Safety and effect of Kanglaite Injection combined with radiation therapy in the treatment of patients aged 75 and above with inoperable esophageal carcinoma

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Dose of radiation therapy for esophageal cancer is currently 50-60Gy and major toxic and side effects are irradiation esophagitis, discomfort in digestive tract, bone marrow inhibition and influence on cardiac and pulmonary functions. Generally, tissue and organ of aged patient have low tolerance and weak invasion of tumor. Expectation of average survival period for aged patient is not high and radiation dose received is normally lower than 40Gy\(^1\). Although radiation therapy has been considered as major treatment method for middle and late-stage inoperable esophageal cancer, result of sole radiation therapy is clinically not satisfactory and lots of oncologists combine radiation therapy with chemotherapy and this makes more severe toxic and side effects. Major ingredient of Kanglaite Injection (KLT) is semen coicis oil scientifically extracted from a TCM plant. KLT is a dual-phase, broad-spectrum anticancer drug to improve body immune function and resist cancer. It can also minimize toxic and side effects caused by radiation therapy and chemotherapy\(^2\). Objective of this study is to evaluate safety and therapeutic effect of KLT combined with radiation therapy to treat patients aged 75 and above with inoperable esophageal carcinoma.

1. Material and method
1.1 General data
From July 2001 to March 2004 we conducted KLT (manufactured by Zhejiang Kanglaite Pharmaceutical Co., Ltd. approval No.: z10970091) combined with radiation therapy to treat 96 cases aged 75 and above with inoperable esophageal cancer and made comparison with cases receiving sole radiation therapy. All patients did not receive any treatment before admission and got systematic examinations including esophagoscope, contrast examination of upper digestive tract and chest CT to confirm pathological diagnosis. Male/female ratio 60/36, age 75-83 (average 77) years, middle and upper segmental carcinoma 72 cases (75%), lower segmental carcinoma 24 cases (25%), stage IIIa 44 cases (46%), IIIb 52 cases (54%). Major symptoms included dysphagia 87% and chest pain 56.3%. Patients had concomitant diseases such as chronic obstructive lung disease 62%, hypertension 15%, chronic heart disease 37% and diabetes 8%. 96 cases were randomly divided into combination group (CG) and single radiotherapy group (RG) with 48 cases in each group. Patients in CG received radiotherapy plus KLT regimen while those in SG only got radiotherapy.

1.2 Method
1.2.1 X-ray linear accelerator 6mV was applied for one anterior perpendicular field followed by two posterior angular fields with 100cm source-skin distance and irradiation scope including primary lesion and adjacent big lymph nodes. Dose for spinal cord was <45Gy and bilateral pulmonary field >30Gy with planned average dose 50Gy (30-60), actual average dose 50Gy (0-60) and irradiation
field daily dose 1.8-2.5Gy. 82 cases completed the plan and 10 cases refused to continue the treatment due to discomfort. Irradiation dose received was 39.6-48Gy. Another 2 patients received doses 39.6 and 48Gy respectively due to other complications.

1.2.2 TCM treatment was KLT 200ml once per day, iv drip, for 21 days.

1.2.3 Response to radiation therapy and result of toxic and side effects were determined by objective examination, symptom of patient and following observation. One week after completion of radiation therapy with KLT treatment and at every 2-3 months, 96 cases received upper digestive tract contrast examination, chest CT and routine chemical examination.

1.3 Statistic processing
Comparison on inter-group rates was tested by X², four-fold table, SAS.

2. Results
2.1 Response to radiation therapy and toxic and side effects
After therapy majority of patients in CG and RG had dysphagia and chest pain notably relieved or improved with no significant difference between 2 groups (P>0.05). However patients in CG had improvement in appetite and fatigue apparently better than that in RG with significant difference (P<0.05). Toxic and side effects in both groups were relatively slight such as grade I-II irradiation esophagitis (12/15 cases), nausea and vomit (7/1 case), irradiation dermatitis (8/17 cases), leucopenia (3/19 cases) and loss of weight (11/10 cases). Toxic and side effects were extinctive 4-5 weeks after completion of treatment. 2 patients in CG had slight phlebitis but could tolerate slow drip. Statistic analysis showed that leucopenia patients in CG were far less than that in RG (P<0.05) while other toxic and side effects had no notable differences between 2 groups (P>0.05). See Table 1.

