

## REVIEW

# A Review of Radiation-Induced Oral Mucositis in Traditional Chinese and Western Medicine Research

DU Ning (杜宁)<sup>1</sup>, YE Pei-zhi (叶霏智)<sup>1</sup>, REN Shuang (任爽)<sup>2</sup>, LIU Li-xing (刘丽星)<sup>1</sup>,  
LIU Xin-qi (刘欣琦)<sup>1</sup>, ZHANG Jie (张杰)<sup>2</sup>, FENG Li (冯利)<sup>1</sup>

1. National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China

2. The First Affiliated Hospital of China Medical University, Shenyang 110001, China

**Correspondence to:** FENG Li, Email: fengli663@126.com

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**ABSTRACT** Radiation therapy is one of the main treatments for head and neck tumors, and radiation-induced oral mucositis (RIOM) is a common serious adverse effect of radiation therapy. We summarized the pathogenesis, prevention and treatment methods of RIOM related to traditional Chinese and Western medicine in recent years. The treatment of RIOM in traditional Chinese medicine should be based on clearing heat and detoxifying, nourishing Yin and promoting fluid, tonifying spleen and stomach, cooling blood and removing blood stasis. Osteopontin, immunoglobulin A and saliva flow tests may be effective clinical indicators in the future. Through analysis, the author believes that the use of integrated intervention of traditional Chinese and western medicine can better benefit patients, and the prevention and predictive diagnostic tools of RIOM should become the future focus of attention.

**KEYWORDS** Radiation therapy; Radiation-induced oral mucositis; Mechanism; Research progress

## INTRODUCTION

Radiation-induced oral mucositis (RIOM) is an inflammatory reaction process of oral mucosa. It is the most common toxic side effect during radiotherapy or concurrent chemoradiotherapy in patients with head and neck malignant tumors, with an incidence of up to 85%–90%.<sup>[1]</sup> It is usually manifested as mucosal redness, swelling and erosion, oral pain and even dysphagia, accompanied by oral infection. The patients' quality of life and treatment compliance were seriously affected. We reviewed the current prevention and treatment methods of RIOM with traditional Chinese and western medicine, and sorted out the relevant biological markers under study, hoping to provide new ideas for the follow-up research and treatment of radiation oral mucositis.

## UNDERSTANDING OF RADIATION MUCOSITIS IN WESTERN MEDICINE

### Pathogenesis

The intact structure of oral mucosa is protective

to the submucosal tissues. The damage of oral mucosal tissues caused by radiotherapy leads to the destruction of the integrity of the mucosa, and then the symptoms of oral redness, swelling, pain, ulcer, erosion and so on. Studies have shown that RIOM is a series of complex molecular reactions, including direct damage of basal epithelial cells, oxidative stress response, inflammatory response, innate immune response and homeostasis imbalance of oral flora.<sup>[2,3]</sup>

Under the induction of radiotherapy, the DNA chemical bond of basal epithelial cells ionizes, generating hydroxyl radical to cut DNA, and DNA double bond break leads to damage and apoptosis of basal epithelial cells and auxiliary bone subcells.<sup>[4,5]</sup> At the same time, radiotherapy can induce the formation of reactive oxygen species (ROS) and NOS, stimulate oxidative stress response, and lead to the imbalance of intracellular REDOX homeostasis, resulting in cell and tissue damage.<sup>[6]</sup> DNA cleavage induces P53, nuclear factor  $\kappa$  B (NF- $\kappa$  B) and other transcription

factors, NF- $\kappa$ B as the central mediator of activation of inflammatory factors, can induce the production of pro-inflammatory factors, adhesion molecules, etc., and trigger subsequent inflammatory molecular pathways.<sup>[7]</sup> Pro-inflammatory factors such as TNF- $\alpha$ , IL-1 $\beta$ , and Interleukin (IL)-6 can initiate ectomymal signaling, which in turn activates sphingomyelinase to exacerbate damage to basal epithelial cells and connective tissue.<sup>[8,9]</sup> NF- $\kappa$ B can also cause cell death by activating the apoptotic pathway, causing further damage to mucosal epithelium and submucosal tissues. Clinical manifestations include epithelial exfoliation, mucosal edema, inflammation, and ulcers.<sup>[10]</sup>

