IntroductIon
Radiation enteritis (RE) is a common radiation injury in patients with pelvic, abdominal, and retroperitoneal malignant tumors during or after radiotherapy. It can occur in any segment of the intestinal tract but generally occurs in the rectum and colon. The incidence is related to radiography and is about 5%–13%.[1] Its progression mechanism involves radiation-induced damage to normal intestinal tissues and bacterial involvement. RE can be divided into acute and chronic stages. Most of the acute stages occur around 1–2 weeks after radiotherapy and are mainly manifested as nausea and vomiting, diarrhea, pain before defecation, varus, and bloody stool. Chronic RE usually occurs after the acute stage or direct irradiation, which causes chronic inflammation due to local tissue ischemia for 6 months. It manifests as recurrent hematochezia, diarrhea, bellyache, intestinal stenosis, ulcer, and fistula.

Currently, symptomatic supportive therapy is still the main treatment for RE, including administration of amifostine (a radioprotective agent), intestinal probiotics, intestinal mucosal protective agent, and amino acid salicylic acid drugs.[2-5] Recently, several novel therapies have also come into play, such as hyperbaric oxygen therapy and fecal bacteria transplantation. However, these therapies have not gained much interest owing to the limited beneficial effect or several side effects. To date, there is no unified, precise, and effective treatment plan. A clinically safe, effective, and economic RE therapy is urgently needed. Recent research data show that the prevention and treatment of RE by traditional Chinese medicine (TCM) has produced good results, but there is still a lack of an effective and reliable standardized treatment of RE using TCM. In this article, the prevention and treatment of RE using TCM is discussed in two aspects: Syndrome differentiation and external treatment.

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Abstract
At present, there is no unified clinical approach for the treatment of radiation enteritis (RE). Clinically, its treatment is mainly based on nutritional support, mucosal protective agents, somatostatin, and microecological preparations. On the basis of syndrome differentiation and treatment, traditional Chinese medicine (TCM) is mainly used for internal administration, enteroclysis, acupuncture, and Tuina. It shows significant advantages in relieving the adverse reactions of radiotherapy and exhibits significant preventive and therapeutic effects against RE. This article reviews two aspects of TCM on RE, including internal and external administration, to explore and develop an effective and reliable standardized Chinese medicine program.

KEYWORDS: Radiation enteritis, traditional Chinese medicine, treatment progress

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pathogenic factor of RE. Traditional medicine considers radiation as an exotic evil, fire, heat, and poison.\[6\] The pathogenesis of this disease is different from that of other acute and chronic diseases. Acute RE mostly manifests itself as excessive syndrome. The pathological sites of Chinese medicine include large intestine, spleen, and stomach. Initial radiation invades the intestinal tract from outside, showing intestinal heat accumulation, damaged meridians, and conduction dysfunction. As the disease progresses, it changes from excess to deficient, or a combination of both. However, it is still mainly based on the excess syndrome. Chronic RE manifests as long-term ailments, such as long-term diarrhea and fecal blood that consumes the body’s Qi, blood, and fluid. This is followed by damage to the spleen and the stomach. Spleen deficiency often results in the lifting of Zhongyang, which is often manifested as the mixture of deficiency and excess, i.e., cold and heat. The disease is mostly caused by heat, toxin, and dampness, and mostly affects the large intestine and spleen. Further progression of the disease leads to Yin-qi injury, followed by Yang-qi injury, which eventually leads to the Yang-deficiency of spleen and kidney.