Table 1  Comparison on symptom and toxic/side effects in two groups after radiation therapy

<table>
<thead>
<tr>
<th>Symptom/Group</th>
<th>Combination group (CG)</th>
<th>Radiotherapy group (RG)</th>
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<tbody>
<tr>
<td>Dysphagia</td>
<td>29/43 (67.4%)</td>
<td>26/41 (63.4%)</td>
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<tr>
<td>Appetite improvement</td>
<td>28/48 (58.3%)</td>
<td>4/48 (8.3%)</td>
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<tr>
<td>Fatigue</td>
<td>10/48 (20.8%)</td>
<td>37/48 (77.1%)</td>
</tr>
<tr>
<td>Chest pain relieved</td>
<td>17/26 (65.4%)</td>
<td>16/28 (57.14%)</td>
</tr>
<tr>
<td>Esophagitis</td>
<td>12/48 (25.0%)</td>
<td>15/48 (31.3%)</td>
</tr>
<tr>
<td>Nausea and vomit</td>
<td>7/48 (14.6%)</td>
<td>1/48 (2.1%)</td>
</tr>
<tr>
<td>Dermatitis</td>
<td>8/48 (16.7%)</td>
<td>17/48 (35.4%)</td>
</tr>
<tr>
<td>Leucopenia</td>
<td>3/48 (6.3%)</td>
<td>19/48 (39.6%)</td>
</tr>
<tr>
<td>Weight loss≤5%</td>
<td>11/48 (22.9%)</td>
<td>10/48 (20.8%)</td>
</tr>
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Compared with combination group: 1) P<0.05

2.2 Size of lesion and disease progression
According to WHO criteria, lesion response is divided into complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD). In CG and RG groups: CR 0/0 case, PR
27(56.25%)/22(45.8%) cases, SD 17(35.42%)/18 (37.5%) cases and PD 4(8.33%)/8(16.7%) cases respectively. There was no significant difference between two groups (P>0.05).

2.3 Comparison on survival period between two groups
Survival period in CG and RG was 6 months: 72.9%/62.5%; 12 months: 41.7%/33.3%; 18 months: 22.9%/18.8% and 24 months : 8.3%/6.3% respectively without notable difference (P>0.05) while average survival period was 10 months in CG and 8 months in RG.

3. Discussion
Esophageal carcinoma is currently one of malignant tumors in the world with high incidence (304/100,000 in certain region). Pathogenic age group is mainly in aged people. Due to inapparent early symptom, patient is already at middle or late stage when diagnosed. For patients aged 75 and above especially for those with middle or upper segmental esophageal cancers, only less than 1/3 receive surgical operation because of operational trauma and high cost. Many patients are not willing to receive or cannot tolerate operation. They only receive supportive treatment or get no treatment. Therefore it was difficult to carry out radical cure for them and local-control treatment (radiotherapy or combined with chemotherapy) became main treatment method for majority cases.

Lonardi et al [3] reported that the radiation therapy on 1,208 cases of 50-70 years old patients with pulmonary and esophageal carcinoma found that acute and chronic toxic and side effects were not related with age and stressed that aged patients could not be excluded from therapeutic radiation therapy while other experts had similar reports [4, 5]. Radiation therapy has been major therapeutic method for middle and late stage inoperable esophageal cancer but its clinical result is not satisfactory and many oncologists tend to adopt radiation therapy combined with chemotherapy. Some scholars [6] held that effect of combination therapy was equal to that of surgical operation. However radiation therapy, when combined with chemotherapy, brings more severe toxic and side effects that lead to more strict clinical selection of patient. Combination therapy is applied only for those young inoperable patients with good physical constitution.

96 patients aged 75 and above with inoperable esophageal cancer received radiation therapy in this study of whom 48 cases simultaneously applied KLT as supportive treatment. Major function of KLT was to enhance body immune capacity, improve appetite and inhibit tumor without apparent side effect. 48 patients received KLT for 21 days as a cycle and only 2 cases had slight phlebitis without other discomfort. Although application of KLT to these patients in combination group had no significant difference in terms of influence on lesion and survival period as compared with data from single radiation group, this study indicated that the addition of KLT could enhance patient immune function, improve appetite, relieve pain and reduce impact of radiation therapy on white cells. This showed that the combination with KLT could safely improve therapeutic effect of radiation therapy.

In spite of limited sampling number and certain deviation in observational indication, we hold that sufficient radiation therapy plus KLT to treat inoperable patients aged 75 and above with esophageal cancer is not only safe but important in controlling disease progression, relieving pain and improving survival quality.
References


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