The formation of ulcers creates a very positive environment for bacterial colonization, which in turn increases inflammation. Some scholars have confirmed that the load of ulcerative epithelial bacteria in oral microorganisms of patients after radiotherapy is significantly increased, indicating that oral bacteria are correlated with RIOM.<sup>[11]</sup> After radiotherapy, the submucosal salivary glands are damaged and the salivary secretion is reduced, which can increase the harmful microorganisms in the mouth. Studies have shown that the oral microbiome promotes the occurrence of mucositis by regulating innate immunity, aggravates the inflammatory response by activating NF- $\kappa$ B and other inflammatory factors, and affects mucosal healing.<sup>[12]</sup>

### Treatment of Radiation Oral Mucositis

The treatment of radiation oral mucositis mainly includes preventing the occurrence of RIOM and promoting the repair and regeneration of oral mucosa. The key reason for the occurrence of RIOM is that the changes in cell biology caused by radiation exceed the physiological self-protection ability, resulting in cell damage. The existing prevention and treatment programs mainly start from the intervention of mucous membrane damage.

### Anti-inflammatory therapy

Inflammation is an important mechanism of RIOM, and anti-inflammatory drugs play a very important role in the treatment of RIOM. Common anti-inflammatory drugs include bendamine, Rebabai and so on. Aniline is a widely used anti-inflammatory drug in clinic. It has anti-inflammatory, analgesic, anesthetic

and antibacterial effects. According to MASCC/ISOO Clinical Practice guidelines, the use of Bendamine mouthwash during moderate dose radiotherapy is recommended for the prevention of RIOM.<sup>[13]</sup> Studies have assessed that the incidence of ulcers and erythematosis can be reduced by 30% with bendamine intervention during radiotherapy compared to control groups. The prophylactic use of rapapai toothbrush significantly reduced the incidence of grade 3 RIOM in patients with head and neck radiotherapy compared with placebo (83.3% vs. 33.3%,  $P=0.036$ ), the mechanism of which was related to the inhibition of IL-8, TNF- $\alpha$  and other inflammatory factors.<sup>[14]</sup> In addition to anti-inflammatory mouthwashes, there are anti-inflammatory ointments, such as topical corticosteroids, as well as natural ingredients, such as mouthwashes containing honey, curcumin, propolis, etc..<sup>[15]</sup> Its effectiveness in relieving aura-related inflammation and pain has been demonstrated in clinical trials.<sup>[16]</sup> In addition, studies have shown that active ingredients extracted from marigold, calendula, and scopolia can also improve the symptoms and incidence of RIOM.<sup>[17]</sup>

### Mucosal repair

The mucosa was damaged after radiotherapy, and the self-repair ability of oral epithelium was also reduced. Studies have shown that prophylactic use of cell growth factor during radiotherapy can effectively reduce the incidence of RIOM, promote the generation of oral mucosal cells, and improve the repair ability.<sup>[18]</sup> At present, cell growth factors include keratinocyte growth factor, epidermal growth factor and so on. Palifermin, a recombinant keratinocyte growth factor (KGF), is currently the only drug approved for mucositis by the US Food and Drug Administration and the European Medicines Agency and has been found to significantly reduce the incidence and severity of RIOM. The mechanism may be related to promoting the proliferation of epithelial cells, increasing the thickness of the non-keratinized layer of oral and gastrointestinal mucosa, activating the anti-inflammatory cytokine IL-13, and inhibiting the inflammatory response.<sup>[19-21]</sup> MASCC/ISOO guidelines recommend the use of low-intensity laser therapy (LLLT) for the prevention and treatment of RIOM in patients with head and neck cancer undergoing radiotherapy.<sup>[13]</sup> As a relatively new treatment method, LLLT can activate signal factors such as

growth factors and detoxifying oxygen free radicals by activating cell signals, promote cell proliferation and mucosal microcirculation, promote cell mucosal repair, and significantly reduce the incidence of grade 3 and grade 4 RIOM.<sup>[22]</sup> Intervention with LLLT has been shown to reduce the incidence of severe RIOM (RIOM grade  $\geq 2$ ) by 62% and shorten the time to complete RIOM remission. There have been no reports of adverse reactions to LLLT, which confirms that patients have a strong tolerance to laser therapy.

