

Yin-Nourishing and Heat-Clearing Therapy for Radiotherapy-Related Adverse Effects in Nasopharyngeal Carcinoma: A Review

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Abstract: *Nasopharyngeal carcinoma is prevalent in southern China, and radiotherapy remains the principal treatment. Despite effective tumor control, radiotherapy often causes oral mucositis, xerostomia, sinusitis, and dermatitis. These adverse effects impair quality of life and may interrupt treatment. This review examines their pathogenesis from biomedical and traditional Chinese medicine perspectives. It then summarizes clinical approaches based on nourishing yin and clearing heat and evaluates pharmacological evidence for representative formulas and medicinal substances. Current findings suggest anti-inflammatory, antioxidant, immunomodulatory, microcirculatory, and tissue-repair effects. However, small samples, heterogeneous interventions, inconsistent outcomes, and indirect mechanistic evidence preclude firm conclusions. Multicenter randomized controlled trials are needed to determine efficacy, safety, optimal timing, and the relationship between pharmacological mechanisms and clinical outcomes.*

Keywords: Nasopharyngeal carcinoma, Radiotherapy-related injury, Nourishing yin, Clearing heat, Traditional Chinese medicine.

1. Introduction

Nasopharyngeal carcinoma (NPC) is a common head and neck malignancy, particularly in Asia and southern China. The deep anatomical location of the nasopharynx, its proximity to critical structures, and the radiosensitivity of NPC make radiotherapy the mainstay of treatment. However, radiotherapy may cause systemic symptoms, including fatigue, nausea, dizziness, and insomnia. It also causes local injuries such as oral mucositis, xerostomia, dermatitis, and sinusitis. These complications reduce quality of life and may compromise treatment adherence. In traditional Chinese medicine (TCM), radiation is viewed as a fire-heat toxin that consumes qi and damages body fluids. Nourishing yin and clearing heat is therefore an important therapeutic principle.

Radiotherapy-related injury comprises interacting symptoms rather than isolated events. Symptom-network analysis has identified oropharyngeal, emotional-sleep, gastrointestinal, and neurological clusters. Dry mouth, difficulty swallowing or chewing, and fatigue are key management targets [1]. In TCM, the pathogenesis is characterized by latent cancer toxin, interaction between stasis and heat, and concurrent depletion of qi and yin. Treatment therefore combines detoxification, cooling and activating the blood, and replenishing qi and yin [2,3]. Clinical observations suggest that yin-nourishing and heat-clearing therapy may reduce acute adverse reactions during concurrent chemoradiotherapy [4]. Prescription-mining studies also identify qi supplementation, yin nourishment, heat clearing, detoxification, and blood activation as common strategies in NPC treatment [5]. Evidence from other postoperative cancers provides only indirect support; studies specific to NPC radiotherapy are still required [6].

2. TCM Understanding of Radiotherapy - related Adverse Effects

2.1 Radiation-induced Oral Mucositis

Radiation-induced oral mucositis (RIOM) is a common complication of NPC radiotherapy and results from ionizing-radiation injury to oral mucosal cells. Clinical manifestations include erythema, edema, erosion, ulceration, severe pain, and impaired oral intake. Prolonged exposure may disrupt the oral microenvironment and alter the microbiota. Changes in specific taxa have been associated with RIOM onset and delayed healing. In TCM, RIOM corresponds to the categories of ‘oral ulcer’ and ‘oral erosion.’ Constitutional deficiency is compounded by radiation-induced heat toxin, which consumes body fluids and qi. Injury to the spleen and stomach impairs the upward distribution of fluids. Persistent toxin and heat damage tissue, while prolonged yin depletion generates deficiency heat and delays healing. Deficiency of healthy qi is therefore considered the root, heat toxin the manifestation, and injury to yin and body fluids the consequence.

RIOM can cause pain, dysphagia, nutritional impairment, and radiotherapy interruption. Preventive care, oral hygiene, nutritional support, analgesia, and infection control should continue throughout treatment [7,8]. TCM management addresses the changing balance among heat, stasis, and deficiency. Heat toxin predominates early, enters the nutrient and blood levels in the middle stage, and is followed by depletion of both qi and yin. The wei-qi-ying-xue framework can therefore guide stage-based treatment [9,10]. Professor Pei Zhengxue similarly proposes that fire-heat toxin affects the lung and stomach, consumes qi and fluids, and injures the collaterals [11]. Network pharmacology and molecular docking indicate that *Dendrobium officinale* may modulate HIF-1, PI3K-Akt, and NF-κB signaling. These findings require confirmation in well-designed clinical studies [12].

