Effect of Honey in Radiation Induced Mucositis in Head and Neck Cancer

John Winkle Medida¹, Bala Sankar Ramavath², Joseph Benjamin Gandi³

ABSTRACT

Introduction: Mucositis is a common side effect of chemo radiotherapy to the head and neck region. It compromises patient’s health and quality of life. Standard treatment is not available at present. Care is limited to symptom control. Honey has anti-bacterial and anti-inflammatory properties. It is naturally available, cheap, and ubiquitous. Hence to know the effect of honey in radiation induced mucositis.

Materials & methods: 56 cancer patients receiving concurrent chemoradiotherapy to head and neck region were recruited in this study from October 2012 to August 2014. Study group consisted 27 patients and control group consisted 29 patients. Study group patients received topical application of honey collected from CAROM plant along with chemo radiotherapy and control group patients received only chemo radiotherapy. All patients were assessed twice a week for the onset and severity of mucositis. Both study and control group patients were advised to take plenty of oral fluids, supplementation with high protein diet and oro dental care.

Results: 15 (55.6%) patients in study group developed mucositis at 13th fraction whereas 15(51.7%) patients in control group developed mucositis at 10th fraction indicating that honey postpones the onset of radiation induced mucositis. The severity of radiation induced mucositis at every assessment showed statistically significant difference between study group and control group. This clearly showed control group patients were with higher grades of mucositis than study group patients.

Conclusion: This prospective interventional study found the usefulness of topical application of honey in reducing the onset and severity of radiation induced mucositis in patients receiving chemo radiation to head and neck cancers.

Keywords: Honey, Radiotherapy, mucositis, Head and neck cancers.

INTRODUCTION

The head and neck cancers form the seventh most common cancer worldwide. They are the most common cancers in developing countries, especially in Southeast Asia. Head and neck cancers are more common in males compared to females. This is mainly attributed to the use of tobacco, areca nut, alcohol etc. Most of the head and neck cancer patients receive radiotherapy at some stage during treatment. Radiotherapy plays a significant role as a primary treatment in early stage and adjuvant treatment later stage head and neck cancers. Due to the radiation-induced DNA damage of surrounding critical structures, radiotherapy can cause debilitating side effects such as skin reactions (erythema, dry desquamation, moist desquamation), oral mucositis (mouth ulceration) xerostomia (dry mouth).

Oral mucositis is caused by a multi-step biological process, which occurs in 30 to 40% of patients receiving chemotherapy, 60% of patients receiving radiotherapy and 92% of patients receiving both chemotherapy and radiotherapy.¹,² It can cause serious secondary complications such as pain, difficulty in eating and swallowing, taste changes, infection, malnutrition and weight loss. It can also lead to a reduction in total dose delivered to the tumor bed and unscheduled treatment breaks. This can have a detrimental effect on local tumor control and thus patient survival.⁴

Management of mucositis is critical to maintain the patients food pathway, avoid interruption in the delivery of radiation treatment and to avoid hospitalization and the need for parenteral or tube feeding. Currently there is no standard treatment for oral mucositis in head and neck cancer patients worldwide. Food and Drug Administration (FDA) have no approved intervention for prevention of radiation induced mucositis. Current management of oral mucositis is limited to symptom control including pain relief and maintenance of good oral hygiene. One of the latest interventions for the management of radiation induced oral mucositis is natural honey.⁵,⁷,⁸ It has antimicrobial properties⁷ and promotes wound healing.

The main objective of this study is to know the effect of topical application of honey on onset and severity of radiation induced mucositis in head and neck cancer patients receiving radiation.

¹Senior Resident, ²Asst professor, ³Professor Department of Radiation Oncology, MNJ Institute of Oncology& Regional Cancer Centre, Hyderabad, India

Corresponding author: Dr. John Winkle Medida, Room no 7, MNJ Institute of Oncology & Regional Cancer Centre, Redhills, Hyderabad, India

How to cite this article: John Winkle Medida, Bala Sankar Ramavath, Joseph Benjamin Gandi. Effect of Honey in Radiation Induced Mucositis in Head and Neck Cancer. International Journal of Contemporary Medical Research 2016;3(1):108-113.
MATERIALS AND METHODS

Present study was done in the department of radiotherapy in MNJ Institute of Oncology & Regional Cancer Centre. The patients were randomly selected from year 2012 to 2014 and were allotted study group and control group.