### Improve symptoms

Pain is usually the first symptom of patients with head and neck radiotherapy 1–2 weeks after the start of radiotherapy. Severe pain will affect the patient's eating and nutritional status, and even delay the treatment time or suspend radiotherapy and chemotherapy. Treatment may include non-steroidal anti-inflammatory drugs such as acetaminophen, lidocaine, or opioid pain medications to relieve pain. The use of analgesic drugs may cause sleepiness, fatigue and other adverse reactions, and we should pay attention to the dosage and duration of use during the use of drugs. Mucosal protectants can cover the damaged area locally and form adhesive complexes at the ulcer to protect the mucosa. They are mostly used to treat early and mild RIOM, but the clinical effect is poor.<sup>[23,24]</sup> At present, it is not recommended as a primary means of preventing and treating RIOM.

In addition to the above treatment, there are many research reports on anti-infection drugs such as chlorhexidine gluconate, granulocyte colony stimulating factor, oral cryotherapy, probiotics, vitamins, oral platelet gel, melatonin, superoxide dismutase mimics and so on. Although we have some research on the pathogenesis and treatment of RIOM, it is still a big challenge for us, so we should pay more attention to the prevention measures of RIOM while focusing on the treatment. At present, there is still a lack of authoritative predictive diagnostic indicators in clinical practice. In this regard, we have sorted out the relevant studies of some clinical scholars on the new detection indicators.

## NEW DETECTION INDEX

Saliva is an important pillar to maintain oral immune environment, and it contains abundant

biological molecules such as glycoproteins and electrolytes.<sup>[25]</sup> The changes of saliva components can regulate the immune response and maintain the homeostasis of oral microflora, which is closely related to the occurrence of RIOM. Changes in the composition of saliva provide a new field for researchers to explore effective indicators to predict RIOM.

Osteopontin (OPN) is a phosphoglycoprotein in saliva that is involved in the protection of mucosal integrity and antibacterial effects,<sup>[26]</sup> and it plays a key role in the occurrence and progression of tumors, inflammatory response, and cell survival and proliferation.<sup>[27]</sup> OPN has been shown to be a poor predictor of overall survival in breast cancer and hematologic malignancies, suggesting its potential as a predictive marker.<sup>[28]</sup> OPN plays an important role in innate and adaptive immune response, tissue damage and repair, suggesting a strong correlation with the pathogenesis of RIOM.<sup>[29]</sup> By observing the levels of osteopontin in saliva and serum of peripheral stem cell transplantation (APSCT) patients who received high-dose preconditioning to produce RIOM, it was found that the level of OPN in the saliva of patients was negatively correlated with the severity of RIOM,<sup>[30]</sup> suggesting that OPN could be used as a potential biomarker for detecting RIOM.

Immunoglobulin A (sIgA) is also a potential indicator for monitoring RIOM. SIgA is a glycosylated protein in saliva and is the first line of defense of the oral mucosa.<sup>[31]</sup> SIgA can inhibit viral action by direct interaction with microbial antigens, and can maintain microbial homeostasis by binding to bacterial lipopolysaccharides.<sup>[32,33]</sup> Some scholars have observed significant changes in the structure of IgA N-glycan in saliva of RIOM patients with different degrees during the treatment of stem cell transplantation, and the changes in saliva IgA reflect the correlation between IgA and local oral immune response. Therefore, sIgA glycoylation may be used as a potential marker to monitor the pathological process of oral cavity and the progression of RIOM.<sup>[34]</sup>

Damage to the salivary glands caused by radiotherapy can lead to reduced saliva flow and changes in saliva composition in the mouth, which is an important factor in the development of RIOM.

Saliva flow test can reflect the degree of salivary gland damage to a certain extent and may be useful for detecting RIOM. Dominika<sup>[35]</sup> demonstrated the suitability of the Schirmer test for detecting dry mouth by attaching the strip to the saliva site, such as the submandibular and sublingual glands, and measuring saliva flow by observing the moistness of the strip over a period of time. Studies have shown that Schirmer test value <25 mm after 3 minutes is insufficient salivation, while Chena<sup>[36]</sup> points out that Schirmer test value <15 mm after 3 minutes can be regarded as severe dry mouth and insufficient salivation after head and neck radiotherapy. Schirmer test can well detect dry mouth in patients with head and neck radiotherapy and chemotherapy, and can be used as a good indicator to monitor dry mouth degree in the prevention and treatment of RIOM.