2.2 Radiation-induced Xerostomia

Reduced salivary secretion is a common long-term complication of radiotherapy. Ionizing radiation damages salivary-gland parenchymal cells and may cause persistent or irreversible functional loss. Patients may experience oral pain, dysgeusia, sleep disturbance, dental caries, and difficulty speaking, chewing, or swallowing. Inadequate intake can lead to weight loss, while chronic oral dryness increases the risk of tooth loss and gingivitis. In TCM, radiation is considered a dry, hot, and toxic pathogen. Heat consumes oral fluids, and dryness injures lung yin and disrupts fluid distribution. Damage to stomach yin and spleen function further reduces the production and transport of saliva. The core pattern is depletion of yin and body fluids by dry heat toxin, leaving the mouth inadequately nourished.

Biomedical mechanisms of salivary-gland radiation injury include damage to acinar and stem/progenitor cells, microvascular and neural injury, oxidative stress, and chronic inflammation. Prevention should therefore combine dose reduction, functional preservation, and tissue repair [13]. Conventional treatments may relieve symptoms but often provide limited long-term benefit. TCM approaches commonly combine nourishment of yin and generation of fluids with heat clearing, detoxification, qi supplementation, and blood activation [14,15]. The 'sweet flavor for sustained tonification' theory emphasizes stage-specific restoration of fluids, support of spleen function, and supplementation of deficiency [16]. The doctrine that the spleen opens into the mouth instead emphasizes strengthening the spleen, replenishing qi, raising clear yang, and distributing fluids [17]. Data-mining studies likewise identify nourishing yin, generating fluids, clearing heat, and detoxifying as the most frequent strategies for post-radiotherapy xerostomia [18].

2.3 Radiation-induced Sinusitis

Radiation-induced sinusitis usually presents with nasal obstruction, yellow purulent discharge, nasal dryness or burning pain, hyposmia, and headache. Radiation damages the nasal epithelium and reduces ciliated, goblet, and basal cells. Acute inflammation and persistent inflammatory signaling cause further epithelial atrophy and compromise the nasal barrier. Although classical TCM texts contain no exact counterpart, the condition resembles biyuan (deep-source nasal discharge). Common patterns include heat toxin with stasis, qi deficiency with phlegm-dampness, and yin deficiency with exuberant fire. Fire-heat toxin obstructs the sinuses and scorches the nasal orifices. Subsequent depletion of lung yin and qi promotes dryness, impaired smell, blood stasis, and phlegm. The central pathogenesis is heat toxin injury to the collaterals, accompanied by qi-yin deficiency and binding of phlegm and stasis.

Otitis media and sinusitis may worsen after NPC radiotherapy. Advanced T stage is a risk factor for otitis media, whereas smoking and advanced T stage are associated with sinusitis. High-risk patients require early screening and intervention [19]. In an allergic-rhinitis model, modified Cang'erzi San inhibited SYK/PI3K/Akt signaling and regulated inflammatory immunity [20]. This result supports a possible anti-inflammatory mechanism but is not direct evidence for radiation-induced sinusitis. Flavonoids and saponins in *Gleditsiae Spina* also have anti-inflammatory and

antibacterial activities, providing a pharmacological rationale for further study [21].

2.4 Radiation-induced Dermatitis

Radiation-induced dermatitis ranges from erythema, dryness, and desquamation to erosion, ulceration, bleeding, and necrosis. Its pathogenesis involves cellular and molecular injury, with free-radical-mediated oxidative stress playing a central role. TCM classifies the condition as a sore or ulcer. Fire toxin enters the skin and damages the vessels, causing erythema and burning pain. Damp-heat causes erosion, exudation, and pruritus. Prolonged heat consumes qi and yin and deprives the skin of nourishment, while collateral injury impairs blood flow and may lead to bleeding or necrosis. The main patterns are exuberant heat toxin, damp-heat accumulation, qi-yin deficiency, and blood stasis obstructing the collaterals.

