At laparoscopy, there was no ascites and the pelvis was free of gross peritoneal disease. A deposit in the region of the falciform ligament was identified and was negative for tumor on assessment. After confirming no air leak with one camera port and second injection port, a solution of cisplatin (12mg) and doxorubicin(2mg) diluted in normal saline was sequentially aerosolized at pressure 200psi, flow 30ml/min, 150ml using a CE-certified nebulizer (CapnoPen ®, CapnoPharm) for 5mins and capnoperitoneum was maintained for 30 mins, the toxic aerosol was safely removed via a closed waste system after the procedure. The patient tolerated the procedure well and discharged the next day.
Systemic chemotherapy was re-started (FLOT, cycle 4) after 4 weeks. Following further multidisciplinary reassessment, he was considered suitable for definitive CRS and HIPEC.

He was taken for CRS and HIPEC, at exploration, peritoneal disease was identified with a PCI of 8. Complete cytoreduction was achieved with a completeness of cytoreduction score of CC-0. The procedure included total gastrectomy with Roux-en-Y GJ, splenectomy, appendicectomy, omentectomy, regional peritonectomy and excision of visible peritoneal deposits. HIPEC was performed using cisplatin (75mg/m^2) and mitomycin-C (15mg/m^2) in 2800 mL of perfusate for 60 minutes at 41-43 Celsius using Medica *Flexiper* pump.

The postoperative recovery was smooth, without major postoperative complications. Systemic chemotherapy was subsequently resumed after 6 weeks of CRS and HIPEC, and the patient completed a total of eight cycles of FLOT, with the final cycle administered on 26th Oct 2025 and is on routine follow-up.

DISCUSSION

Peritoneal metastasis remains a major therapeutic challenge in gastric cancer. Systemic chemotherapy remains the backbone of treatment however the peritoneal compartment represents a distinct therapeutic environment in which adequate drug penetration is limited. This is the reason for increasing interest and birth of various intraperitoneal drug delivery mechanism like NIPS, EPIC, HIPEC and PIPAC.[3]

PIPAC was first introduced into clinical practice by Reymond and colleagues on 5th Nov 2011 in Germany, followed by clinical studies demonstrating the feasibility of repeated procedures.[7] Since then, the technique has progressively expanded world wide as a locoregional treatment option for patients with PM.

In gastric cancer, PIPAC has predominant role in unresectable PM. A systematic review involving 18 studies and 751 patients reported median OS ranging from 8 to 19.1 months, however the evidence in heterogenous and no phase III trial is available.[6] The use of PIPAC as a potential bridge to definitive surgery is particularly relevant to the present case. The use of PIPAC as a neoadjuvant therapy before CRS and HIPEC is reported where radiological regression was observed in seven of nine patients and major histological regression was observed in eight patients, allowing subsequent CRS and HIPEC in selected patients (5.2%), with mean number of 3.5+/-0.9 cycles though this study include different primary malignancy and not particularly gastric cancer.[4]

The significance of this case report lies in the introduction of PIPAC as a treatment modality for peritoneal metastasis (PM) in Nepal, this represents the first reported case from Nepal in which PIPAC was utilized for the management of PM secondary to gastric cancer. A similar case of gastric cancer with concomitant liver and peritoneal metastases was successfully managed using a multimodal approach comprising neoadjuvant PIPAC, definitive surgery and systemic chemotherapy resulting in a favorable outcome.[8]

In our case, PCI increased from 3 at staging laparoscopy to 8 at the time of CRS, this may be due to underestimation during laparoscopy as PCI estimation may vary between open and laparoscopic assessment with underestimation occurring in a substantial proportion of patients.[9]

This experience demonstrates the feasibility of integrating advanced intraperitoneal therapy technique with systemic chemotherapy and subsequent CRS-HIPEC in a resource-constrained setting in the management of patients with PM.

CONCLUSION

PIPAC may have a potential role as a neoadjuvant or conversion component of multimodal treatment for carefully selected gastric cancer patients with limited peritoneal metastasis. In this case, PIPAC was successfully integrated between FLOT chemotherapy and subsequent CRS-HIPEC, achieving CC-0 cytoreduction and allowing completion of systemic treatment. This first reported experience from Nepal demonstrates the feasibility of establishing PIPAC

within a multidisciplinary gastric cancer program. However, the single-case nature and short follow-up preclude conclusions regarding long-term oncological efficacy.

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