Compared with other body fluids, saliva has many advantages, such as convenient collection, non-invasive and painless, low cost, etc., and is currently a very active research field of new detection indicators. OPN has a wide range of biological activities and plays an important role in innate and adaptive immune responses, tissue damage and repair, suggesting that it is strongly correlated with the pathogenesis of RIOM, so OPN is a strong candidate as a novel biomarker. Saliva contains more than 1,000 glycosylated proteins. sIgA may be used as a detection marker to monitor the pathological process of oral mucosa, and it also shows that other glycosylated proteins have great potential for research. The Schirmer test is simple and can provide additional information for predicting RIOM by detecting dry mouth in patients with oral salivary flow responses.

## UNDERSTANDING OF RADIATION MUCOSITIS INTRADITIONAL CHINESE MEDICINE

### Pathogenesis of Traditional Chinese Medicine

Radiation induced oral mucositis in traditional Chinese medicine has no direct corresponding disease name, based on its clinical manifestations can be classified as "throat arthralgia (喉痹)", "aphtha (口疮)", "mouth malnutrition (口瘡)" category. "Aphtha" was first discussed in *Huangdi Neijing* <<黄帝内经>>, *The question•Qi alternations* <<素问•气交变大论>> said: "the age of Jin is less than, the

fire up... People suffer from oral sores, and even heartache." Fire is flaming upwards in nature, which can burn the tongue, cause oral sores, at the same time will evaporate the water in the body, consume the qi, and even cause blood stasis and phlegm congestion. The causes of aphthous ulcer are mainly exogenous heat evil, improper diet, emotional discomfort, lack of endowment and so on. It can be found that the pathogenesis of aphthous ulcer lies in fire, but fire divided into real fire and empty fire, and the disease also has virtual and real. The causes of aphtha can be summarized as follows.

### Heat accumulated in the heart and spleen

*Shengji General Record* <<圣济总录>> said: "heart qi through the tongue... One's temper runs through one's mouth. Excessive heat in the viscera affects the heart and spleen, qi rushed to the mouth and tongue, so that the mouth and tongue sore also." Aphthous ulcer is caused by the evil of fire along the two channels of heart and spleen on the mouth. *Shengji General Record* also has a similar statement: "People with oral sores have heat in the heart and spleen, qi rushing up to scorch, fumigating the mouth and pretending to be sores". The two channels of the heart and spleen accumulate heat, shall not diverge, attack the upper jiao, then see the mouth and tongue sore, red swelling heat pain. The clinical presentation includes ulceration of the oral mucosa, burning pain, restlessness, increased thirst, and dry stools.

### Flaring up of deficient fire

*Shengji General Record* said: "Stomach qi is weak, valley qi is less, deficiency yang and aphthous ulcer, can not be held to one thing, should seek to receive this also." *Medicine* <<医贯>> said: "Oral ulcer, upper jiao solid heat, middle jiao deficiency cold, lower jiao yin fire, each jing fu (transmission) change caused by it should be treated separately." In addition to excess fire, there is weakness in the middle burner, resulting in impaired ability to receive and digest food and fluids. The failure to restrain the uprising of Stomach Qi and inability of the Kidney essence to regulate the ministerial fire leads to the development of oral ulcers. Clinically, recurrent ulceration of the oral mucosa with burning pain is



observed, which hampers eating and persists over a prolonged course. Other accompanying symptoms may include fatigue, lassitude, and soreness of the waist and knees.

### Yang Qi deficiency

Lack of Yang qi, zang-fu cold can also cause the formation of oral ulcers. *Shou Shi Bao Yuan* <<寿世保元>> mentioned: "oral ulcer white, spleen cold." *Medical Extracts* <<医学摘粹>> said: "spleen and stomach dampness cold, bile fire inflammation, and produce oral sores." It refers to cold and damp depression and heat, damp and heat steaming and resulting in aphthous sores. Ming Dynasty *Secret key and class prescription for Diagnosis and Treatment• Volume 10•Mouth* <<秘传证治要诀及类方>> 卷十 said: "the lower deficiency on the top, resulting in mouth and tongue sore." It is pointed out that the lower deficiency and upper excess are the mechanism of aphthous ulcer. The upper excess refers to the upper jiao qi and Yang heat. Lower deficiency refers to deficiency of kidney yang. The deficiency of Kidney Yang leads to the accumulation of Cold and Dampness, which transforms into Heat. The upward flaring of this Heat results in the development of oral ulcers. This condition manifests as an imbalance with weakness in the upper part of the body and excessive activity in the lower part. Clinical evidence: oral mucosa ulceration, long difficult to heal, longer course of the disease is and slight pain, fatigue, pale face, fear of cold, etc.

