Clinical and Experimental Study on Prevention and Treatment of Acute Radiation Injury in Nasopharyngeal Carcinoma Patients by Yiqi Huoxue Yangyin Recipe (益气活血养阴方)

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ABSTRACT  Objective: To observe the effect of Chinese herbal medicine in alleviating acute toxic-adverse effect of radiotherapy and on growth of stromal cells in bone marrow. Methods: Seventy-two patients with nasopharyngeal carcinoma (NPC) were randomly divided into two groups. Radical radiotherapy was applied to both groups. In the radiotherapeutic period, to the 36 patients in the treated group, Yiqi Huoxue Yangyin Recipe (YHYR) was given additionally by oral taking and compressing on radiation area, and to the 36 patients in the control group, vitamin B12 solution was given for gargling or compressing. Experimental study was carried out in rats of two groups, irradiated with 5.0 Gy X-ray and treated with YHYR or normal saline intraperitoneally, to observe the colony forming unit-fibroblastoid (CFU-F) in cultured bone marrow stromal cells (BMSC), taken from the rats at different time. Results: The oral mucomembranous radiation damage occurred in 47.2% of the treated group when the dose of radiation reached to 41.4 ±9.4 Gy, while in the control group, it was 91.7% when the dose reached to 30.9±8.9 Gy. The skin radiation damage occurrence rate in the two groups was 13.9% and 33.3% respectively when the dose of radiation reached to 50.2±5.6 Gy and 43.2±6.3 Gy respectively. Comparison of the two groups showed significant difference (P<0.01), the radiation damage was significantly slighter in the treated group. Experimental study showed that the rats in the two groups were significantly different in occurrence and degree of bone marrow function inhibition, P<0.01. The numbers of CFU-F in cultured BMSC of radiation damaged rats taken at respective different culture time were also significantly different between the two groups, P<0.01. Conclusion: YHYR could significantly reduce acute radiation damage of mucomembrane and skin, alleviate the inhibition on bone marrow function, and eliminate the injury of radiation on BMSC.

KEY WORDS Yiqi Huoxue Yangyin Recipe, nasopharyngeal carcinoma, acute radiation injury, bone marrow stromal cell

The oral mucomembranous and skin damages are the most commonly seen acute reaction to radiation besides leukopenia. This study was carried out by administering Yiqi Huoxue Yangyin Recipe (益气活血养阴方, YHYR, a TCM recipe for reinforcing Qi, activating blood circulation and supplementing Yin) to prevent and treat acute radiation injury in nasopharyngeal carcinoma patients and observe its influence on the radiation injury of bone marrow stromal cells (BMSC).

CLINICAL STUDY

Clinical Materials

Seventy-two patients of nasopharyngeal carcinoma (NPC), hospitalized from September 1995 to July 1997, whose diagnosis were confirmed by pathology and who have received radiotherapy in the author's hospital, were divided randomly into the treated group (A) and the control group (B). There were 33 males and 3 females in each group, their age ranged 45—74 years (mean 58.6 years) in Group A and 47—73 years (mean 56.9 years) in Group B. The stage of tumor in patients, according to “Norm of Diagnosis and Treatment of Often Encountered Malignant Tumor in China”(1), were listed in detail in Table 1. The clinical materials of the two groups were comparable (P>0.05).

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Table 1. Stage of Tumor in the Two Groups (Cases)

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>TNM</th>
<th>T</th>
<th>N</th>
<th>N₀</th>
<th>N₁</th>
<th>N₂</th>
<th>N₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>36</td>
<td>1 6</td>
<td>19</td>
<td>10</td>
<td>3</td>
<td>14</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>B</td>
<td>36</td>
<td>1 5</td>
<td>20</td>
<td>10</td>
<td>2</td>
<td>16</td>
<td>15</td>
<td>3</td>
</tr>
</tbody>
</table>

Note: The M stage of tumor in all patients is M₀.

Treatment

Radio-therapy applied to both groups was the routine method of X-ray radiation using 6 MV medical linear accelerator. That is: set the radiation fields on bilateral preauricular areas and anterior nasal area, the total dose applied was 66—70 Gy on nasopharyngeal region, 55—66 Gy on neck region for treatment and 45—55 Gy for prevention. Radiotherapy was carried out 5 times in a week, 2 Gy every time, once a day and completed within 6.5—7 weeks.

YHYR was administered additionally to Group A at the same time, which consisted of red sage root, spatholobus stem, red poppy root, astragalus root, pseudostarwort root, glehniae root, each 30 g, grossy privet fruit 20 g, figwort root and rehmannia root, each 15 g. If the patients complained about throat pain, belamcanda rhizome 10 g, scutellaria root 15 g and flavescent sophora root 30 g were added. The recipe was given one dose every day made to decoction by water, starting from 2 days before the beginning of radiotherapy and lasted to 2 days after the end of radiotherapy. The decoction was also used, with 30 g of glauber salt added in, to make hot-wet compress on the radiation fields in the same period of oral taken.

Instead of the administration of Chinese herbal medicine, 150 ml solution of "Weisike" (维斯克, a trade name of vitamin B₁₂ product made by Yunfeng Pharmaceutical Factory, Zhangjiakou) was given to patients in Group B when they revealed I degree of radiation reaction on oral mucomembrane, by adding in 400 ml normal saline for gargling frequently, and for wet compressing on radiation field.

Blood routine examination was monitored 1—2 times every week. Radiotherapy would be ceased when white blood cell count lowered to less than $3.0 \times 10^9$/L. The condition of tumor was examined at the end of the treatment.

Radiation Injury Grading

The injury on oral mucomembrane and skin was graded as following: grade 0, with normal mucomembrane and skin; grade I, with slight congestion of mucomembrane or pigmentation of skin; grade II, with severe congestion of mucomembrane or desquamation of skin; grade III, with albuginea scattering on mucomembrane or moist dermatitis on skin; grade IV, with albuginea fusing in pieces on mucomembrane, diameter $\geq$ 1 cm, or erosive skin area larger than half of radiation field.

The inhibition degree of bone marrow was graded according to the standard of WHO$^{(2)}$.

Statistical Analysis

Chi-square ($\chi^2$) test was used for comparison of rates and $t$ test for comparison of mean values between the two group using the statistic software Stata (version 3.01, USA).

Results

In Group A, skin injury occurred in 6 patients, when the dose of radiation reached to $50.2 \pm 5.6$ Gy, while in Group B, it occurred in 20 patients when the dose reached to $43.2 \pm 6.3$ Gy. The results showed that when compared with Group B, the occurrence of skin injury patient was less, and the dose of radiation for inducing skin injury was higher in Group A, $P < 0.05$. Similar