**Differentiation between Syndrome and Treatment**

The pathogenesis of RE is the basic pathology mechanism was mainly solid for this empty sign, actual situation mixture. The treatment mainly focuses on strengthening the body’s resistance to eliminate pathogenic factors. The body’s resistance is strengthened to nourish qi, consolidate the root, nourish the spleen and kidney, contract the intestine and stop diarrhea, and eliminate pathogenic factors by alleviating heat and toxins, clearing damp heat, activating blood circulation and removing blood stasis, and promoting qi. Among them, detoxification, dampening of heat, and activating blood circulation are the main treatment mechanisms followed by >60% of all therapeutic modalities reported in the literature. Meta-analysis on the employment of TCM in treating RE, reducing the blood temperature and maintaining hemostasis are the two most common treatment approaches.\[7\] However, as far as the author is concerned, the clinical symptoms of this disease are complex and variable, discouraging the use of similar prescriptions and medicines for different cases. The key to resolve this limitation is syndrome differentiation. According to the patient’s physical condition, duration of disease, symptoms, and related research in recent years, the disease can be roughly divided into the following five types of syndromes.

**Qi stagnation and blood stasis**

This type of syndrome is prevalent among patients at the initial stages of radiotherapy. Fire-heat toxin invades the human body, burns qi and blood, plunders yin fluid, and causes qi stagnation. The main symptoms of this syndrome include abdominal pricking pain, discomfort after diarrhea, and fixed pain. The accompanying symptoms include dark complexion, chest swelling, irritability, dry mouth, no desire to drink fluids, occasional fever (especially at night), bruises on the edge of the tongue or dark red tongue, pulse strings, and astringent. Treatment approaches include activating Qi and blood circulation, alleviating heat, and removing blood stasis. Representative prescription involves chaishuhsugan powder with or without Qingying decoction. Most of the patients with this type of syndrome are in the acute stage of RE. Previously, Song Xiaocon used Qingying decoction to treat 38 cases of RE, with a total effective rate of 95%.\[8\] Xingy’s et al. study treated 35 patients with acute RE using the prescription specific for alleviating heat, detoxifying, cooling, and activating the blood.\[9\] The assessment of the overall clinical and colonoscopy effects showed that this method could effectively reduce intestinal mucous membrane injury and improve tolerance of the intestinal tract to radiation.

**Dampness-heat pouring downward**

Radiation is the evil of fire, heat, and poison. It can straighten the intestine and stomach during radiotherapy, which leads to dysfunction of the spleen and stomach. Spleen dysfunction results in endogenous dampness, which, combined with external fire poison in the intestine, causes diarrhea, and bloody stool. These are the most common type of clinical syndromes. The main symptoms include sharp abdominal pain, blood and pus, and anal burning. The accompanying symptoms include a lower volume of red urine, fatigue, yellow sticky coating, pulse slippage, or immersion. Treatment principles involve alleviating heat and dampness, nourishing blood, and stopping bleeding. Representative prescriptions include GegenQinlian and HuanglianJiedu decoctions. For instance, Ruqin et al. used GegenQinlian decoction and Lisha et al. used modified Qi Fang. Zhongni et al. used Professor Zhang Zhifang’s prescription of a Lianjiang formula to treat damp-heat injection RE. All the above investigators achieved good results.\[10-12\]

**Liver-spleen disharmony**

This type of syndrome is found in tumor patients, suffering from illness for several years, whose liver-qi stagnation transverses to the spleen and renders it dysfunctional, leading to diarrhea. The main symptoms include abdominal pain, bowel sounding, painful diarrhea, and pain relief after diarrhea. The accompanying symptoms involve gasteremphraxis and pain, hiccup, acid and noise, vomiting, thin white or greasy tongue coating, and pulse string. Treatment principles involve soothing the liver, strengthening the spleen, dispelling dampness, and stopping diarrhea. Representative prescriptions include Tong-Xie-Yao-Fang with or without Xiaoao powder. Lu Wenzeng treated 42 cases of RE of liver and spleen disharmony using Tong-Xie-Yao-Fang, which calmed the nerves and dispelled melancholy, with a total effective rate of 95.24%, which was significantly different from that of the control group.\[13\] Yu et al. treated acute RE patients using Tong-Xie-Yao-Fang; they observed that the onset time of 30 patients in the treatment group was significantly delayed, and the severity was lighter than that of the control group (P < 0.05).\[14\]

