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COLORECTAL / GASTRIC / OTHERS DIGESTIVE PERITONEAL METASTASES

BC01

HIPEC FOR GASTRO-INTESTINAL NEUROENDOCRINE NEOPLASMS: AN PROPENSITY SCORE MATCHED ANALYSIS OF ALL HIPEC CENTERS IN THE NETHERLANDS AND BELGIUM

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Objectives

Cytoreduction and hyperthermic intraperitoneal chemotherapy (HIPEC) is the only potentially curative treatment option for patients with peritoneal metastases (PM) of colorectal cancer. Its value for patients with PM of gastro-intestinal neuroendocrine neoplasms (GI-NENs) remains unclear. This study compared outcomes of cytoreduction and HIPEC to surgery alone for peritoneally metastasized GI-NENs: typical neuroendocrine tumors, neuroendocrine carcinomas, goblet cell carcinoids (GCCs), and mixed adeno-neuroendocrine carcinomas (MANECs). These data are presented in the light of a systematic review.

Methods

Data from two cohorts of GI-NEN patients with PM were obtained: (1) a cohort treated with cytoreduction and HIPEC in all thirteen Dutch and Belgian HIPEC centers; (2) a cohort treated with surgery alone from the Netherlands Cancer Registry. Primary and secondary outcomes were overall survival (OS) and morbidity and mortality, respectively. After propensity score matching to adjust for selection bias, OS was tested in univariate and multivariate survival analysis. A systematic review was conducted according to the PRISMA guidelines.

Results

After correction for gender, tumor stage, lymphnode stage, and the presence of liver metastases, cytoreduction and HIPEC was associated with improved survival compared to surgery alone in GCC and MANEC patients. This difference was significant in univariate (39 versus 12 months, $p < 0.001$) and multivariate analysis (HR 4.27, 95%-CI 1.88–9.66, $p = 0.001$). No improved OS was seen in other GI-NEN subgroups. Relatively low grade III-IV morbidity (17.5%) and mortality (0%) were seen after HIPEC. The present results are comparable with the literature found in the systematic search.

Conclusion

Cytoreduction and HIPEC could improve survival in patients with PM of GCCs and MANECs and is a safe treatment option. Treatment of GI-NEN patients in high-volume centers and prospective registries should provide the evidence enabling clinical decision-making on HIPEC in other GI-NEN subgroups.

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COLORECTAL / GASTRIC / OTHERS DIGESTIVE PERITONEAL METASTASES

BC02

PRESSURIZED INTRAPERITONEAL AEROSOL CHEMOTHERAPY (PIPAC) FOR NONRESECTABLE PERITONEAL METASTASIS FROM GASTRIC CANCER

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Objectives

PIPAC is a recent approach for intraperitoneal chemotherapy with promising results for patients with peritoneal metastasis (PM). We aimed to evaluate survival and postoperative outcome of PIPAC in patients with non-resectable PM from gastric cancer.

Methods

This is a retrospective analysis of prospective maintained PIPAC database of Lyon Sud university hospital of all patients diagnosed with non-resectable PM from gastric cancer before January 2017 and underwent at least one PIPAC procedure. PIPAC with Cisplatin 7.5 mg/m² and doxorubicin 1.5 mg/m² were administrated for 30 min at 37 °C and 12 mmHg at 6-week intervals. The treatment schedule proposed alternating 2 systemic chemotherapy cycles followed by 1 PIPAC procedure. Outcome criteria were survival, adverse events according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

Results

One hundred sixty-three PIPAC were applied in 42 consecutive patients including 22 (52%) female. At the time of the first PIPAC, median age was 51.5 years (32–74). Median PCI was 17 (1–39). Twenty (47.6%) patients underwent more than 2 lines of preoperative chemotherapy. Median consecutive PIPAC cycles were 3 (1–12). Overall and major complications (CTCAE - III, IV) occurred for 10 PIPAC (6.1%) and 5 (3.1%) respectively. Two patients died within 30 days after the PIPAC procedure due to small bowel obstruction for one and pulmonary embolism for the other patient. Overall Survival was 17.5 months. Four (9.5%) patients became resectable and underwent complete cytoreductive surgery and HIPEC.

Conclusion

PIPAC with low-dose cisplatin and doxorubicin is safe and feasible in association with systemic chemotherapy. Survival data are encouraging and justify further clinical studies in this indication.

