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A CONCEPTUAL STUDY ON THE ROLE OF AYURVEDA IN MANAGEMENT OF CHEMO RADIATION INDUCED ORAL MUCOSITIS

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ABSTRACT

Chemo/Radiation induced oral mucositis is a significant problem in cancer patients undergoing therapy. It is a major dose-limiting toxicity of chemo-radiation therapy in various cancers. Ayurveda has explained conditions such as sarvasaramukha paka which are disease conditions similar to oral mucositis. There are various ayurvedic herbs with proven effect in managing and preventing chemo-radiation induced oral mucositis. Ayurveda can offer a healthy alternative to management of chemo/radiation induced oral mucositis. Future research can point to the specific ayurvedic treatments in oral mucositis imbibing the principles of Ayurveda and not focusing just on the pharmaco analytical profile of certain plants alone.

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INTRODUCTION

Oral mucositis points to erythematous and ulcerative lesions in the oral mucosal layer seen in patients having cancer while being treated using chemotherapy and radiation therapy or both to areas adjacent to and including the oral cavity. The oral mucositis lesions are very painful and can affect nutrition and oral hygiene and increase the risk of local and systemic infection to the patient. Mucositis can also affect other areas of the alimentary tract; such as, gastrointestinal region which can manifest as diarrhea. Mucositis, hence, is a highly clinically relevant and at-times dose-limiting complication of cancer therapy^{1,2}.

Oral mucositis is a significant problem in patients undergoing chemotherapeutic management and was reported to affect 51% of patients receiving chemotherapy for solid tumors or lymphoma.³ An even higher percentage (approximately 75–80%) of patients receiving high-dose chemotherapy before hematopoietic cell transplantation are reported to develop clinically significant oral mucositis.⁴ Patients who are being treated with radiation therapy for head and neck cancer typically receive an approximately 200 cGy daily dose of radiation, five days per week, for 5–7 continuous weeks are found to be susceptible to oral mucositis invariably. Many studies have reported that severe oral mucositis is found in 29–66% of all patients receiving radiation therapy for head and neck cancer^{5,6}. Infections accompanying oral mucositis lesions can result in life-threatening systemic sepsis during cycles of immunosuppression⁷. Moderate to severe oral mucositis has been found to have positive correlation to systemic infection and transplant-related mortality⁸. In patients having hematologic malignancies and allogeneic hematopoietic cell transplantation, it was found that there is an increased severity of oral mucositis associated resulting in total parenteral nutrition and parenteral narcotic therapy.⁹ It can also cause increased incidence of fever, infection, hospital admission and increased total inpatient charges¹⁰.

A major chunk of patients who are being managed by radiation therapy for head and neck cancer are found to suffer from inability to continue eating by mouth due to mucositis pain and often receive nutrition through a nasogastric tube or intravenous line.¹¹ It has been shown that patients with oral mucositis are significantly more prone to have severe pain and a weight loss of $\geq 5\%$.¹² In a study, approximately 16% of patients receiving radiation therapy for head and neck cancer were hospitalized due to mucositis¹³. Further, 11% of the patients receiving radiation therapy for head and neck cancer had unplanned breaks in radiation therapy due to severe mucositis. Thus, oral mucositis is a major dose-limiting toxicity of radiation therapy to the head and neck region.

Oral mucositis at the outset presents as erythema or redness of the oral mucosa which later progresses to erosion and ulceration of the mucosal layer. The ulcerations are often found to be covered by a white fibrinous pseudomembrane and the lesions mostly heal in an approximate duration of 2–4 weeks after the last dose of chemotherapy or radiation therapy.¹⁴ Immunosuppressed patients (eg. patients undergoing hematopoietic cell transplantation) may have resolution of oral mucositis seen associated with temporary granulocyte recovery.¹⁵

This conceptual review looks at the role of Ayurveda in preventing and managing chemoradiation induced oral mucositis.