**Spleen deficiency and dampness encumbrance**

Most of the patients with this syndrome suffer from chronic RE and have a long course of the disease. Tumor patients...
often suffer from deficiency. After the invasion of heat poison, the blood and qi are depleted. Zhengqi becomes increasingly deficient. This syndrome is also characterized by dysfunction of the spleen and stomach, indiscriminate turbidity, obstruction of qi, and retention of damp pathogens due to deficiency of the spleen and dampness. The main symptoms include diarrhea, mucus or bloody stool, increased frequency, and anal drop. The accompanying symptoms include poor appetite, epigastric distension, dull pain, physical fatigue, lazy, fat tongue or dental marks on the edge, white tongue coating, and weak pulse. Treatment principles involve invigorating the spleen and eliminating the dampness. Representative prescriptions include shenlingbaizhu powder and xiangshaliujunzi decoction. Shenglian et al. used Baizhu powder to treat 30 RE cases. Their results showed that the degree of abdominal pain and diarrhea in the treatment group was significantly lower than that in the control group. The total effective rate was 83.3% in the treatment group and 60% in the control group. There was a significant difference between the two groups (P < 0.05). Gufeng et al. treated 38 RE patients using Jianpi Qinghua decoction. They showed that the total effective rate of the treatment group (treated with Jianpi Digestion decoction) was 89.47%, which was higher than that of the control group (65.79%) that was treated using levofloxacin capsule and montmorillonite powder (P < 0.05).

**Deficiency of the spleen and kidney yang**

Tumor patients with this syndrome exhibit deficiency in vital energy failed spleen-qi, weak spleen-yang, and cannot warm up the middle soil, leading to the accumulation of cold and dampness. In addition, their diarrhea lasts for a long time, Yin is exhausted, and Yin and Yang are damaged, which leads to the deficiency of the spleen and kidney Yang. The main symptoms include chronic diarrhea, feces with sticky frozen samples, and a small amount of blood, or tenesmus. The accompanying symptoms include boriing diet, head and body fatigue, cold limbs, sour waist and knee, white tongue coating, and pulse sinking. Treatment principles involve warming the kidney and reinforcing the spleen, fixing the intestine, and stopping diarrhea. Representative prescriptions include Zhenwu and Fuzi Lizhong decoctions. Sen Yongqin treated 16 cases of RE with spleen and kidney deficiency and cold type syndrome with ZhenrenYangzang decoction and Taohua decoction, with an effective rate of 87.5%. Zhengxiang used Zhenren Yangzang decoction to treat diarrhea after colorectal cancer surgery, with a total effective rate of the treatment group of 92.73%, which was significantly better than that of the control group (89.09%; P < 0.05).

**EXTERNAL TREATMENT OF TRADITIONAL CHINESE MEDICINE**

**External treatment of enema**

Chinese herbal enema is an efficient, fast, safe, and less toxic route of drug administration. Studies have shown that intestinal administration is more rapid than oral administration, and its absorption rate and total absorption following intestinal administration was comparable to that following intravenous administration. The bioavailability through this route is increased by 100%. TCM enema is most commonly used in the treatment of acute RE. This type of administration is simpler and can lead to the better curative effect. Yixiao’s et al.’s study showed that 36 cases were treated by retention enema with Chinese herbal decoction by alleviating heat, detoxifying wind, and removing dampness. Compared with metronidazole enema in the control group, the intestinal mucosal condition, KPS score, and symptom score of patients in the treatment group were significantly better (P < 0.05). Yang Zhiyong et al. used compound Baiji powder for enema RE patients and found that the effective rate of the observation group was significantly higher than that of the conventional enema control group (P < 0.05). He Weimei et al. randomly divided 195 patients into groups A, B, and C treated with western medicine alone, Kangfuxin plus dexamethasone enema, and Kuijie enema, respectively. Their results showed that Kuijie enema improved the clinical symptoms of patients with radiation proctitis II most effectively.