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TRANSLATIONAL RESEARCH

BC03

A FIRST IN MAN STUDY OF DIRECT INJECTION OF BROMELAIN AND N-ACETYLCYSTEINE INTO RECURRENT PSEUDOMYXOMA PERITONEI OF APPENDICEAL ORIGIN

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Objectives

Appendiceal neoplasms account for approximately 1% of all colorectal malignancies. Advanced disease is often the result of tumour perforation and seeding of tumour cells within the peritoneal cavity, leading to pseudomyxoma peritonei (PMP). The combined modality of complete CRS/HIPEC is considered standard of care for appendiceal tumours with curative intent. Many patients with PMP achieve long-term survival although in a significant proportion, recurrence following CRS/HIPEC occurs, and repeat interventions have a negative impact on quality of life, risks of the procedure outweigh the benefits, and is a considerable strain on health systems. In an attempt to modify these outcomes, mucin and mucin-producing tumours have remained the two main targets of our research. We discovered remarkable synergy between Bromelain (Br) and N-acetylcysteine (NAC), and together this new method of treatment was able to completely dissolve PMP mucin in vitro and in the peritoneum of rodents.

Methods

We recently began a phase I study to examine in a clinical setting, the efficacy and safety of applying Br/NAC directly into recurrent PMP deposits in 20 patients with low grade or mucinous appendix tumours that are found to be unsuitable for repeat surgery. As at April 2018, nine patients have been enrolled and three patients have been treated. The aim of this study is to assess whether the application of Br/NAC dissolves the tumour, allowing for it to be aspirated. The efficacy of this intervention will be assessed by follow up radiological imaging with the expectation that this combination treatment will result in dissolution and removal of the tumour.

Results

No haematological side effects have been seen. One patient complained of pain after the injection, which was managed with analgesia (PCA). All patients received multiple injections. Patient 1 had six doses into multiple peritoneal tumours across days 1, 7, 12 and 17. Patient 2 had 3 doses into a large pelvic tumour across days 1 and 3. Patient 3 had two doses into a pelvic sidewall tumour on day 1. After treatment, it was possible to aspirate large volumes of viscous tumour from the cavities. Follow up computed tomography scans at 1 week demonstrated significant reduction in the diameter of tumour areas treated.

Conclusion

Based on these preliminary clinical results and extensive laboratory and animal data, direct injection of Bromelain and N-acetylcysteine may provide a new, minimally invasive therapy for removal of recurrent PMP.

I.a) Best communications**PERITONEAL MESOTHELIOMA AND PSEUDOMYXOMA PERITONEI****BC04****CYTOREDUCTIVE SURGERY AND MULTIVISCERAL SMALL BOWEL TRANSPLANTATION.**

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Cytoreductive surgery and HIPEC can cure Pseudomyxoma. With extensive small bowel involvement or recurrence inevitable disease progression causes small bowel obstruction, abdominal wall failure with fistulation and nutritional failure. Poor quality of life results and is eventually fatal. TPN improves nutrition but does not palliate massive abdominal distention and abdominal wall failure. Multi visceral small bowel transplantation could offer a life prolonging option in endstage disease.

Methods

Between 2013–2018, 15 patients were referred for possible transplantation. 2 not fit died, 1 died on waiting list, 4 currently under assessment and 8 end stage pmp patients, following discussion at the Peritoneal Malignancy SMDT and National Transplant MDT, underwent small bowel transplantation. The peritoneal malignancy and transplant teams jointly performed the procedures.

Results

3 patients had radical debulking and 5 complete cytoreduction followed by transplantation. Organs transplanted: 2 isolated small bowel transplants 6 modified multivisceral transplants including stomach, duodenum-pancreatic complex, small bowel and abdominal wall; 4 received colon and 1 kidney. Operation time dropped from 18 hrs to 13 hrs and transfusion requirements from 35 to 6 units. Mortality: 5 alive at time of review, 36, 31, 20, 17 and 6 months from surgery; 3 died (Day 26, 64 and 5 months post op) 1) anastomotic leak Graft versus host disease (GVHD) and chest sepsis 2) GI bleed and anastomotic leak 3) GVHD and bone marrow failure (perfect match). No rejection of intestinal grafts seen. Surviving patients independent of TPN and well at home. One has radiological progression of disease and symptomatic extensive thoracic disease and two with areas of radiological recurrence and two currently disease free

Conclusion

Multi-visceral small bowel transplantation is technically feasible for endstage PMP. It is life transforming giving an extra 6–36 months independent of TPN and excellent quality of life to date. Long term outcomes remain to be determined. This major surgical intervention requires close collaboration between peritoneal malignancy and transplant teams.

