TITLE: Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Carcinomatosis: Clinical Effectiveness and Guidelines

DATE: 01 November 2016

RESEARCH QUESTIONS

1. What is the clinical effectiveness of hyperthermic intraperitoneal chemotherapy for the treatment of peritoneal carcinomatosis?

2. What are the evidence-based guidelines regarding hyperthermic intraperitoneal chemotherapy for the treatment of peritoneal carcinomatosis?

KEY FINDINGS

Two systematic reviews, two randomized controlled trials, four non-randomized studies, and one evidence-based guideline were identified regarding hyperthermic intraperitoneal chemotherapy for the treatment of peritoneal carcinomatosis.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2011 and October 17, 2016. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.
SELECTION CRITERIA

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Adult patients with peritoneal carcinomatosis/carcinosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Hyperthermic intraperitoneal chemotherapy (HIPEC)</td>
</tr>
<tr>
<td>Comparator</td>
<td>Alternate cancer treatments (e.g., systemic chemotherapy), placebo, no treatment</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Clinical benefits and harms (e.g., survival, morbidity and mortality), guidelines</td>
</tr>
<tr>
<td>Study Designs</td>
<td>Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, evidence-based guidelines</td>
</tr>
</tbody>
</table>

RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and evidence-based guidelines.

Two systematic reviews, two randomized controlled trials, four non-randomized studies, and one evidence-based guideline were identified regarding hyperthermic intraperitoneal chemotherapy for the treatment of peritoneal carcinomatosis. No relevant health technology assessments were identified.

Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

Two relevant systematic reviews\(^1,2\) (SRs) were identified. One review\(^1\) examined the literature regarding hyperthermic intraperitoneal chemotherapy (HIPEC) for the treatment of gastric peritoneal metastasis. The authors identified a small number of relevant trials and concluded that HIPEC may be effective when a complete, or almost complete, resection of the peritoneal metastases can be successfully done. The second SR\(^2\) focused on patients with colorectal cancer with liver and peritoneal metastases who underwent resection and HIPEC. The authors identified a trend towards an increase in median survival for patients who underwent resection of both types of metastases with HIPEC as compared to similar patients who underwent modern systemic chemotherapy.

Two randomized controlled trials\(^3,4\) and four non-randomized studies\(^5-8\) were identified. The characteristics and results of these studies are summarized in Table 2.

One guideline\(^9\) from the American Society of Colon and Rectal Surgeons was identified that recommends “the treatment of patients with peritoneal carcinomatosis should be
multidisciplinary and individualized and may include surgical cytoreduction. The role of intraperitoneal chemotherapy remains insufficiently defined." (page 838)

<table>
<thead>
<tr>
<th>Table 2: Summary of Clinical Study Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First Author, Year</strong></td>
</tr>
<tr>
<td>--------------------------</td>
</tr>
<tr>
<td><strong>Randomized Controlled Trials</strong></td>
</tr>
</tbody>
</table>
| Rudloff, 2014⁴ | Patients with measurable metastatic gastric adenocarcinoma involving the peritoneum N = 17 | Gastrectomy, metastasectomy, HIPEC and systemic FOLFOXIRI versus FOLFOXIRI alone | • Median OS was 11.3 months for the combined intervention and 4.3 months in the chemotherapy group  
• Two patients in the combined group survived beyond 12 months |
| Yang, 2011⁵ | Peritoneal carcinomatosis of gastric cancer N = 68 | CRS + HIPEC versus CRS alone | • Median survival  
  o HIPEC group = 11.0 months  
  o surgical group = 6.5 months  
• Median follow-up of 32 months  
  o 85.3% of patients in the HIPEC group had died  
  o 97.1% of patients in the surgical group had died  
• The authors suggested surgery + HIPEC may improve survival with acceptable morbidity |
| **Non-Randomized Studies** |
| Boemer, 2016⁶ | Peritoneal carcinomatosis of gastric cancer N = 38 | Gastrectomy + CRS + HIPEC versus Palliative management (with or without gastrectomy) | • Median survival time  
  o CRS + HIPEC = 17.2 months  
  o Palliative = 11.0 months  
• Two year survival  
  o CRS + HIPEC = 35.8%  
  o Palliative = 16.9% |
| Huang, 2014⁵ | Colorectal cancer peritoneal carcinomatosis | CRS + HIPEC versus | • Complete cytoreduction  
  o CRS + HIPEC = 42.4% |
<table>
<thead>
<tr>
<th>First Author, Year</th>
<th>Patient Characteristics</th>
<th>Intervention and Comparator</th>
<th>Results and Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 62</td>
<td>CRS alone</td>
<td></td>
<td>o CRS alone = 31.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Median OS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>o CRS + HIPEC = 13.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>o CRS alone = 8.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• SAEs 30-days post-operative</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>o CRS + HIPEC = 28.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>o CRS alone = 9.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• The authors concluded that CRS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+ HIPEC could improve OS for</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>these patients</td>
</tr>
<tr>
<td>Marcotte, 2014^7</td>
<td>Appendiceal peritoneal</td>
<td>CRS + HIPEC (oxaliplatin)</td>
<td>• 5 year OS for the whole</td>
</tr>
<tr>
<td></td>
<td>carcinomatosis</td>
<td>versus</td>
<td>cohort = 66.2%</td>
</tr>
<tr>
<td></td>
<td>N = 78</td>
<td>No CRS or HIPEC;</td>
<td>o HIPEC = 77%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative second-look with</td>
<td>o No HIPEC = 9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>no HIPEC</td>
<td>o Second-look = 100%</td>
</tr>
<tr>
<td>Cashin, 2012^8</td>
<td>Peritoneal carcinomatosis from colon cancer</td>
<td>HIPEC versus SPIC</td>
<td>• Median OS</td>
</tr>
<tr>
<td></td>
<td>N = 32</td>
<td></td>
<td>o HIPEC = 36.5 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>o SPIC = 23.9 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Median disease-free survival</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>o HIPEC = 22.8 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>o SPIC = 13.0 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Morbidity was not significantly different between groups</td>
</tr>
</tbody>
</table>

CRS = cytoreductive surgery; EPIC = early postoperative intraperitoneal chemotherapy; FOLFOXIRI = folinic acid, fluorouracil, oxaliplatin, irinotecan; HIPEC = hyperthermic intraperitoneal chemotherapy; OS = overall survival; SPIC = normothermic sequential postoperative intraperitoneal chemotherapy.
REFERENCES SUMMARIZED

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses


Randomized Controlled Trials


Non-Randomized Studies


Guidelines and Recommendations


PREPARED BY:
Canadian Agency for Drugs and Technologies in Health
Tel: 1-866-898-8439
www.cadth.ca
APPENDIX – FURTHER INFORMATION:

Systematic Reviews – Only Executive Summary Available in English


Clinical Practice Guidelines – Methodology Not Specified


Consensus Statements


Non-Randomized Studies

No Comparator Group


Alternate Comparators


Alternate Interventions


Quality of Life


Review Articles