Ayurvedic Perspective

Shalaky Tantra is one of the eight branches of Ayurveda which particularly deals with the diseases occurring in head, neck, eyes, ear and oral cavity.¹⁶ Mukhagata Roga or diseases of oral cavity is described in ancient Ayurvedic texts like Sushrut Samhita, Charak Samhita, Astanga Sangraha, Yoga Ratnakar, Madhav Nidan, etc. Mukha stands for oral cavity and sarvasara includes the sarvabhaga of the mukha viz-osta, danta, dantamoola, jihwa, talu and kanta.¹⁷ Disease of oral cavity are 65 in number, which occur in seven locations of mouth such as lips-8, gums-15, teeth-8, tongue-5, palate-9, throat-17, sarva mukha-3.¹⁸

Among this Sarvasaramukha paka or aananpaka, (oral cavity) can be considered a close apparition of oral mucositis. It is recognized as pittanantmajavikara and ratkapradoshajvikara and treated as such. Paka refers to inflammation or ulceration symptomatically similar to oral mucositis. There are 5 types of Mukha Paka – i) Vataj Mukha Paka – In this, vitiated Vata dosha causes a single or multiple ulcers in the oral mucosa with acute inflammatory changes. The disease is progressive in nature, very painful, mucosa becomes dry and rough. The associated symptoms are inflamed lips, tongue and palate, difficulty in opening the mouth and sensitivity to cold items, etc.

ii) Pittaj Mukha Paka – In this, vitiated pitta dosha causes inflammation and ulceration of oral mucosa. Smaller reddish yellow papules develop throughout the mouth and causes severe burning, altered taste, difficulty in mastication and deglutition.

iii) Kaphaja Mukha Paka – In this, vitiated Kapha dosha causes inflammation and ulceration of oral mucosa. The mouth becomes sweet and sticky with itching sensation and negligible pain. Small cysts or tumors develop and become more severe by compression and excision.

iv) Sannipataja Mukha Paka – All the symptoms of Tridosha and Rakta dosha are present in this disease.

v) Raktaj Mukha Paka – All the signs and symptoms and treatment are like Pittaja Mukha Paka¹⁹

It is evident from the predominant nature of the symptoms that the various dosha involvements point to an increasing severity and chronicity of the disease rather than different disease conditions. Looking at the patho physiology, the disease is pitha Rakthaja in nature. The nidana of radiation/chemotherapy are also suitable to cause this Pitha Vrudhi due to its Theekshna, Ushna, Vyavayi and Vikashi in nature.

General line of treatment includes Snehana, Swedana (oleation) and Shodhana Karma (Vaman, Virechan, Nasya, Rakta mokshan) from a systemic point of view.²⁰

Kavalgraha / Gandusha is the primary line of treatment to attain local cure in all conditions. Medicines vary according to dosha pradhanatha such as Triphala Kashaya, Rasnadi Kashaya, Dashmoola Kashaya, Vatahara Taila or Ghrita for vata, Panchvalka Kashaya, Pancha Tikta Kashaya, Yashtimadhu Kashaya, milk, sugarcane juice and ghee for Pitha and Khadiradi Taila, Haridradi Taila, Trikatu Kashaya for Kapha predominance.²¹

Snehika Dhoomapana (medicated smoking), Lekhana, Pratisarana and Raktha mokshana are also indicated.²²

Existing Evidence on the efficacy of Ayurvedic Drugs in Chemo/Radiation induced Oral Mucositis

