



ORIGINAL RESEARCH PAPER

Oncology

EFFECT OF TOPICAL APPLICATION OF HONEY IN RADIATION INDUCED MUCOSITIS IN HEAD AND NECK CANCER PATIENTS

KEY WORDS: Head and Neck Cancers, Concurrent Chemo Radiation, Topical application of Honey, Radiation induced Mucositis.

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ABSTRACT

Background : The Head and Neck forms the 7th most common cancer world wide. They are the most common cancer in developing countries in South east Asia. Head and Neck more common in males compared to females. Radiation therapy plays a significant role as a primary treatment in early stage cancers and in the Adjuvant treatment of later stage Head and Neck cancers. In this study the patients were belongs to all subsidies of Head and Neck cancers irrespective of stage expect for Metastasis.

Aims and Objective :

Aims :

1. To know the effect of topical application of honey on the onset of mucositis in Head and Neck cancer patients receiving concurrent chemo radiation.
2. To assess the effect of topical application of honey on severity of mucositis in Head and Neck cancer patients receiving concurrent chemo radiotherapy.

Methods : Total 56 Head and Neck cancer patients who were to receive concurrent chemo radiotherapy treatment were recruited in this study. Out of 27 were allocated in study group and remaining 29 were allocated into control group. Study group received honey for topical application along with chemo radiotherapy where as control group received chemo radio therapy.

Results: Two types of mocositis seen in this study :

1. On set of radiation induced of mocositis : Most of the patients in this study group developed mucositis (92.6%) by the end of 13th fraction. Majority of patients (51.7%) in control group developed mucositis in 10th fraction.
2. Severity of Radiation induced Mucositis : Severity of mucositis was less in study group compared to control group.

Conclusion : Topical application of honey reducing in the onset as well as severity of radiation induced mucositis in patients receiving radiation to Head and Neck cancers.

INTROUDCTION

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.

HNSCC in the developing world differ from those in the Western world in terms of age, site of disease, etiology and molecular biology. Poverty, illiteracy, advanced stage at presentation, lack of access to health care, and poor treatment infrastructure pose a major challenge in management of these cancers. 1

Head and neck cancers are common in several regions of the world where the prevalence of tobacco and alcohol consumption is high.

Radiation therapy plays a significant role as a primary treatment in early stage cancers and in the adjuvant treatment of later stage head and neck cancers. However, due to the radiation-induced DNA damage of surrounding critical structures, radiation therapy can cause debilitating side effects in patients such as skin reactions (erythema, dry desquamation, moist desquamation), xerostomia (dry mouth) and oral mucositis (mouth ulceration).

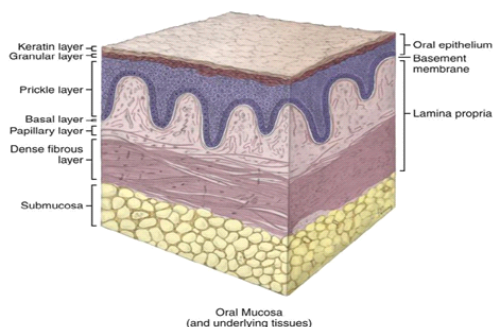


Fig-1: Layers of Oral Mucosa

Oral mucositis is caused by a multi-step biological process, which will occur in 30 to 40% of patients receiving chemotherapy, 60% of patients receiving radiation therapy and 92% of patients

receiving both chemotherapy and radiation therapy. 6,7,11 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 tumour bed and unscheduled treatment breaks. This can have effect on local tumor control and patients survival.

Table no.1: INCIDENCE OF ORAL MUCOSITIS AMONG CANCER PATIENTS

| Head & Neck Sub site | Men (%) | Women (%) |
|----------------------|---------|-----------|
| Lip, Oral Cavity | 11.3 | 4.3 |
| Nasopharynx | 0.6 | 0.2 |
| Other Pharynx | 6.6 | 1.3 |
| Larynx | 4.8 | 0.5 |
| Thyroid | 0.7 | 1.9 |
| TOTAL | 24 | 8.2 |

One of the latest interventions for the management of radiation-induced oral mucositis is natural honey. It has antimicrobial properties 15 and promotes wound healing.

