Effect of Intraperitoneal Hyperthermic Chemoperfusion to Control Malignant Ascites in Patients with Peritoneal Carcinomatosis

KOKURIKI KOBAYASHI*, SHIGERU FUJIMOTO, MAKOTO TAKAHASHI, TAKAAKI MUTOU, TADASHI TOYOSAWA, YASUHIRO OHTSUKA, TAKESHI OGASAWARA

Department of Surgery, Social Insurance Funabashi Central Hospital, 6-13-10, Kaijin, Funabashi, Chiba, JAPAN

Abstract: How to control malignant ascites is one of the important problems for the patients with peritoneal carcinomatosis. In order to assess the efficacy of intraperitoneal hyperthermic chemoperfusion (IHCP), clinical outcome of the 8 patients who had malignant ascites and received IHCP was investigated. The origins of their peritoneal carcinomatosis were gastric cancer in 5 patients, ovarian cancer in 1 patient and unknown in 2 patients. IHCP was performed for 90–120 minutes just after cytoreductive surgery under hypothermic general anesthesia. Heated perfusate with 10 µg/ml of mitomycin C (plus 15–30 µg/ml of CDDP in 2 patients) was circulated in the peritoneal cavity through a closed circuit. The inflow temperature and the outflow temperature of the perfusate were controlled to be 44–46°C, and 43–44°C, respectively. The mean amount of ascites of the 8 patients was 5425 ± 3253 ml (1200–10000 ml). After the treatment, ascites disappeared in 7 of 8 patients (87.5 %). The median ascites free duration of these 7 patients was 5 months (3–17 months). IHCP is suggested to be effective to control malignant ascites of the patients with severe peritoneal carcinomatosis. It may also give them better quality of life and opportunities to receive further treatment.

Key Words: malignant ascites, peritoneal carcinomatosis, intraperitoneal hyperthermic chemoperfusion

Introduction

When we treat patients with peritoneal carcinomatosis, how to control malignant ascites is one of the important problems from the standpoint of treatment strategy and of patient’s quality of life. Although advances have been made these days in chemotherapeutic approaches for the patients with peritoneal carcinomatosis, it is often still difficult to treat these patients, especially when they have already developed considerable amount of malignant ascites.

Since 1986, intraperitoneal hyperthermic chemoperfusion (IHCP) has been performed in our hospital mainly for the patients with gastric cancer for the purpose of treating or preventing peritoneal seeding. Sometimes we also apply this treatment to the patients with peritoneal carcinomatosis of
other origins. In order to assess the efficacy of IHCP treatment to control malignant ascites, we investigate here the clinical outcome of the patients with peritoneal carcinomatosis who had relatively large amount of ascites and received this treatment.

**Patients and Methods**

**Patients**

From July 1993 through December 2002, a total of 30 patients with histologically confirmed peritoneal carcinomatosis underwent IHCP combined with surgery at Funabashi Central Hospital. Among these patients, relatively large amount of ascites (≥1000 ml) was observed at the time of surgery in 8 patients. These 8 patients consisted of 4 men and 4 women with a mean age of 56.5 ± 12.3 years (41 to 77). Their peritoneal carcinomatoses were originated from gastric cancer in 5 patients and ovarian cancer in 1 patient. In 2 patients, the origins of their peritoneal carcinomatoses were not determined even by surgical exploration (Table I).

**IHCP**

IHCP was performed just after surgery under hypothermic general anesthesia. IHCP equipment was set up and inflow and outflow tubes were inserted into the upper abdominal cavity and the Douglas’ cavity respectively. Before the start of IHCP, the body temperature of the patient was lowered with a cooling mat placed under the trunk and ice bags placed around the head and the neck. Heated perfusate (3000–3500 ml) which contained 10 μg/ml of mitomycin C (plus 15–30 μg/ml of CDDP in 2 patients) was circulated in the peritoneal cavity through a closed circuit using 3 pumps (Fig. 1, Fig. 2). The circulation rate of the perfusate was around 2000 ml/min. During IHCP treatment,

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**Table I. Characteristics and outcomes of the patients**

<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>Sex</th>
<th>Primary Organ</th>
<th>Amount of Ascites (ml)</th>
<th>Surgery</th>
<th>Ascites Free Duration (month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>52</td>
<td>M</td>
<td>stomach</td>
<td>1200</td>
<td>laparotomy</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>63</td>
<td>F</td>
<td>unknown</td>
<td>7000</td>
<td>laparotomy</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>67</td>
<td>M</td>
<td>stomach</td>
<td>1300</td>
<td>gastrostomy</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>42</td>
<td>M</td>
<td>stomach</td>
<td>2900</td>
<td>total gastrectomy</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>41</td>
<td>F</td>
<td>stomach</td>
<td>8000</td>
<td>bilat. salpingo-oophorectomy</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>57</td>
<td>F</td>
<td>ovary</td>
<td>10000</td>
<td>hysterectomy</td>
<td>17</td>
</tr>
<tr>
<td>7</td>
<td>53</td>
<td>M</td>
<td>stomach</td>
<td>7000</td>
<td>gastrostomy</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>77</td>
<td>F</td>
<td>unknown</td>
<td>6000</td>
<td>omentectomy</td>
<td>3</td>
</tr>
</tbody>
</table>

*Fig. 1. A view of IHCP equipment in use*
the inflow temperature and
the outflow temperature of
the perfusate were controlled
to be 44~46°C, and 43
~44°C, respectively.