Woon sup yoon et.al has substantiated shown the positive effect of Thriphala on radiation induced acute intestinal mucosa damage in Sprague Dawley rats.²³ RK Mamgain et al has shown in a pilot study the superior efficacy of an ayurvedic preparation of yashtimadhu (*Glycyrrhiza glabra*) on radiation-induced mucositis in head-and-neck cancer patients when given along with conventional management when compared to conventional management alone.²⁴ Yashtimadhu was observed to be effective and delayed the development of severe form of mucositis. Ahmadi A²⁵ postulated that Oral aloe vera mouthwash has anti-inflammatory and wound healing properties thus preventing the development of radiation induced mucositis. Though Su et al.²⁶, in their study concluded that oral aloe vera was not beneficial adjunct to head and neck radiotherapy and didn't decreased mucositis or improved patients' well being. Naidu MU et.al²⁷ studied a mixture of herbal agent used as an oral gel wafer including extracts of glycyrrhizin, *Centella asiatica*, *Polygonumcuspidatum*, *Angelica sp* and *Camellia sinensis*. A pilot study showed the positive effect of the combination in oral mucositis, however, further studies should confirm these results. The efficacy of pure natural honey for the treatment of mucositis was reported in patients under radiation therapy and/or chemotherapy in several clinical trials. We have found many clinical trials associated with the preventive and therapeutic effects of honey and its relative products for management of radiation- and chemotherapy-induced mucositis.²⁸ In a randomized single blind clinical trial, 40 patients who suffered from head and neck cancer and required radiation to the oropharyngeal mucosa were randomly divided into 2 groups. Patients received 20 mL pure natural honey from bees fed on thyme and astragale in the Alborz Mountains of Iran, 15 minutes before, then 20 mL doses again at 15 minutes and 6 hours after radiation therapy. They washed their mouths with honey and engorged slowly to cover the oral and pharyngeal mucosa. A significant reduction in mucositis in patients treated with honey was observed as compared with controls.²⁹ The same results in reduction of mucositis were observed in another study, in which 40 patients received topical applications of 20 mL pure honey before and after radiation therapy.³⁰ In a clinical trial, the effect of natural honey and 0.15% benzydamine hydrochloride on onset and severity of radiation mucositis was assessed and compared with control. The patients were randomized into three groups of 20 patients. Group 1 patients received topical application of natural honey; groups 2 and 3 received topical application of 0.15% benzydamine hydrochloride and 0.9% normal saline, respectively. The onset of mucositis and the severity of mucositis were graded during the course of the radiotherapy and 2 weeks after radiotherapy. A significant reduction of mucositis in patients treated with honey was compared with 0.15% benzydamine hydrochloride, 0.9% normal saline applied to patients was observed. The differences between the groups were statistically significant.³¹ Results of other studies showed that prophylactic use of natural honey was effective in reduction of mucositis subjective symptoms from radiotherapy and/or chemotherapy. Honey reduces wound pain by postponing tissue oxygenation through blocking exposure of the damaged mucosa to oxygen.³² Biswal et al³³ suggested that the effectiveness of honey on wound healing might be because of the hygroscopic nature of honey, its viscosity, its acidic pH, which prevents bacteria growth on the mucosa, inhibin (hydrogen peroxide) converted from glucose oxidase and gluconic acid, enzymes which probably are growth factors and tissue nutritive minerals and vitamins that help repair the tissue directly.

Shinobu Okada et.al³⁴, in a pilot study in hematopoietic cancer patients suggested that topical application of sesame oil, which has both antioxidative and anti-inflammatory activities, is useful for retardation of chemotherapy-induced oral mucositis. In the same study, cytological examination further demonstrated that inflammation induced by chemotherapy is reduced by sesame-oil application.

CONCLUSION

Mucositis affects most patients undergoing chemotherapy and radiotherapy and is a major clinical and economic burden that severely affects patient survival and quality of life.³⁵ However, management of mucositis largely involves the control of symptoms using antibiotics, anesthetics, and analgesics,³⁶ and there are very limited therapeutic agents available for mucositis treatment. Ayurveda with its wide range of therapeutic options can offer a solution to this debilitating clinical condition thereby saving the health, wealth and quality of life of the patients undergoing chemo/radiotherapy. Future research can point to the specific ayurvedic treatments in oral mucositis imbibing the principles of Ayurveda and not focusing just on the pharmaco analytical profile of certain plants alone.

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Competing Interests

The authors declare no conflict of interest.

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