The present study was designed to know the effect of topical application of natural honey which was collected from Carom plant and certified by NIRD (National Institute of Rural Development), on the onset and severity of Radiation Induced Mucositis in Head and Neck Cancer patients receiving concurrent Chemo Radiotherapy.

AIMS AND OBJECTIVES

The aims of present study were

- 1) To know the effect of topical application of honey on the onset of mucositis in head and neck cancer patients receiving concurrent chemo radiotherapy.
- 2) To assess the effect of topical application of honey on severity of mucositis in head and neck cancer patients receiving concurrent chemo radiotherapy.

METHODOLOGY

Total 56 Head and Neck cancer patients who were to receive concurrent chemo radiotherapy treatment were recruited in this study. Out of 27 were allocated in study group and remaining 29 were allocated into control group. Study group received honey for

topical application along with chemo radiotherapy where as control group received chemo radio therapy.

In study group, patients were given 10ml of natural honey collected from Carom flowers for topical application in oral cavity 10min before and after every radiation fraction.

The above treatment was taken throughout the course of radiotherapy

Honey: Honey collected from CAROM plant (Trachyspermum copticum) was used in this study.

SELECTION CRITERIA:

INCLUSION CRITERIA:

- a) Histopathologically confirmed non-metastatic Squamous cell carcinoma of head and neck
- b) Age less than 70 years
- c) ECOG performance status of 0-2.
- d) Patients should receive Concurrent Chemo radiotherapy as primary treatment.

EXCLUSION CRITERIA:

- a) Tumors of non-squamous histology.
- b) Age greater than 70 years.
- c) Performance status ECOG PS >2.
- d) Any prior treatment received for the tumor.
- e) Any co-morbid condition or acute infection where treatment is contraindicated
- f) Evidence of Distant Metastasis.

INITIAL EVALUATION AND ENROLEMENT:

1. Full medical history and physical examination.
2. Local examination as initial clinical assessment of tumor stage.
3. Endoscopic assessment of site, nature and extent of the disease.
4. Diagnostic workup consisting of hemoglobin, total and differential WBC count,
5. platelet count, renal function tests (Urea, Creatinine, 24hours urinary creatinine)

Radiation Treatment Planning and Delivery:

Positioning and immobilization: All the patients were treated in a supine position and properly immobilized by a thermoplasticcast (orfit cast).

Simulation and delineation of target volume and organs at risk (3D-CRT)

Phasel: 44Gy/22 fractions, 5 fractions per week to volume comprising the gross disease with extension and nodal areas at risk.

Phasell :22 Gy/11 fraction, 5 fraction per week to boost volume , sparing the spinal cord which includes the gross tumor volume with margin.

Radiotherapy was delivered by linear accelerator (LINAC) using 6MV X rays. Patients in both arms received concurrent chemotherapy with cisplatin 40 mg/ m2 given weekly with radio therapy.

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 complication development. Development of mucositis was assessed using clinical examination under good light.

RESULTS

Patients Characteristics:

Age and Sex:

Patients were in the age group of 25-58 years in study group

whereas 30-62 in control Group. The mean age of patients in study group was 40.6 with standard deviation of 9.31. The mean age of patients in control group was 48.03 with standard deviation of 10.01. The following table shows the age range and number of patients in each group. 5 out of 27 patients were females in study group whereas 7 out of 29 were females in control group.

Table no.8: Study Group

| Range | Male | Female | Total |
|-------|------|--------|-------|
| 20-30 | 3 | 0 | 3 |
| 31-40 | 9 | 1 | 10 |
| 41-50 | 5 | 3 | 8 |
| 51-60 | 4 | 1 | 5 |
| 61-70 | 0 | 0 | 0 |
| Total | 22 | 5 | 27 |