**External treatment of acupuncture and tuina**

In addition to oral and enema treatment with TCM, there are non-drug therapies, such as acupuncture, tuina, etc. These non-drug therapies have recently been applied in the treatment of RE and led to beneficial effects. Yemei and Chuncheng found that the total effective rate of the combined group was 90%, which was better than that of the control group (66.67%). Jingyan et al. used health gymnastics combined with Zusanli acupoint massage to prevent the occurrence of acute RE in patients with malignant tumors. Their results showed that the incidence of acute RE in the control group was significantly higher than that in the observation group (P < 0.05).

**SUMMARY AND PROSPECT**

At present, the research regarding RE has entered into the domain of molecular mechanisms. It involves the study of microvascular injury, inflammatory cytokines, intestinal flora disorder, cell structure changes, and other aspects involved in the process of RE occurrence and helps form a preliminary theoretical framework. However, modern medicine has not yet come up with a comprehensive and systematic treatment plan for RE. Symptomatic treatments, such as fasting and enteral nutrition, intestinal mucosal protection, maintaining hemostasis, and encountering inflammation, hyperbaric oxygen therapy, and probiotics and somatostatin supplementation, are still the main treatments for RE. However, the curative effect is not good. Finally, 1/3 chronic RE patients require surgical treatment for the alleviation of symptoms. The incidence of complications, such as hemorrhage, infection, and short bowel syndrome, is about 30% in patients undergoing surgery. The leakage rate of the anastomotic stoma is as high as 10%, which seriously affects the quality of life of the patients. Chinese medicine has made some progress in the prevention and treatment of RE, with a positive curative effect. However,
there are some limitations: (1) Most of the existing studies are still in the clinical stage, and the main challenge of the study is the compound preparation of Chinese medicine. There have been some deficiencies in the study of the molecular mechanism during the treatment of RE with TCM. Further studies are needed on the mechanism and target of drug action. (2) Clinical studies are mostly based on the observation of curative effect, although the inclusion, exclusion, diagnostic, and curative effect criteria have also been discussed. However, some problems still prevail, such as lack of randomized control, small sample size, incomplete curative effect indicators, and lack of research reports on chronic RE. (3) There is still a lack of unified evaluation criteria and treatment guidelines of TCM efficacy in the clinic. (4) At present, the external treatment of RE in TCM is mostly focused on retention enema, but there is still no unified standard for the specific operation of retention enema of TCM, such as the depth, the speed of intubation, and the temperature of medication. (5) The research on the internal treatment of RE with TCM is limited, and most of them do not conduct syndrome differentiation analysis. They only involve clinical trials of simple or ancient prescriptions. Therefore, it is necessary to strengthen the research on syndrome types of RE, statistically analyze the distribution of clinical syndrome types, and study the sensitivity of different syndrome types to drug use. (6) With respect to current clinical data, more treatment and less prevention fail to achieve full potential of the advantages of “preventive treatment” of TCM. (7) TCM and Western medicine provide certain curative effect on RE. However, the approach to efficiently combine them organically is urgently needed to be elucidated. It is very important to determine the time and form of participation involved in the prevention and treatment of RE by TCM. For example, it needs to be elucidated if, during abdominal and pelvic radiotherapy, oral Chinese medicine and enema preventive treatment could be added in advance; if the intervention of TCM must be continued even after the treatment and for how long. Furthermore, future studies should also focus on the potential synergistic effects of TCM and Western medicine, when they are used simultaneously during the treatment. This review only pays attention to clinical syndrome differentiation and external treatment and does not involve the research progress of RE in modern medicine in recent years. In addition, based on the modern biological, psychological, social, and medical models, this paper does not focus on the psychological intervention of the patients.

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