Key pathological processes include barrier disruption, oxidative stress, persistent inflammation, and defective repair. In an animal model, Compound Sophora flavescens Gel inhibited PI3K/Akt phosphorylation and reduced IL-1 β , IL-6, and TNF- α [22]. Sophora flavescens and its active constituents may also regulate ion channels, inhibit excessive keratinocyte proliferation, and strengthen antioxidant defenses [23]. Clinically, a blood-cooling, blood-activating, and detoxifying decoction improved radiation dermatitis in patients with NPC [24]. A medical radiation-protection spray combined with Kangfuxin Liquid reduced inflammation in radiation dermatitis associated with another malignancy [25]. This finding provides indirect evidence only. Aloe constituents have anti-inflammatory, antibacterial, antioxidant, and wound-healing activities [26]. The principle of supporting healthy qi while resolving stasis may also inform treatment of chronic lesions involving the collaterals [27].

3. Clinical Applications of Yin-nourishing and Heat-clearing Therapy

3.1 Radiation-induced Oral Mucositis

Clinical treatment of RIOM commonly centers on nourishing yin and clearing heat. One randomized trial compared Kangfuxin Liquid alone with Kangfuxin Liquid plus Banlangen Granules. The combined regimen achieved a higher response rate and greater improvements in symptom, pain, and quality-of-life scores. Another study added nebulized Shenmai Injection to chlorhexidine gargle and montmorillonite; mucosal injury decreased and the clinical response improved. In severe RIOM, Compound Kushen Injection plus a locally prepared gargle shortened ulcer duration and promoted mucosal healing. It also improved TCM symptoms, oral microbial balance, and local inflammation. A cooling-decoction gargle plus Kangfuxin spray delayed the onset of radiation stomatitis and reduced C-reactive protein and TCM syndrome scores. Oral *Dendrobium officinale* tea also alleviated symptoms associated with yin deficiency and exuberant fire during radiotherapy.

Banlangen Granules contain alkaloids, organic acids,

glycosides, and polysaccharides with antimicrobial, anti-endotoxin, anti-inflammatory, and immunomodulatory activities [28]. These properties provide a pharmacological rationale for their use in oropharyngeal inflammation. Reviews of integrative RIOM treatment recommend combining local care, mucosal protection, anti-inflammatory analgesia, and syndrome-based herbal therapy to address its multifactorial pathogenesis [29].

3.2 Radiation-induced Xerostomia

Several clinical studies have evaluated yin-nourishing interventions for xerostomia. Lugen Shengmai Yin given during concurrent chemoradiotherapy reduced adverse reactions and xerostomia, preserved salivary-gland function, and improved quality of life compared with placebo. Modified Zengye Decoction plus Kangfuxin Liquid improved xerostomia associated with yin deficiency and exuberant fire more than Kangfuxin Liquid alone. Zhigancao Decoction, used first as a rinse and then swallowed, reduced visual analogue scale scores and increased salivary secretion. It also lowered IL-17 and increased IL-10 at the end of radiotherapy and six months later. A blood-activating, yin-nourishing, and detoxifying decoction combined with symptomatic Western treatment improved xerostomia, TCM syndrome scores, and Karnofsky performance status. A yin-nourishing and pathogen-eliminating decoction added to radiotherapy and Kangfuxin Liquid also improved symptoms and syndrome scores.

Shashen Maidong Ganlu Yin improved radiation-induced oral dryness and related quality-of-life outcomes, providing direct clinical support for nourishing yin and generating fluids [30]. A yin-nourishing and dryness-moistening formula combined with acupuncture increased salivary flow, reduced salivary-gland injury, and improved immune-regulation indices [31].

3.3 Radiation-induced Sinusitis

In a randomized study, modified Cang'erzi San plus nasal irrigation achieved a higher response rate and a lower incidence of radiation-induced sinusitis than irrigation alone. Negative-pressure sinus replacement using Gleditsiae Spina granules improved postnasal discharge, nasal obstruction, olfactory loss, retained secretions, and mucosal edema compared with saline. Chinese herbal ultrasonic nasal inhalation added to irrigation also reduced sinusitis incidence. It improved headache, obstruction, discharge, olfactory function, and Lund-Kennedy scores and lowered high-sensitivity C-reactive protein and TNF- α .