Graph no.1: The graph showing age range of study group

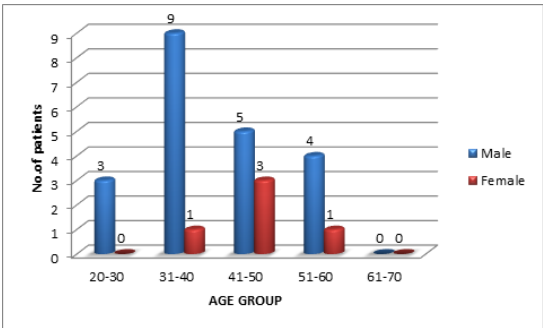
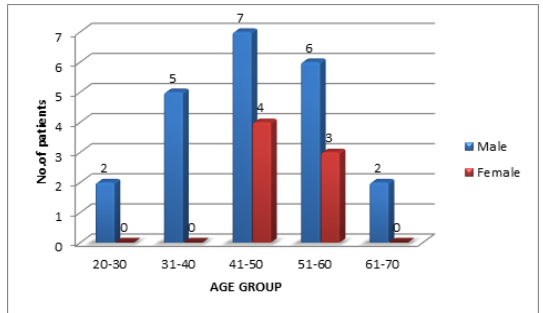


Table no.9: Control Group

| Range | Male | Female | Total |
|-------|------|--------|-------|
| 20-30 | 2 | 0 | 2 |
| 31-40 | 5 | 0 | 5 |
| 41-50 | 7 | 4 | 11 |
| 51-60 | 6 | 3 | 9 |
| 61-70 | 2 | 0 | 2 |
| Total | 22 | 7 | 29 |

Graph no.2: The graph showing age range of control group



The patients were assessed regularly twice a week for the onset of mucositis and severity of mucositis according to RTOG mucositis grading system.

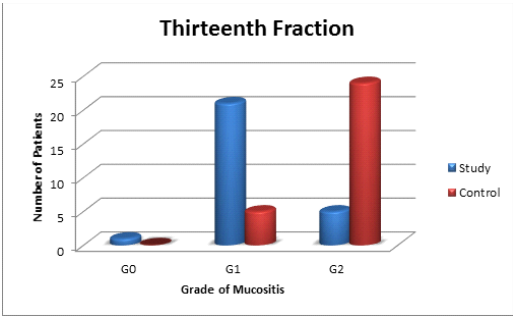
Mucositis :

Two types of mocositis seen in this study :

1. On set of radiation induced of mocositis : Most of the patients in this study group developed mucositis (92.6%) by the end of 13th fraction. Majority of patients (51.7%) in control group developed mucositis in 10th fraction.
2. Severity of Radiation induced Mucositis : Severity of mucositis was less in study group compared control group.

Table no-2: Study group at thirteenth fraction

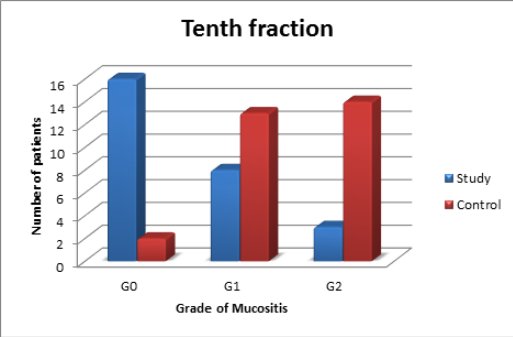
| 13# | Study | Control | Df | X ² |
|-----|------------|------------|----|----------------|
| G0 | 1 (3.7%) | 0 (0%) | 2 | 0.000 |
| G1 | 21 (77.8%) | 5 (17.2%) | | |
| G2 | 5(18.5%) | 24 (82.8%) | | |



Thirteen fraction assessment of mucositis: 1(3.7%) patient had no mucositis, 21(77.8%) patients developed grade1 mucositis. 5(18.5%) patients developed grade2 mucositis in study group. 5(17.2%) patients developed Grade1 mucositis and 24(82.8%) patients developed grade 2 mucositis in control group.

Table no-3: Study group at tenth fraction

| 13# | Study | Control | Df | X ² |
|-----|------------|------------|----|----------------|
| G0 | 16 (59.3%) | 2 (6.9%) | 3 | 0.000 |
| G1 | 8 (29.6%) | 13 (44.8%) | | |
| G2 | 3 (11.1%) | 14 (48.3%) | | |



Tenth fraction assessment of mucositis: 16(59.3%) patients did not develop any mucositis, 8(29.6%) patients developed grade1 mucositis, 3(11.1%) patients developed grade2 mucositis in study group. 2(6.9%) patients developed no mucositis, 13(44.8%) patients developed grade1 mucositis, 14(48.3%) patients developed grade 2 mucositis in control group.



