CLINICAL EXPERIENCES

Effect of Yangyin Humo Decoction (养阴护膜饮) on Oral Mucomembranous Reaction to Radiotherapy*

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ABSTRACT **Objective:** To observe the effect of Yangyin Humo Decoction (养阴护膜饮, YHD) on oral mucomembranous reaction in patients with head-neck tumor undergoing radiotherapy. **Methods:** Forty-two patients with head-neck tumor undergoing radiotherapy were randomized equally into two groups. The conventional Western medical treatment was administered to all, including intravenous dripping of 2% lidocaine 20 mL, dexamethasone 5 mg, gentamycin 80 000 units, vitamin B_{12} 5 mg, dissolved in saline 250 mL, and 5% sodium bicarbonate solution for gargling, but to the patients in the tested group, YHD was given additionally. The medication was started simultaneously all through the whole course of the radiotherapy. Patients were examined every day to observe and compare the degree, initiating time, and repairing time of their oral lesions; the dosage of radiation they received was recorded as well. **Results:** The degree of mucomembranous reaction that appeared in most patients in the test group was of grade 1-2, while in the control group, it was grade 2-3. The average time for oral lesion of 1, 2, 3 grades to be initiated in the test group was 12.0±1.1, 11.0±1.3 and 10.0±0.8 days, respectively, after radiation started, which was later than that in the control group (P<0.01). Moreover, the average repairing time for the lesions of grades 1, 2, and 3 in the test group was 3.0±0.7, 10.0±1.3 and 19.0±0.8 days, which were shorter than those in the control group respectively (P<0.01). The radiation applied on the primary tumor of patients with oral lesion of grade 1-3 in the test group was 24.2±2.2, 42.0±2.6 and 58.0±1.6 Gy on the average, respectively, which were higher than that applied on patients in the control group (P<0.05 or P<0.01). **Conclusion:** The Chinese herbal preparation YHD could alleviate oral mucomembranous reaction to radiation applied in patients with head-neck tumor.

KEY WORDS radiotherapy, Chinese herbal treatment, radio-protector

Morbidity of head-neck tumor accounts for about 30% of all tumors. Radiotherapy occupies an important role in the treatment of head-neck tumors owing to its good effect on them, since most of head-neck tumors are radio-sensitive, also because there are many vital organs located on head-neck region which are intercrossed mutually, making complete resection impossible[1]. However, radiotherapy could cause injury on normal tissues, among which oral mucomembranous reaction (OMMR) is an ever encountered acute adverse reaction to radiation on head-neck tumors. It exhibits clinically as dryness and ulceration in the oral cavity and pharyngeal region to cause difficulty in swallowing or in severe cases makes patients incapable to take food, which seriously impacts the quality of life (QOL) of patients, or it also affects the therapeutic efficacy due to the interruption of radiotherapy. It has been reported that if the therapeutic course is prolonged for 14 days, the local control rate would be reduced by 13%-24%[2].

We have treated 42 patients with head-neck tumors from January 2008 to December 2008, using Chinese herbal medicine Yangyin Humo Decoction (养阴护膜饮, YHD) to alleviate the OMMR to radiation in them with satisfactory results. It is now reported as follows.

METHODS

Clinical Materials

All the patients enrolled were inpatients at the authors' hospital, their diagnoses of head-neck tumor were confirmed by pathologic and iconographic examinations, and their Karnofsky integral[3] over 70 scores. They were randomized equally into the test group and the control group. The 21 patients in the test group were 11 males and 10 females, ages from 30 to 71 years, 51.5 years on the average; the 21

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patients in the control group were 10 males and 11 females, ages 25 from 69 years, 52.1 years on the average. The standard for staging of nasopharyngeal carcinoma[3], recommended at the Fuzhou Meeting (1992), and Cots worlds staging standard[4] were used as reference for lymphoma, and for other kinds of tumor, the International Union Against Cancer (UICC) Tumor Node Metastasis Classification of Malignant Tumors stage (2002)[5] was complied. Clinical materials in the two groups were comparable (P>0.05).