### Yin-yang imbalance

There is a saying in *Chong Lou Yu Yao Xu Bian* <<重楼玉钥续编>> that "there are those who injure dryness and make oral sores".<sup>[37]</sup> *New An Zheng Otorhinolaryngology Clinic* <<新安郑氏喉科>>, believes that dryness and evil are more likely to damage body fluid than fire evil. When Yang is excessive, yin diseases may arise. This can further lead to an imbalance between yin and yang, resulting in a two-level differentiation.<sup>[38]</sup>

### TCM Syndrome Differentiation Treatment Ideas

Chinese medicine treatment is based on the whole concept, although oral mucositis is located in the oropharynx, the treatment should pay attention to the local and the connection between the viscera.

During treatment, syndrome differentiation can not only effectively relieve symptoms, but also better promote mucosal repair. Based on the modern doctors' views on RIOM, the dialectical thinking can be summarized as follows:

### Excessive heat can injure Yin

Chinese medical master Zhou Daihan proposed that radiation syndrome is a fiery evil.<sup>[39]</sup> The fire evil poison invades the human body, injures the fluid and consumes the qi, burns the yin fluid, and the fire is endogenous, resulting in local red swelling heat pain, dry mouth, dry nasopharynx, irritated heat, dry stool and so on. Scholars such as Kong Jiaxin also adopted the methods of clearing heat and detoxifying, invigorating qi and nourishing yin, and used Puji Disinfection Decoction (普济消毒饮) to treat oral mucosal reaction of patients with nasopharyngeal carcinoma after radiotherapy, which achieved remarkable results and found that the incidence of grade 3 and 4 RIOM could be significantly reduced.<sup>[40]</sup> The prescriptions often used in treatment include Zengye Decoction (增液汤), Yiwei Decoction (益胃汤), Shashen Maidong Decoction (沙参麦冬汤), etc..<sup>[41-43]</sup> Among them, Shengdi (*Raw rehmannia glutinosa*, 生地) and Maidong (*Ophiopogon japonicus*, 麦冬) moistening dryness, nourishing yin clearing heat, promoting saliva secretion, relieving dry mouth and thirst symptoms. Clearing heat and detoxifying, such as Huangqin (*Scutellaria baicalensis*, 黄芩) and Baihuashecao (*Spreading Hedyotis Herb*, 白花蛇草), with Dangshen (*Codonopsis*, 党参) tonifying spleen and stomach, promoting production of body fluid and benefiting qi.

### Lung and stomach stasis heat, deficiency fire floating

Wang Yueping and other scholars believe that the pathogenesis of RIOM is the stagnation of lung and stomach heat and the emergence of weak fire, and the treatment should be the method of clearing lung and stomach heat and nourishing yin and promoting fluid, and the treatment should be based on Xianfang Hongming Yin (仙方活命饮) to emphasize clearing heat and detoxifying and nourishing yin and promoting fluid.<sup>[44]</sup> Zhang Yongxi et al. found that the use of Yangyin Shengjin Decoction (养阴生津汤) can significantly increase the amount of saliva secretion and improve the symptoms of dry mouth in patients

