Photodynamic Therapy for the Treatment of Advanced Gastrointestinal Tumours

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Abstract. In the study, 120 patients with advanced gastrointestinal tumours were treated by PDT; 5 mg/kg of HpD was intravenously given 48–72 h prior to PDT. The light source was an argon dye laser with an output beam of 630 nm. The irradiation time varied from 15–25 min with a power of 100–350 mW cm\(^{-2}\). The entire tumour was irradiated with a light dose of 100–250 J cm\(^{-2}\). Of the 120 patients, 20 had cancer of esophagus, 72 had cancer of the gastric cardia, 18 had cancer of the stomach and 10 had cancer of the rectum. Eighty-eight patients (73.3%) had a response to PDT. Twelve patients with CR were followed up for one to five years, two patients died during the two years after PDT.

INTRODUCTION
The application of photodynamic therapy (PDT) in gastrointestinal tumours (GIPDT) is now under investigation in a few countries. PDT of upper gastrointestinal tumours was first reported by Hayata et al (1). The Japan Cooperative Group, chaired by Professor Hayata, has treated over 100 cases in the early stage of upper gastrointestinal tumours. The longest survivor was treated more than 5 years ago. In China, clinical application of PDT was started in September 1981 (2). The Cooperative Group on GIPDT has reported the use of laser photodynamic therapy with haematoporphyrin derivative (HpD) for the treatment of gastrointestinal tumours in about 260 cases. We have reported the use of PDT in 52 cases of upper gastrointestinal tumours (3). In this report, we describe our experience of photodynamic therapy with HpD in advanced gastrointestinal tumours and note long-term follow-up results.

METHODS

Haematoporphyrin Derivative (HpD)
We used two types of HpD which was provided by the Beijing Institute of Medicine (B-HpD) and Yangzhou Pharmaceuticals Ltd. Skin sensitivity tests were performed before intravenous injection of HpD to avoid anaphylactic reactions; 5 mg HpD per kg body weight was given by slow intravenous injection. Laser treatment was given 48–72 h after HpD injection and subsequent protection from sunlight lasted about 4 weeks.

Light sources
For therapeutic procedures an argon dye laser was employed. The pumped dye laser with rhodamine B which can be tuned to emit light with a wavelength of 630 nm. Two types of quartz fibre were used, a flat-cut bare fibre and a cylindrical fibre, which was passed down the biopsy channel of endoscope.

Procedure
PDT was performed 48–72 h after injection of HpD. The power output was adjusted to 100–300 mW at the fibre tip. The tip of flat-cut bare fibre was held 10–20 mm away from superficial lesions. Exophytic areas of esophageal, cardia and rectum cancer were treated interstitially by using the 30 mm cylindrical fibre. In large tumours the cylindrical fibre was placed in several positions. In cases of protruding lesions, movement of the cylindrical fibre caused variation in the field illuminated. The light-energy
dose applied was given as an estimated energy dose (EED) based on the endoscopist’s assessment of the average illumination field. The entire tumour received an EED of 100–250 J cm\(^{-2}\).

**Evaluation of therapeutic results of PDT**

The tumour response to PDT was evaluated endoscopically, histologically or cytologically. The tumour response was classified into four grades: complete remission (CR) means no tumour was visible at endoscopy and histologic or cytologic findings; partial remission (PR) means that 50% or more of the tumour volume disappeared macroscopically for at least one month; mild remissions indicated that the tumour volume had been reduced by less than 50% but 25% or more disappeared; and no remission means that less than 25% of the tumour volume disappeared, increased or death occurred (3).

**RESULTS**

The 120 patients with gastrointestinal tumours who were treated by PDT ranged from 39–91 years of age and they consisted of 104 males and 16 females. The carcinoma was diagnosed by endoscopic biopsy and histological examination. All patients had advanced tumours. The extent of each tumour was confirmed by endoscopy, radiography, ultrasonography. CT (Computed Tomography) was performed on some cases. On the basis of endoscopy biopsy, 21 tumours were squamous carcinoma and the others were adenocarcinoma. Seventy-five patients were inoperable, 45 postoperative patients had recurrence. All patients with oesophagus and cardia cancer had dysphagia initially. Table 1 shows the site of the tumours.

<table>
<thead>
<tr>
<th>Type</th>
<th>Cancer of esophagus</th>
<th>Cancer of cardia</th>
<th>Cancer of stomach</th>
<th>Cancer of rectum</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>20</td>
<td>72</td>
<td>18</td>
<td>10</td>
<td>120</td>
</tr>
</tbody>
</table>

An argon ion laser with wavelength 514.5 nm and output 50 mW was used to observe the fluorescence of tumours before PDT. Ninety-six per cent showed typical orange-red fluorescence. The multiple points of laser therapy was fixed according to the size of fluorescence area. In large tumour masses, it must be irradiated at multiple points until the aforementioned dose is reached. Seven patients had second or third photodynamic therapy. The therapeutic effect has been evaluated in all patients.

<table>
<thead>
<tr>
<th>Location of tumours</th>
<th>Therapeutic effect*</th>
<th>Therapeutic effect</th>
<th>Therapeutic effect</th>
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<th>Therapeutic effect</th>
<th>Therapeutic effect</th>
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<th>Therapeutic effect</th>
<th>Therapeutic effect</th>
<th>Therapeutic effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagus</td>
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<td>5</td>
<td>4</td>
<td>10</td>
<td>20</td>
<td></td>
<td></td>
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<tr>
<td>Cardia</td>
<td>8</td>
<td>32</td>
<td>16</td>
<td>16</td>
<td>72</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td>2</td>
<td>4</td>
<td>8</td>
<td>4</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td>1</td>
<td>7</td>
<td>0</td>
<td>2</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>48</td>
<td>28</td>
<td>32</td>
<td>120</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

* CR = Complete remission; PR = Partial remission; MR = Mild remission; NR = No remission.

Twelve patients (10%) had CR; 48 (40%) had PR and 28 (23.3%) had MR. The total of these patients (CR, PR and MR) were 88 patients (73.3%) had a response to PDT. The percentage of effectiveness of the patients with cardia cancer and stomach cancer was 77.8%. The patients with rectal cancer had 80%. But the patients with oesophageal cancer had 50%. Complete remission could be obtained for only one patient. In 10 out of 12 patients in the CR group, the size of tumours ranged from 10 to 50 mm in diameter. The other two patients had tumours of 60 and 100 mm in diameter.

All patients were re-examined by endoscopy and biopsy after four weeks. Histologic changes following the treatment were degeneration, vacuolar and necrosis of tumour cells, and infiltration of lymphocytes and plasmacytes in the stroma to different degrees. The tumour necrosis was observed at a depth of about 10 mm.

The follow-up survey of the results of PDT lasted from 6 to 60 months. Cases showing good results received endoscopic examination every 3–6 months. The CR group was followed up for 13–62 months. Table 3 shows the current status of these patients.

During the course of the survey, two patients died at 25 months. Four patients have been followed up for more than 24 months without signs of recurrence.

In the PR and MR groups 36.4% patients are alive after having PDT for 12 months. All patients in the NR group died less than one year after PDT. The histologic changes of 14 patients were sustained for 1 to 12 months after one PDT. In 50% of the patients the tumour cells