Treatment

The conventional radio-therapeutic program was applied on both groups using linear accelerator with 6 MV-X ray and 9 MeV electron stream, mainly radiation on bilateral face-neck combined parallel opposite field, bilateral pre-auricular field and facio-buccal field. The dosage for the primary tumor is 6 000-7 000 cGy/6-7 weeks, the full cervical preventive dosage 4 000-5 500 cGy/4-6 weeks, dosage for cervical lymph node metastasis 6 000-6 500 cGy/6-7 weeks, 200 cGy/FX; for Hodgkin's lymphoma 3 600 cGy/23 FX, and for non-Hodgkin's lymphoma 4 500-5 000 cGy/28-31 FX. The radiation was implemented once daily, five times per week.

As accessory treatment, 20 mL of 2% lidocaine, 5 mg of dexamethasone, 80 000 units of gentamycin, and 5 mg of vitamin B12 were added into 250 mL saline for gargling before and after meals, or at night, 2 min every time, accompanied with buccal puffing and sucking actions alternately to make the full contact of the solution with various parts in oral cavity. Besides, 5% sodium bicarbonate solution was given for gargling, the using method is similar to that of the above-mentioned solution.

YHD, a Chinese preparation, formulated depending on the concerted prescription at the authors' department, was given to the test group additionally as accessory, which (one dose) consisted of honeysuckle flower 15 g, forsythia fruit 9 g, scullcap root 15 g, glehnia root 15 g, lilyturf root 15 g, crude rehmannia root 15 g, figwort root 15 g, red peony root 10 g, red sage 10 g, milkvetch root 10 g, asiabell root 10 g, balloon flower root 10 g, arctium fruit 10 g, and liquorice 6 g. It was decocted in water, boiling down to 150 mL of decoction, one dose daily, administered in six times by keeping it in the mouth for 2 min and then swallowed.

All the above-mentioned accessory treatment was administered synchronously with the radiotherapy.

Items of Observation

The severity, initiating time and repairing time of OMMR and the radiation applied on the oral mucous were observed. The severity of OMMR was graded according to the standard for grading of acute radiation injury issued by the Radiation Therapy Oncology Group (RTOG)[3], namely, Grade 0 denoted no change; Grade 1 denoted appearance of congestion and possibly mild pain but no need to take analgesic; Grade 2 denoted appearance of flaky catarrh, or inflammatory exudation, with moderate pain, and with analgesic needed; Grade 3 denoted the appearance of fused fibrous mucositis, accompanied with severe pain, with narcotic required; and Grade 4 denoted appearance of ulcer, bleeding, even necrosis.

Statistical Analysis

Adopting the software SPSS 11.5, the data were analyzed by non-parametric rank sum test.

RESULTS

Effects on OMMR Initiating Time and Repairing Time of Different Grades

The radiotherapy was completed in all patients in both groups, with the highest grade of OMMR that appeared in one patient in the whole illness course taken as the standard for measure. No severe reaction of grade 4 was found in the patients of the test group. Most of the OMMR revealed in them were grade 1-2, while those in the control group, were grades 2-3.

OMMR of different severities was initiated at different time points, generally, the later the initiating time, the lower the grade of appearance. Comparison between groups showed that the initiating time of the same grade OMMR was later in the test group than that in the control group. Correspondingly, the

Table 1. OMMR Initiating Time of Different Grades (Days, $\bar{x} \pm s$)

Group	n	Initiating time			
		Grade 1	Grade 2	Grade 3	Grade 4
Control	21	9.0±0.8 (4)	8.0±1.1 (10)	7.0±1.4 (6)	6.0 (1)
Test	21	12.0±1.1 (10)**	11.0±1.3 (7)**	10.0±0.8 (4)*	0.0 (0)

Notes: number in the bracket denote is the case number of that grade; *P<0.05, **P<0.01, as compared with the control group; Grades (Cases) in the two groups, ũ = 5.0883, P<0.01

Table 2. Repairing Time of OMMR and Radiation Applied ($\bar{x} \pm s$)

Group	Cases	Repairing time (Day)				Radiation applied (Gy)			
		Grade 1	Grade 2	Grade 3	Grade 4	Grade 1	Grade 2	Grade 3	Grade 4
Control	21	6.0±0.8	18.0±1.1	28.0±1.4	40.0	18.0±1.6	32.0±2.1	43.3±2.1	60.0
Test	21	3.0±0.7**	10.0±1.3**	19.0±0.8**	0.0	24.2±2.2**	42.0±2.6*	58.0±1.6**	0

Notes: *P<0.05, **P<0.01, compared with the control group

repairing time of OMMR depended on its severity too, the severer the reaction, the longer the repairing time needed. For the OMMR of the same grade, the repairing time in the test group was shorter than that in the control group. Moreover, the dosage of radiation applied on patients revealing OMMR of the same grade was higher in the test group than in the control group, suggesting that the tolerance to radiation in patients of the former was comparatively higher (Table 1 and 2).