with radiotherapy.<sup>[45]</sup>

### Treatment through spleen

Zhong Yanping and other scholars treat RIOM with the spleen, the spleen and stomach belong to the middle jiao, and the spleen is transferred upward to nourish the lung yin. When the spleen loses its healthy function of transportation and transformation, there is a deficiency in the production and transformation of qi and blood (脾失健运, 生化乏源), affect the upper jiao body fluid distribution, dry mouth, thirst and other symptoms, treatment to tonify the spleen and stomach. Professor Song Aiyong<sup>[46]</sup> believed that due to the burning of yin and jin by fiery evil poison, most patients with this disease were the body of yin deficiency and fire abundance, and the treatment of regulating the spleen and stomach, nourishing yin and moistening dryness could significantly alleviate the symptoms of dry mouth of patients with Yiwei Decoction. Qi yin deficiency, spleen and stomach weakness, On the basis of nourishing yin and generating fluids, it is recommended to add spleen-tonifying and stomach-nourishing herbs such as Dangshen, Baizhu (*Atractylodes macrocephala* Koidz, 白术), and Gancao (*Licorice*, 甘草), in order to treat patients with qi deficiency weakness, sweating, fatigue and other diseases.

### Theory of stasis heat

Professor Zhou Zhongying, a Chinese medical master, put forward the theory of blood stasis and heat on radiation oral mucositis,<sup>[47]</sup> believing that radiation causes hot toxic pathogens to jam in the blood. Blood heat and blood stasis mutually combine, leading to the development of pathological conditions. The prevention and treatment theory of cooling blood and removing blood stasis, nourishing yin and replenishing qi was put forward, and Xijiao Dihuang Decoction (犀角地黄汤), Shashen Maidong Decoction (沙参麦冬汤) and Si Junzi Decoction (四君子汤) were taken as representative prescriptions. Scholars such as Fan Jinzhao found that the use of Liangxue Huoxue Granules (凉血活血颗粒) has a good prevention and control effect on radioactive damage.<sup>[48]</sup>

For patients with acute mucositis caused by

radiotherapy, heat toxicity is more serious, and the syndrome is heat toxicity. Clearing heat and detoxification should be emphasized on the basis of nourishing yin and promoting fluid.<sup>[49]</sup> People with hot toxicity can have irritability, sore throat, and even oral mucosa erosion and congestion. Such patients can be given Puji disinfection drink (普济消毒饮), Xijiao Dihuang Decoction, etc.. Huangqin, Shagan (*Belamcanda chinensis*, 射干) and Lianqiao (*Forsythia*, 连翘) can clear heat and detoxify, relieve wind and soothe pharynx, relieve oral inflammation and promote mucosal recovery. Baicalin Huangqin has antipyretic, analgesic and anti-inflammatory effects.<sup>[50,51]</sup> Xiakucao (*Prunella*, 夏枯草) and Banzhilian (*Melea*, 半枝莲) can detoxify and dissipate knots. At the same time Xuanshen (*Scrophulina*, 玄参) and Maidong nourishing qi and yin. For the tongue purple dark, mucous membrane swelling pain, burning feeling worse, can add heat cooling blood, blood circulation and blood stasis drugs. Commonly used drugs are Suiniujiao (*Buffalo horn*, 水牛角), Shengdi, Danpi (*Tree peony bark*, 丹皮) and so on. For patients with poor sleep due to mucosal inflammation, Fuling (*Poria cocos*, 茯苓), Wuweizi (*Schisandra*, 五味子) and Sharen (*Amomum villosum*, 砂仁) can be given to calm the heart and calm the mind; Those who cough up blood and ulcerate can be treated with Baiji (*Bletilla*, 白芨) and Sanqi (*Pseudo-ginseng*, 三七).

To sum up, the pathogenesis of radioactive oral mucositis is characterized by a combination of genuine deficiency and apparent excess, with an intricate intermingling of deficiency and excess. Although the disease location is in the mouth, it is closely related to the heart, lung, spleen, stomach and kidney. The differentiation of symptoms in this condition can include patterns of both true heat and false heat. Additionally, the pathological factors of heat, deficiency, and blood stasis can coexist simultaneously, mutually influencing and contributing to the development of the disease. Clinical dialectical treatment should take both specimens into consideration, with clearing heat and detoxifying, invigorating qi and nourishing yin as the main treatment principles. Radiation is hot and solid evil. According to "warm and clear", the method of clearing heat and detoxification should be carried through the