3.4 Radiation-induced Dermatitis

Topical Kangfuxin Liquid combined with fresh Aloe provided greater protection against radiation dermatitis than either treatment alone. Compound Kushen Injection administered during definitive chemoradiotherapy reduced the grade of acute dermatitis without compromising the short-term tumor response. In patients with qi-yin deficiency, an oral qi-supplementing and yin-nourishing formula plus topical basic fibroblast growth factor delayed dermatitis onset, shortened healing, and reduced injury severity and pain.

4. Pharmacological Basis and Critical Appraisal

Radiotherapy-related injury in NPC is generally characterized by qi-yin deficiency as the root and heat toxin, phlegm, and stasis as the manifestations. Yin-nourishing and heat-clearing therapy should complement, not replace, standard oral care, mucosal protection, analgesia, infection control, and other supportive measures. Studies of Compound Kushen Injection suggest possible effects on radiation injury, cellular immunity, inflammation, energy metabolism, and tumor-related signaling [32,33]. However, small samples, heterogeneous regimens, and inconsistent outcomes limit confidence in these findings.

Pharmacological evidence for herbs used to treat xerostomia is also multi-targeted. Phragmitis Rhizoma contains polysaccharides, flavonoids, and organic acids with antioxidant, anti-inflammatory, and immunomodulatory activities [34]. Rehmanniae Radix has anti-inflammatory, immunoregulatory, and hematopoietic-protective properties [35]. Dendrobium officinale polysaccharides may exert antioxidant, immunomodulatory, and mucosal-protective effects [36]. Total glycosides and other constituents of Scrophulariae Radix show anti-inflammatory, antioxidant, and metabolic-regulatory activity in models of yin deficiency with exuberant fire [37,38]. Chrysanthemum indicum and Zhigancao Decoction provide further support for heat-clearing, detoxifying, anti-inflammatory, and tissue-protective effects [39,40]. Salvia miltiorrhiza and its herb pairs improve microcirculation and have anti-inflammatory, antioxidant, and antifibrotic activities [41,42]. However, direct links between these pharmacological findings and clinically meaningful salivary outcomes remain to be established.

Management of radiation-induced sinusitis should integrate risk-factor control, local nasal care, and syndrome-based therapy. Gleditsiae Fructus and Gleditsiae Spina come from the same plant but differ in medicinal part, chemical composition, dosage, and safety. They should not be used interchangeably [43]. Future studies should standardize symptom scales, nasal endoscopy scores, inflammatory markers, and follow-up periods.

Radiation-induced dermatitis involves skin-barrier disruption, oxidative stress, persistent inflammation, and defective repair. Combining internal and local treatments appears promising. Nevertheless, results from animal models and other disease settings provide mechanistic support only and should not be treated as direct clinical evidence in patients receiving radiotherapy for NPC.

5. Conclusion and Outlook

Radiotherapy-related oral mucositis, xerostomia, sinusitis, and dermatitis share several pathological features: heat toxin injury, depletion of qi and yin, inflammation, oxidative stress, microcirculatory disturbance, and impaired tissue repair. A treatment strategy centered on nourishing yin and clearing heat is consistent with TCM theory and emerging pharmacological evidence. Detoxification, qi supplementation, blood activation, and local therapy may be

added according to the affected site and disease stage. Current clinical studies suggest possible improvements in symptoms, salivary function, mucosal and skin healing, inflammatory regulation, and quality of life.

The evidence remains limited by small, single-center samples; variable formulas and dosages; inconsistent control interventions; and heterogeneous outcome definitions. Some mechanistic conclusions come from animal models or unrelated diseases and cannot be directly generalized to NPC radiotherapy. Future studies should use multicenter randomized controlled designs, standardized diagnostic and outcome criteria, prospective safety monitoring, and longer follow-up. Objective biomarkers, salivary and imaging measures, microbiome profiles, and patient-reported outcomes may help identify patients most likely to benefit and clarify how pharmacological mechanisms translate into clinical effects.

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