DISCUSSION

Modern medicine holds that radiation could cause congestion, swelling, and degeneration of the local capillary endothelial cells, leading to increasing of vascular permeability and slowing down of blood flow and vascular obstruction, which manifests as a figure of non-specific inflammation in tissues. The congestive and swelling mucous membrane with much exudation becomes liable to local infection[6], which would impact repairing and curing of local injury due to its poor blood supply and would induce pain as well due to the pressure on nerve endings. When the salivary gland is affected, its secretion disorder would induce dryness in the mouth and weaken the self-cleaning action of oral mucous membrane, so as to cause more incidents of infection. In severe cases, pseudo-membrane comes into being by the fusion of exfoliated epithelia, infiltrated white blood cells and other exudates, and it even reveals ulceration, bleeding, etc[7]. Electric dissociation and provocation of ionizing radiation on water molecules would produce free radicals to induce critical changes of organic molecules and would last injure or even destroy the sub-cellular and membranous structure. Generally, clinical treatments on OMMR are mainly anti-inflammation, anti-biotics, abating swelling and analgesic, and drugs used are dexamethasone, lidocaine, gentamycin, vitamin B12, sodium carbonate, etc.

Chinese medicine holds that the suffering by radiation belongs to evil fire-heat, which is motive and flaming, tends to compel liquid to leak out and burn body fluid and blood away and injure yin and qi. Then, blood stasis forms due to fluid injury, qi deficiency or fiery heat, and finally syndrome of fire-toxin accumulation, yin-deficiency, fluid insufficiency, blood stasis and Pi (脾)-Fei (肺) qi-deficiency would be developed.

YHD is prescribed chiefly for clearing heat and removing toxic substance by honeysuckle flower, forsythia fruit, and scullcap root, for nourishing yin and producing fluid with crude rehmannia root, figwort root, glehnia root, and lilyturf root, for supplementing qi by milkvetch root, and asiabell root, for cooling blood by rehmannia and figwort root, and for activating blood circulation to remove stasis by red peony root and red sage as the assistant. Balloon flower root and arctium fruit are also used, functioning to remove toxin and smoothen throat, which also to lead the power of drugs directly to the oropharyngeal region as medicinal guiding agents.

Pharmaceutical studies proved that honeysuckle flower, forsythia fruit and scullcap root have the actions of broad anti-biotics; rehmannia, licorice root, honeysuckle flower and red sage could alleviate and inhibit non-specific inflammation induced by radiation; red sage could improve microcirculation, reduce the proliferation of fibrous tissues and advance the growth of granular tissues; glehnia root and crude rehmannia could promote the formation of fibroblast and vascular endothelium and provide the necessary substantial basis for curing ulceration[8]. Moreover, asiabell and red sage show a good anti-radiation action.

This study showed that OMMR was reduced more significantly in the test group than in the control group, with later initiating time and shorter repairing time, and patients treated with YHD possessed higher endurance to radiation. All these results illustrated the evident effects of YHD. By the virtue of its comprehensive prescription and convincing efficiency, YHD was deemed as an outstanding remedy for

OMMR.

However, some of its disadvantages have also been found, for example, because the nature of YHD tends to be cold, which could injure Pi-Wei (胃) in long-term administration, it has to be used accompanied with some drugs of warm nature for regulating qi and strengthening Pi; since the symptoms of thick-greasy tongue coating and poor appetite were frequently found in patients with head-neck tumor, which shows the existence of dampness accumulated in Pi and impeded the digestive function in patients, it is better to administer drugs for strengthening Pi, regulating qi, removing dampness before YHD is used. We will mend these deficits in our future work.

All in all, YHD shows favorable effects in alleviating OMMR in patients with head-neck tumor undergoing radiotherapy. Also, it could improve the QOL of patients and help them in completing their therapeutic program.

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