Results

All the 8 patients in this
study had severe peritoneal
carcinomatosis. At the time
of surgery, innumerable
numbers of metastases could
be seen all over the whole
peritoneal surface in any of
these patients. A mean
amount of ascites of 5425±
3253 ml (1200~10000 ml) was observed in the peritoneal cavity of these patients at the beginning of
surgery (Table I).

In 2 patients whose original sites of the tumor had not been known before surgery, biopsies revealed
adenocarcinoma which might be originated from ovarian cancer. However adhesions and
carcinomatosis of these 2 patients were too severe in the abdominal cavity to determine their origins during surgery.
For all these patients, we tried to remove as much tumor as possible for cytoreduction during surgery. However, while 6 of these 8 patients underwent cytoreductive surgery for original tumors and/or metastatic lesions, 2 patients received only laparotomy without being able to remove any lesion.
IHCP was performed for 90~120 minutes. Temperature of the perfusate was maintained between 44°C and 46°C throughout IHCP. The body temperatures of the patients were lowered to 31~32°C before the start of IHCP and they went up to 39~40°C at the end of the treatment. Soon after the treatment, about 2 weeks after surgery when all the drainage tubes had been removed from the abdomen, ascites disappeared in 7 of 8 patients (87.5%). The median ascites free duration of these 7 patients was 5 months (3~17 months). In one patient, ascites could not be controlled by the treatment, and the patient died of the disease one month after surgery (Table I) (Fig. 3, Fig. 4).

Discussion
Intraperitoneal hyperthermic chemoperfusion was originally designed to treat and prevent peritoneal metastasis from gastric cancer. Favorable outcomes have been achieved by IHCP treatment in patients with advanced gastric cancer. In addition, it sometimes has been observed that IHCP exerted its effect also in treating the patients with peritoneal metastasis from other origins.
In general, patients with peritoneal carcinomatosis are treated by means of chemotherapy either intravenously or intraperitoneally (or sometimes orally).

![CT scans of patient No.6 show remarkable reduction of ascites (a) before IHCP, (b) 1 month and (c) 14 months after IHCP](image)
Although some progresses have been made these days in the field of chemotherapeutic approach for the patients with peritoneal carcinomatosis, their effects are usually limited and not satisfactory \(^1\) \(^2\) \(^7\). When the patients already have some amount of ascites and need surgical treatment with laparotomy, not a few surgeons experienced the difficulty in controlling ascites after surgery.

Although previous studies have shown favorable effects of IHCP for the treatment of patients with peritoneal carcinomatosis, long-term survivals could not be expected even by IHCP when their metastases already have spread the whole peritoneal cavity \(^5\). However, the effect of IHCP to reduce ascites is remarkable even when the patients already have severe peritoneal carcinomatosis. In fact, in this study 7 of 8 patients had their massive malignant ascites controlled soon after IHCP treatment. This may be explained by the following characteristic mechanism of antitumor effects of IHCP. As well as being enhanced by hyperthermia \(^8\), the antitumor effect of the chemotherapeutic agents is distributed equally all over the peritoneal surface by circulating a large quantity of the perfusate at a high speed. By approaches other than IHCP, it may be difficult to distribute chemothrapeutic agents in every corner of the peritoneal surface which has a large area and whose shape is very complicated and irregular.

When we manage to treat patients with malignant ascites, it has an important meaning for us to be able to control the amount of ascites. It will not only have great benefit to the patients’ quality of life, but also give them opportunities to receive other treatment options under more favorable condition. Especially when the patients with malignant ascites need surgery because of tumor bleeding or gastrointestinal obstruction, it could be crucial whether we have means to control ascites after surgery.

In conclusion, IHCP is suggested to be an effective treatment to control malignant ascites of the patients with severe peritoneal carcinomatosis, especially when they need abdominal surgeries.

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腹水を伴う癌性腹膜炎患者における
腹腔内温熱化学灌流療法の腹水抑制効果

小林国力・藤本 茂・高橋 誠・武藤 誠明・豊沢 忠
大塚 恭 寛・小笠原 猛

要 | 病性腹膜炎の治療において、腹水のコントロールは重要である。今回、比較的多量の腹水を
有する癌性腹膜炎の症例における腹腔内温熱化学灌流療法（Intraperitoneal Hyperthermic
Chemoperfusion - IHCP）の腹水抑制効果を検討した。対象は当院で手術と IHCP を施行した癌性腹水を
伴う患者 8 例である。男性 4 例、女性 4 例。平均年齢は 56.5 ± 12.3 歳（41 歳～77 歳）。原因は胃癌 5 例、卵巢
癌 1 例、不明 2 例であった。これらの症例に手術と同時に IHCP を施行した。IHCP は手術終了直後に低
体温全身麻酔下に行行った。Mitomycin C 10μg/ml（2 例では CDDP 15～30μg/ml も併用）を含む加温した
灌流液を用いて、90～120 分間灌流した。灌流液の流入温は 44℃～46℃、流出温は 43℃～44℃に調節した。
8 例全例で、手術時に腹腔内全域に多数の腹膜播種を認め、高度の癌性腹膜炎であった。開腹時に認めた
腹水の量は 1200 ml～10000 ml、平均 5425 ± 3253 ml であった。術後に 1 例を除く 7 例で腹水が消失した
(87.5%)。腹水が消失した 7 例の腹水の消失持続期間は、3ヶ月～17ヶ月、中央値 5ヶ月であった。IHCP は
比較的多量の腹水を伴う癌性腹膜炎症例の開腹手術後にも、良好な腹水抑制効果を示した。このような症
例において開腹手術を施行する場合、IHCP は有効な腹水抑制手段と思われ、患者の QOL 向上に役立つ
とともに、さらに延命、治療の機会を提供する可能性が示唆された。