whole course of the syndrome of Weiqi Ying blood disease. *Su Wen•Regulating the Classics* <<素问•调经论>> recorded: "Yin deficiency generates internal heat", fiery and abundant evil consumes yin and jin, yin deficiency causes endogenous deficiency heat, then nourish yin and jin at the same time to eliminate internal heat; Spleen and stomach for the acquired this, "diet into the stomach, spleen for the operation of its elite qi, Although it is said to "spread to all organs," in reality, it first enters and affects the lungs (虽曰周布诸脏, 实先上输于肺), lung first benefit, is for the spleen soil lung gold, lung by the spleen benefit, then the more prosperous qi, water decline, and the body", so the treatment should be used to supplement the spleen and stomach method throughout, spleen and stomach health is filled with qi, take the meaning of supplementing the spleen soil lung gold; The fiery evil poison is worse, invading blood points, fighting blood for stasis, then the stasis heat fight, viscera damage, consume yin qi, as *Reading Medical Essay* <<读医随笔>> said "body fluid for fire exhaustion, then the blood line more stagnant", manifested as mucosal rupture, erosion, even appear bleeding, hemoptysis. At this time, we should make good use of products that clear heat and cool blood and promote blood stasis to help restore the operation of qi and blood. The early prevention and treatment of RIOM can mainly promote qi and yin, and the symptoms of RIOM are gradually emerging in the middle stage. It should focus on detoxifying and cooling blood on the basis of qi and yin, and pay more attention to the recovery of qi and yin in the later stage, remove stasis and heat, prevent the disease and evil from remaining unclear and healthy qi no longer. So we should pay attention to the pathogenesis at any time during the treatment, weigh the deficiency and real.

## DISCUSSION

By studying the mechanism of RIOM, we realized that the occurrence of RIOM is a series of complex biological reactions. The mucositis caused by radiotherapy is not only the direct injury of epithelial cells, but also the result of activation of a series of signals triggered by cell injury. There are many potential therapeutic targets in the pathogenesis of RIOM, which may become new research directions in the future. Western medicine mainly starts from the physiological and pathological mechanism of

RIOM. In clinical application, drugs such as morphine mouthwash, cell growth factor and benzydamine mouthwash are used for pain relief, anti-inflammatory, antibacterial treatment and mucosal growth promotion. Low-intensity laser therapy and oral cryotherapy are used as means to prevent and reduce the incidence of RIOM. But strong preventive interventions are still needed. Through sorting out the new indicators, such as osteopontin, serum IgA, oral saliva flow and other indicators may become a strong candidate in the future. In addition to osteopontin and serum IgA, saliva contains thousands of glycoprotein components. As an important molecule involved in immune response and inflammation-related reactions, it provides a novel and active potential field for our future research. TCM treatment is based on the study of the occurrence and changes of diseases, the analysis and diagnosis from the overall idea, through the means of syndrome differentiation and treatment, to clear heat and detoxification, nourishing Yin and promoting fluid, tonifying spleen and stomach, and cooling blood and removing blood stasis as the treatment principle, while alleviating patients with dry throat, dry mouth, annoying heat, constipation and other dry symptoms, at the same time, tonifying spleen and stomach, tonifying spleen and qi throughout the treatment process. Improve the symptoms of qi deficiency and fatigue, and cool blood to remove blood stasis. During the treatment period, attention should be paid to observe the pathogenesis changes and weigh the use of drugs at any time. On the basis of improving the symptoms, Chinese medicine treatment can also enhance the physique of patients, remove the evil and support the right, and have a good effect on the anti-tumor treatment and subsequent recovery of cancer patients. In clinical practice, the author suggests the use of integrated traditional Chinese and western medicine to get better results.

## SUMMARY AND CONCLUSIONS

Pain, eating disorders, sleep disorders, etc. caused by oral mucositis will not only affect our quality of life, but also may affect anti-tumor therapy and thus affect the treatment effect. At present, there are many clinical studies on its pathogenesis, but the treatment of RIOM is still a great challenge for us. We should strengthen research on evidence-

based interventions and develop authoritative predictive diagnostic tools. The pathogenesis of mucositis is similar to the side effects of other forms of radiotherapy and chemotherapy, so successful intervention for RIOM may stimulate new ideas for other areas such as radiation-associated dermatitis, proctitis, and pneumonia.

In the treatment of radiation mucositis, we should always pay attention to the pathogenesis changes, with yin-enriching and fluid-producing therapy, invigorating spleen and qi and clearing heat and cooling blood as the basic methods, focusing on different times, adding or subtracting appropriate drugs to the symptoms, and finding suitable treatment methods for patients.

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