

# Prevention of Oral Mucositis Induced by Chemoradiotherapy in Head-and-Neck Carcinoma Patients – A Comparative Study

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## Abstract

**Introduction:** Radiation-induced mucositis is quite bothersome due to acute complications in patients receiving radiotherapy (RT) and even more pronounced with the combined chemoradiotherapy. Mucositis manifests itself as erythema, edema, or ulceration that can be accompanied by a mild burning sensation.

**Aim:** This study aims to compare the efficacy of oral glutamine in the prevention of chemoradiotherapy-induced oral mucositis in head-and-neck cancer patients.

**Materials and Methods:** A total of 40 patients with malignancy confirmed in histopathology who were undergoing conventional RT for head-and-neck cancer were divided into two groups, Group A receives oral glutamine 10 g in 1000 ml of water 2 h before the RT and Group B undergoes conventional RT. The outcome was measured in the 6<sup>th</sup> week of RT and 3<sup>rd</sup> week of post-RT.

**Results:** Twenty-six patients (65%) had carcinoma of the oropharynx, while 14 patients (35%) had carcinoma of the larynx. In this study, 75% of patients in Group A and 85% of patients in Group B are in Stage IV cancers. Supplementation with oral glutamine before RT shown a significant reduction in incidence of mucositis compared to the control group. Post-RT, there was a significant reduction in number mucositis cases in Group A than Group B.

**Conclusion:** Oral glutamine decreased the incidence of chemoradiotherapy-induced oral mucositis.

**Key words:** Oral glutamine, Oral mucositis, Radiotherapy

## INTRODUCTION

Head-and-neck cancer represents the sixth most common cancer worldwide.<sup>[1]</sup> It is one of the most common cancers in developing countries like India.<sup>[2]</sup> In India, it is the most common cancer in males and forms 30% load of India's cancer burden.<sup>[2]</sup>

Radiation therapy plays an important role in the treatment of patients with head-and-neck cancer. Regulated by the location of the malignancy (primary tumor and lymph node metastases), necessarily, the salivary glands, oral mucosa, and jaws have to be included in the radiation treatment

protocols.<sup>[3]</sup> Although, that may result in short- and long-term side effects, this kind of treatment is more effective than the others. Possible side effects include mucositis, osteoradionecrosis, taste loss, hyposalivation, radiation caries, periodontal disease, trismus, and so on.<sup>[4]</sup> Among the acute clinical side effects, disruption in the function and integrity of the mouth are the most important cases. These complications can result in severe ulceration called mucositis. Recently, many studies have been published on the radiation-induced oropharyngeal mucositis associated with the treatment of head-and-neck tumors. The mucositis may be accompanied with other complications such as oral discomfort, pain, poor nutrition, delays in drug control, increased hospitalization, and costs as well as life-threatening infection in some patients. For all of these reasons, oral mucositis should be prevented or minimized as much as possible.<sup>[5]</sup>

## Aim

This study aims to compare the efficacy of oral glutamine in the prevention of chemoradiotherapy-induced oral mucositis in head-and-neck cancer patients.

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## MATERIALS AND METHODS

This prospective comparative study was conducted in the Department of Radiotherapy at Tirunelveli Medical College from January 2019 to June 2019.

### Inclusion Criteria

Patients with malignancy confirmed in histopathology who were undergoing conventional radiotherapy (RT) for head-and-neck cancer were included in the study.

### Exclusion Criteria

Patients with a previous history of receiving RT, uncontrolled systemic or disseminated disease, and presence of the synchronous double malignant tumor were excluded from the study.

Patients were randomized into two groups; Group A receives oral glutamine 10 g in 1000 ml of water 2 h before the RT and Group B undergoes conventional RT.

All patients treated with cobalt-60 teletherapy unit by two-dimensional technique with concurrent weekly cisplatin 50 mg.