Inclusion Criteria
Histo-pathologically confirmed non-metastatic Squamous cell carcinoma of head and neck region, age less than 70 years, ECOG performance status of 0-2, Patients should receive Concurrent Chemo radiotherapy as primary treatment.

Exclusion criteria
Tumors of non-Squamous histology, age greater than 70 years, ECOG performance status of >2, any prior treatment received for the tumor, any co-morbid condition or acute infection where treatment is contraindicated, evidence of distant Metastasis.

Patients Recruitment
56 patients receiving concurrent chemo radiotherapy to head and neck cancers were recruited in this study during October 2012 to august 2014. 27 were taken in study group and remaining 29 were taken into control group. Study group received 10ml of natural honey(Carom Plant) procured from NIRD(National Institute of Rural Development) for topical application in oral cavity 10min before and after radiation treatment. They were asked to swirl honey in oral cavity and swallow it slowly so that it can be smeared on oral and pharyngeal mucosa before and after every radiation fraction. Control group patients received only chemo radiotherapy. Both study group and control group patients were advised to take plenty of oral fluids, supplementation with high protein diet and oro-dental care.

Radiation Treatment Planning and Delivery
All patients underwent pre RT oro-dental care. Radiotherapy was delivered by linear accelerator (LINAC) using 6MV X rays. Computer based CT planning was done for all patients in two phases with total dose of 66Gy/33#. PhaseI: 44Gy/22 fractions, 5 fractions per week PhaselI: 22 Gy/11 fraction, 5 fraction per week, sparing the spinal cord.

Patients in both arms received concurrent chemotherapy with cisplatin 40 mg/ m2 given weekly with radiotherapy

Toxicity Assessment
All Patients were assessed twice a week (3#&5# in 1wk, 8# &10# in 2wk, 13# &15# in 3wk,18# &20# in 4wk, 22# in 5wk, 25# &28# in 6wk, 30# &33# in 7wk) for tumor response and development of mucositis. Mucositis was examined clinically under good light. RTOG (Radiation Therapy Oncology Group) grading system was utilized to grade the mucosis.
Onset of Mucositis

The onset of mucositis in study group and control group was as follows:

1 (3.7%) patient in study group and 12 (41.4%) patients in control group developed grade 1 mucositis at 8th fraction. 10 (37%) patients in study group and 15 (51.7%) patients in control group developed grade 1 mucositis at 10th fraction. 15 (55.6%) patients in study group and 2 (6.9%) in control group developed mucositis at 13th fraction.

The mucositis was assessed twice a week. The following table shows the grades of mucositis on every assessment.

None of the patients in study group and control groups developed mucositis at 3#.

DISCUSSION

Radiation-induced mucositis is a normal accompaniment of radiotherapy to the head and neck area. Normally, the oral mucosa has a relatively high cell-turnover rate. Exposure to ionizing radiation leads to mucosal erythema, small whitish patches and ultimately results in confluent mucositis. In later phases, oral ulceration and bleeding become a dose-lim-
onset of radiation induced mucositis.

Onset of Radiation Induced Mucositis

No patients developed RIM at 5th fraction assessment either in study group or control group. The onset of mucositis in control group patients at 8th (41.4%) & 10th (51.7%) constituted 93.1% of control group patients whereas the onset of mucositis at 10th (37%) & 13th (55.6%) in study group patients constituted 92.6% of patients of study group.

Biswal et al. (2003) conducted a clinical trial investigating the effect of tea plant honey on oral mucositis in patients receiving radiation therapy. In their study, 40 patients with oropharyngeal carcinoma were divided into two groups to receive radiation alone or radiation plus topical application of pure natural honey. They reported a significant reduction in the severity of oral mucositis in those patients treated with honey. Only 25% of patients in the honey group developed grade three or four mucositis compared to 75% in the control group.

Sadakshetram Jayachandran et al. (2012) conducted a study to evaluate the effect of natural honey and 0.15% benzylamine hydrochloride on the onset and severity of radiation induced mucositis. They assessed patients daily, for the onset and severity of mucositis. The onset of mucositis for honey group was on 14th day compared to 12th day for 0.15% benzylamine and control group.

The present study results also showed the onset of mucositis for majority of study group patients was at 13th fraction whereas for control group patients was at 10th fraction inferring honey postpones the onset of mucositis.

SEVERITY OF MUCOSITIS

The current study assessed mucositis twice a week till the end of radiation treatment. Thus patients were assessed at 3rd, 5th, 8th, 10th, 13th, 15th, 18th, 20th, 22nd, 25th, 28th, 30th and 33rd fractions.