Fig-2 : Grades of Muositis

Mean muositis score for study group and control group:

Table no-04: Study Group:

| Fraction | Mean mucositis score |
|----------|----------------------|
| Eight | 0 |
| Ten | 0.4 |
| Thirteen | 1.1 |
| Fifteen | 1.4 |
| Eighteen | 1.8 |

| | |
|--------------|-----|
| Twenty | 2.2 |
| Twenty two | 2.4 |
| Twenty five | 1.7 |
| Twenty eight | 1.3 |
| Thirty | 1.1 |
| Thirty three | 0.9 |

Graph no.17: Study Group Patients

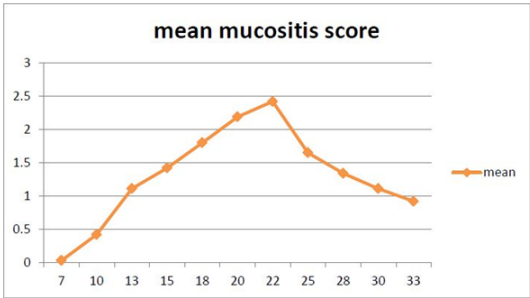
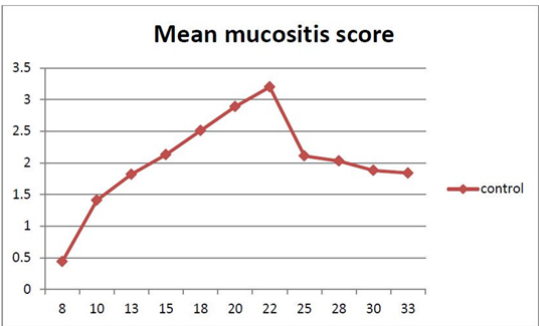


Table no-04: Control Group:

| Fraction | Mean mucositis score |
|--------------|----------------------|
| Eight | 0.44 |
| Ten | 1.41 |
| Thirteen | 1.82 |
| Fifteen | 2.13 |
| Eighteen | 2.51 |
| Twenty | 2.89 |
| Twenty two | 3.2 |
| Twenty five | 2.11 |
| Twenty eight | 2.03 |
| Thirty | 1.88 |
| Thirty three | 1.84 |

Graph no.18: Control Group Patients



DISCUSSION

The main aim of study was to know the effectiveness of honey on topical application over mucosa while patients were on treatment.

Exposure to ionizing radiation leads to mucosal erythema, small whitish patches and ultimately results in confluent mucositis. In the later phases, oral ulceration and bleeding become a dose-limiting toxicity.

In this study the age group of patients varied from 25 -58 years in study group and 30-62 years in control group.

Our study :

Total 56 Head and Neck cancer patients who were to receive concurrent chemo radiotherapy treatment were recruited in this study. Out of 27 were allocated in study group and remaining 20 were allocated into control group. Study group received honey for topical application along with chemo radiotherapy where as control group received chemo radio therapy.

In study group, patients were given 10ml of natural honey collected from Carom flowers for topical application in oral cavity 10min before and after every radiation fraction.

The above treatment was taken throughout the course of radiotherapy

Honey: Honey collected from CAROM plant (*Trachyspermum copticum*) was used in this study.

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 complication development. Development of mucositis was assessed using clinical examination under good light.

Other study :

Sadakshetram jayachandran et.al, in their comparative study to evaluate the effect of natural honey and 0.15% benzydamine hydrochloride on the onset and severity of radiation induced mucositis and to compare with the control, they have assessed the 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% benzydamine and control group.⁷⁵

Assessed 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. The onset of mucositis in earlier fractions and severity of mucositis during later fractions were noted.

CONCLUSION

Topical application of honey reducing in the onset as well as severity of radiation induced mucositis in patients receiving radiation to Head and Neck cancers.

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