The patients were evaluated by the same observer at the 3<sup>rd</sup> and 6<sup>th</sup> weeks during the treatment protocol and the 3<sup>rd</sup> week post-RT. All patients had completed dental and oral examination before treatment and underwent oral care. For symptomatic mucositis, oral paracetamol tablets 500 mg or tramadol 100 mg was administered according to the severity of pain. The need for painkillers, adverse events associated with the study drugs, and patient non-adherence to treatment were recorded.

## RESULTS

In this study, a total of 20 patients were included in the study. There were divided into two groups; Group A receives oral glutamine 10 g in 1000 ml of water 2 h before the RT and Group B undergoes conventional RT.

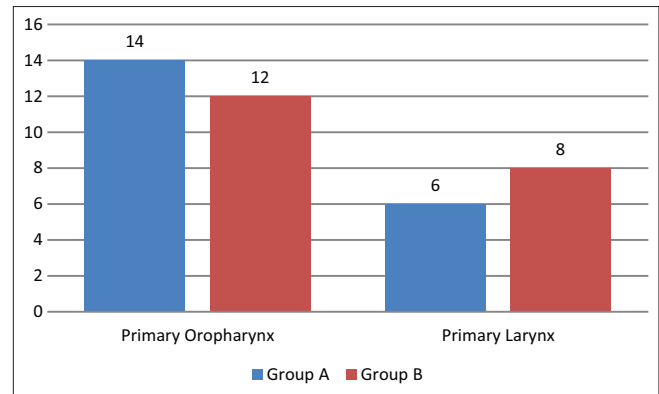
In this study, higher number of patients was in the age group between 51 and 60 years in both groups. Male predominance was noted in both groups. There was no statistical difference noted in the demographics of patients [Table 1 and Figures 1-4].

Twenty-six patients (65%) had carcinoma of the oropharynx, while 14 patients (35%) had carcinoma of the larynx.

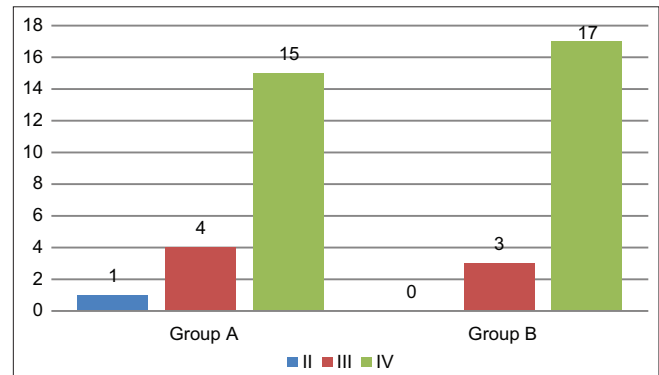
In this study, 75% of patients in Group A and 85% of patients in Group B are in Stage IV cancers.

**Table 1: Distribution of the study parameters**

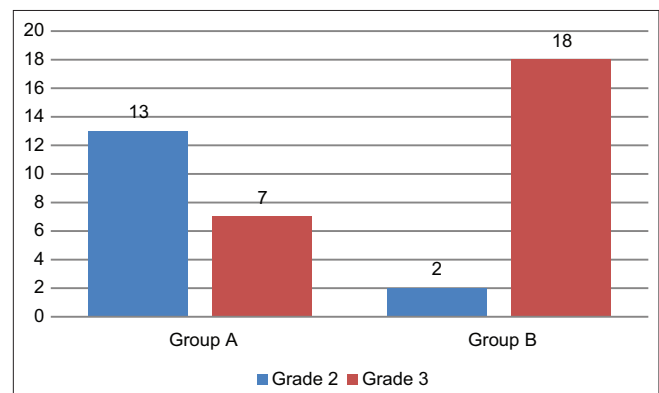
Parameters	Group A	Group B
Age group		
40–50 years	4	4
51–60 years	11	12
>60 years	5	4
Gender		
Male	18	19
Female	2	1