Pattern of mucositis

All patients developed mucositis during radiation treatment. The severity of mucositis was increased as the fractions were increased and towards the end of the treatment severity was decreased in both groups.

The majority patients in study group developed mucositis around 10th & 13th fraction (92.6%) and majority of patients in control group developed around 8th & 10th fraction (93.4%). The severity of mucositis assessed at every fraction showed a statistically significant difference between study and control groups with p value of <0.01.

The results of this study were consistent with the following randomized controlled clinical trials investigating the effect of honey on oral mucositis, using a similar study protocol. Motallebnejad et al. (2008) and Rashad et al. (2008) conducted similar trials using honey in Iran and Egypt respectively. Motallebnejad et al. (2008) evaluated 40 patients with 20 in each arm to receive and not to receive honey. Mucositis...
was assessed with oral mucositis assessment scale (OMAS). The results showed significant reduction in mucositis among honey received patients compared with controls with p value of 0.000. Rashad et al. (2008) randomized 40 patients to study group to receive honey topically along with radiotherapy and control group only with radiotherapy. Patients were assessed weekly for the development of mucositis. No patients in the study group developed grade 4 mucositis and only 15% of patients developed grade 3 mucositis whereas 65% of patients developed grade 3/4 mucositis in control group (p<0.05). Motallebnejad et al. (2008) used saline mouthwashes and Rashad et al. (2008) used Benzydamine HCl mouthwashes for all patients.

Sadaksharam Jayachandran et al. evaluated 60 patients and divided them into 20 patients each group taking honey orally, 0.15% benzydamine chloride and normal saline during radiation treatment. They found pure natural honey delays the onset of radiation induced mucositis and significantly reduce the severity of mucositis. The differences between the groups were statistically significant (P < 0.001).

Important factors that influence the effectiveness of honey: Its hygroscopic nature, acidic pH prevents bacteria growth when applied to the mucosa, Inhibin (hydrogen peroxide) converted from glucose oxydase and gluconic acid, Enzymes (growth factors?) and tissue-nutritive minerals and vitamins help repair tissue directly.

The antibacterial property of honey depends upon its concentration. The effect on radiation mucositis in honey treated patients might be due to the bacteriostatic effect of viscid honey. Pure honey is acidic, with a pH of around 3.9. The solubility reducing factor present in honey can activate in absence of saliva. Honey applied on radiation induced xerotic mucosa increases the micro hardness of enamel, thereby preventing caries. Hence, it has been postulated that honey is less Cariogenic in dry mouth patients.

There are currently no approved agents or strategies that reliably prevent RIM, although several agents are under investigation. The current recommendations for mucositis are directed at limiting its extent and/or severity by appropriate treatment selection, attention to RT planning details, and the use of supportive and palliative care including basic oral care, aggressive use of analgesics, the use of feeding tubes in selected cases, and swallowing exercises and therapy. Honey has been found effective in burn wounds, oral infections and acceleration of surgical wound healing. Pure honey is ubiquitous, cheap and natural, and exhibits antibacterial, analgesic and tissue nutritive factors to stimulate re epithelization in the damaged mucosa, and is thereby a justified agent to try in radiation mucositis. Through this study, topical application of honey can be used as an effective intervention to prevent the radiation induced mucositis.

CONCLUSION

1. This small prospective interventional study found the usefulness of topical application of honey in reducing the onset as well as severity of radiation induced mucositis in patients receiving radiation to head and neck cancers.

2. The results of the study are similar with three overseas studies Biswall et al., 2003; Motallebnejad et al., 2008 and Rashad et al., 2008 and one Indian study by Sadaksharam Jayachandran and Narasimhan Balaji, 2010.

Limitations
1. The sample of patients is small.
2. The study group is not representative of entire head and neck cancer patients.
3. Non randomization of patients.

Recommendations
This study evaluated patients for radiation induced mucositis twice a week. By this, the exact fraction/dose of development of mucositis can not be assessed properly. Instead if assessed daily, the exact fraction/dose at which the mucositis starts can be known. The effect of honey on the radiation dosimetry should be studied, if it is adopted as one of the modality of treatment of radiation induced mucositis.

REFERENCES

9. Khanal B1, Baliga M, Uppal N. Effect of topical honey on limitation of radiation-induced oral mucosi-


Source of Support: Nil; Conflict of Interest: None

Submitted: 21-11-2015; Published online: 05-12-2015