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PERITONEAL MESOTHELIOMA AND PSEUDOMYXOMA PERITONEI

BC05

DOES HYPERTERMIC INTRAPERITONEAL CHEMOTHERAPY HAS AN ADDITIONAL BENEFIT OVER CYTOREDUCTION ALONE IN PSEUDOMYXOMA PERITONEI? A PROPENSITY SCORE ANALYSIS OF THE PSOGI DATABASE

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Objectives

We evaluated the differences in survival and side effects associated with HIPEC after Cytoreductive surgery (CRS) in pseudomyxoma peritonei (PMP).

Methods

From the PSOGI database containing 3400 PMP cases we selected 1924 patients with complete information regarding the main prognostic factors and intraperitoneal treatments: age, prior surgical score (PSS), prior chemotherapy (PCT), histological subtype (high & low grade [WHO]), lymph node status (LN), completeness of cytoreduction (CC), peritoneal cancer index (PCI), and HIPEC/EPIC. We built multivariable logistic models containing the above-mentioned prognostic factors and EPIC treatment (yes, no) to estimate the propensity score (PS) for HIPEC treatment. Inverse probability treatment weighting (IPTW) based on PS was used to balance the comparisons between CRS alone group and CRS/HIPEC group and in the following prognostic scenarios: overall PMP (376 vs. 1548 pts), completely cytoreduced cases (164 vs. 1352 pts), cc-2 (37 vs. 79 pts), cc-3 (175 vs. 117 pts), low-grade PMP (197 vs. 1056 pts), and high-grade PMP (179 vs. 492 pts).

The standardized mean difference (SMD) was used to evaluate the balancing results.

The outcomes of interest were overall survival (OS) and severe morbidity (NCI-CTCAEv3). Differences in OS and odds ratio (OR) of severe morbidity were assessed by means of IPTW weighted log-rank tests and logistic regression models.

Results

The SMD of all prognostic factors and EPIC treatment between the CRS and CRS/HIPEC groups did not overcome the threshold level of 0.1 across all prognostic scenarios indicating very good balancing. HIPEC was not statistically associated with different risk of severe morbidity in none of the comparisons performed, even being protective in the cc-3 subgroup (OR: 0.61, p-value = 0.032). Finally, with the exception of the cc-2 subgroup, HIPEC was associated with a significantly better weighted 5-yr OS: 58% vs. 46% (p: 0.004) in overall PMP; 77% vs. 71% (p: 0.009) in cc-0/1; 27% vs. 13% (p: 0.019) in cc-3; 74% vs. 64% (p: <0.001) in low grade PMP; and 40% vs. 27% (p: 0.002) high-grade PMP.

Conclusion

HIPEC was associated to better OS when performed after CRS in PMP without increased risk of severe morbidity. The prognostic benefit was not observed in cc-2 patients.

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ANESTHESIA / EARLY RECOVERY / PREOPERATIVE PREPARATION / NUTRITION

BC06

ASSOCIATION BETWEEN EPIDURAL ANALGESIA AND OUTCOME IN PATIENTS OPERATED WITH CURATIVE INTENT OF PERITONEAL CARCINOMATOSIS: A COHORT STUDY OF 606 PATIENTS

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Objectives

Local anesthetics could have beneficial effects on cancer-related recurrence and mortality. The aim of this study was to evaluate the effect of local anesthetics on progression-free survival (PFS) and overall survival (OS) in patients with peritoneal carcinomatosis (PC) who received Hyperthermic Intra Peritoneal Chemotherapy (HIPEC).

Methods

Between 2006 and 2016, 606 patients were operated with curative intent for PC arising from digestive or ovarian cancer with or without an intra and postoperative epidural analgesia. Complete cytoreductive surgery and HIPEC was performed in 85% of the cases. Demographic characteristics, ASA score, carcinomatosis origin and completion of complete resection were recorded. A propensity score matching was used to obtain 2 similar groups (epidural versus without epidural). Propensity score model included main demographic and prognostic variable. Primary outcome was PFS; secondary outcomes included OS, hospital length of stay (LOS) and postoperative complications (POC).

Results

The study population was 58 years old patients, 56% female, with an ASA score of II (72%). Primitive cancers were colorectal (52%), peritoneal pseudomyxoma (15%) and ovarian (11%) cancer. 66% of patients received an epidural and 73% reached complete resection of PC. There was a significant increase in PFS (HR 0.75, 95% CI: 0.58–0.99) and OS in the epidural group (HR 0.59 (95% CI: 0.35–0.98), that was not confirmed after propensity score matching analysis. We also found an increase in PFS in the group of patients with an epidural and complete resection or with peritoneal pseudomyxoma. There was no significant difference for LOS and POC.

Conclusion

This study suggests that local anesthetics administration via an epidural may reduce recurrence in specific groups of patients with PC especially when complete resection is achievable or patient with peritoneal pseudomyxoma.