**Figure 1: Distribution of site**

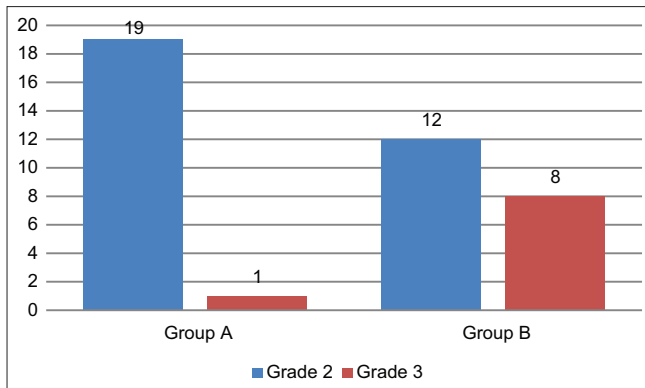


**Figure 2: Distribution of AJCC stage**



**Figure 3: Distribution of outcome at the 6<sup>th</sup> week of radiotherapy**

Supplementation with oral glutamine before RT shown a significant reduction in incidence of mucositis compared to the control group.



**Figure 4: Distribution of outcome after 3 weeks of radiotherapy**

Post-RT, there was a significant reduction in the number of mucositis cases in Group A than Group B.

## DISCUSSION

Radiation-induced mucositis is quite bothersome due to acute complications in patients receiving RT and even more pronounced with the combined chemoradiotherapy. Mucositis manifests itself as erythema, edema, or ulceration that can be accompanied by a mild burning sensation.<sup>[3]</sup> Extreme appearances are characterized by large and painful ulcers that have a large impact on patient's quality of life. It may seriously restrict simple activities such as speaking, eating, or even swallowing saliva.<sup>[6]</sup> The early clinical sign of mucositis is erythema appearing at cumulative doses of head-and-neck radiation of about 10 Gy.

In general, oropharyngeal mucositis occurs in more than 90% of patients who receive radiation and/or chemotherapy for head-and-neck tumors.<sup>[7]</sup> It occurs in almost all the patients who are treated for cancers of the mouth, oropharynx, nasopharynx, and in approximately two-thirds of those treated for cancers of the hypopharynx or larynx.<sup>[8]</sup> Vera-Llonch *et al.* reported that 80% of patients undergoing radiation therapy showed oropharyngeal mucositis and 29% developed severe oropharyngeal mucositis.<sup>[9]</sup>

Glutamine is one of the 20 amino acids encoded by the standard genetic code. Glutamine is also used by cells of the immune system, such as lymphocytes and macrophages. Some studies have suggested that dietary supplementation with glutamine may protect the gut from the side effects of both RT and chemotherapy.<sup>[10,11]</sup>

Some studies have shown that glutamine increases collagen synthesis in human fibroblasts by a direct stimulatory effect and as a proline and hydroxyproline residue precursor.<sup>[12,13]</sup> It also enhances the immune system and is an important fuel for both macrophages and lymphocytes. IV glutamine

supplementation reportedly increased immunoglobulin A production in rats.<sup>[14]</sup>

Leitão *et al.* showed that glutamine or alanyl-glutamine accelerated mucosal remodeling from 5-fluorouracil-induced oral mucositis by increasing glutathione stores in hamster mucosa.<sup>[15]</sup> Nose *et al.* demonstrated that bolus enteral glutamine prevented cisplatin-induced intestinal mucosal injury in rats, possibly resulting in increased intracellular glutathione.<sup>[16]</sup> Several clinical studies have shown the protective effects of glutamine on the mucosal epithelium.<sup>[17-19]</sup>

## CONCLUSION

The ideal management of oral mucositis that develops during radiation therapy which is even more pronounced with chemoradiotherapy remains a challenging problem. Prophylactic treatments can help reduce the severity of oral mucositis. Considering the morbidity associated with concurrent chemoradiation due to mucositis, interventions like supplementation with oral glutamine will prove beneficial for the patients.

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