Evaluation of Topical Application of SIDR Honey in the Management of Radiotherapy Induced Oral Mucositis

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Abstract

Oral mucositis is a common side effect of cancer therapies, particularly radiation therapy for head and neck cancer and to a less extend with various forms of chemotherapy. Honey has been used widely in the medical field due to its antimicrobial, antioxidant effects which enhance tissue healing. To evaluate clinically the effectiveness of the Sidr Honey in the management of oral mucositis. This study was conducted on twenty patients suffering from oral mucositis and receiving radiotherapy. The patients were selected upon the inclusion and exclusion criteria. Ten patients (test group) (group I) will gargle with 5ml honey diluted with water 15 to 30 minutes prior to the treatment, and 6 hours after the radiation therapy treatment, Topical application with concentrated honey twice daily for 2 weeks in addition to the conventional treatment. Ten patients (study group) (group II) will use the conventional treatment including antifungal, analgesics and systemic antibiotics. Regarding the mucositis severity scores, test group showed significant decrease at the 5th day till the end of the study and for the VAS, test group showed significant decrease at the 1st day and the decrease continued till the 14th day while the control group showed a significant decrease in the mucositis severity score and VAS only at the 14th day. Sidr honey may be of benefit in the management of radiotherapy induced oral mucositis.

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Introduction

Cancer is a major international health problem. According to the international agency for research on cancer, each year there is about 10.9 million new cases, 6.7 million deaths and 24.6 million persons alive with cancer around the world, oral cavity and pharyngeal cancers account for 75% of head and neck cancers and are the fourth most spread cancer in men.[1]

Although the 21st century has seen remarkable advances in early cancer detection, treatment and prevention, the incidence, prevalence and mortality rates for all types of cancer have increased worldwide.[2] The world cancer report 2008,[3] stated that cancer burden doubled in the last thirty years. Years ago,[4, 5] cancer was considered a disease of western, industrialized countries. Today, the situation has changed considerably, since more than half of the global cancer burden is now borne by developing countries. The World Health Organization (WHO) estimates that in 2007, about 72% of all cancer deaths occurred in low- and middle-income countries.[2] In contrast, in 1970, the developing world accounted for only 15% of newly reported cancers.[3]

In Egypt, which shares most of the environmental problems of developing countries,[6] the cancer registries are unavailable. Mortality statistics from death certification may be a particular source of cancer statistics.[7] Head and neck cancers are classified as malignancies of the upper aero-digestive tract including the mouth, pharynx, larynx, nasal cavity and sinuses. They are the sixth most common type of cancer, representing approximately 4% of all cancers

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worldwide with an estimated 650,000 registrations and 350,000 deaths worldwide annually.[1]

Surgery, chemotherapy and radiotherapy are the options for treatment of head and neck cancers.[8] However, Radiotherapy and chemotherapy are not tissue-specific. They act by inhibiting rapidly dividing cell growth, interfering with cell division mechanisms[9] but do not differentiate between rapidly dividing cancer cells and normal cells.[10, 11] Oral Mucositis (OM) is defined as inflammation and ulceration of the oral mucosa,[12] while the fibrinous exudates that is colonized by bacteria and covers the ulcer referred to as "pseudomembrane".[13, 14]

The resulting ulceration and infection of the oral mucosa has a marked impact on patients ability to eat and swallow,[15] it impairs their quality of life, including social and daily functioning.[16] Also it increases the risk for bacterial and fungal colonization and for systemic infection in immuno-compromised patients.[17] Moreover, the progression of oral lesions and its impact on general conditions of the patient may require parenteral nutrition.[18]

Furthermore, patients with severe oral Mucositis are at higher risk of unplanned breaks/delays in radiation therapy which adversely affecting tumor control and treatment outcome.[19, 20] Breaks in the treatment often result in tumor repopulation and reduced local control rates.[21] General management of oral Mucositis, has been essentially palliative and restricted to relief the painful symptoms and maintenance of good oral hygiene. It is very difficult for the clinician to choose from the different treatment modalities, many interventions have little evidence supporting their effectiveness, so no intervention has been conclusively shown to be effective.[22]

Honey has been used medically throughout history since Egyptian civilizations. Honey is a byproduct of flower nectar which becomes concentrated by dehydration inside a beehive.[23] It has an acidic ph (3.9), high viscosity and osmolarity which inhibit microbial growth and enhance epithelialization thus promoting wound healing, also it is effective in treatment of acute and chronic wounds such as ulcers and burns.[24]

Sidr honey becomes well documented in Ayurvedic and Yunanu medicine, the sidr honey is made from bees who only feed on the nectar of Sidr tree. Sidr honey is a known antibacterial agent, used as wound dressing, stomach ulcers, boots immune system and digestive problems.[25] Since the efficacy of honey in treatment of acute and chronic wounds such as ulcers and burns was evaluated, but its usefulness for management of mucositis still needed to be proved and that is why the current study has been conducted. Hence, the aim of the current study is to evaluate clinically the effectiveness of the Sidr Honey in the management of oral mucositis.

Materials and Methods

Selection of patients

The study was conducted on twenty patients suffering from oral mucositis and receiving radiotherapy on head and neck region. Patients were selected from Department of Clinical Oncology, Faculty of Medicine, Alexandria University.

Study design

Randomized clinical trial.

Study sample

Twenty patients are selected from the Department of Clinical Oncology, Faculty of Medicine, Alexandria University.

Inclusion criteria

1. Age above 20 years.
2. Patients clinically diagnosed with oral mucositis according to WHO scale.[16]
3. Patients receiving radiotherapy treatment.

Exclusion criteria

1. Smoking tobacco and Alcohol intake.
2. Patients with systemic diseases as diabetes, viral hepatitis and those under anticoagulant therapy.
3. Pregnancy and lactation.
4. Patients receiving chemotherapy treatment.

Pre-study assessment

1. Detailed information regarding the study protocol and therapy was fully illustrated.
2. Informed consent was obtained.
3. A complete detailed data set (patients' examination record) was

documented.

4. Oral hygiene instructions were carried out to all patients.[26]
5. Adequate hydration was advised.[27]

Diagnosis of radiotherapy induced oral mucositis based on

1. History

Full history was obtained from the selected patients including name, age, sex, onset, smoking habit, symptoms, medical history, drug history and any previous treatments.

2. Clinical examination

Examination of all clinical signs of oral mucositis was done according to WHO scale.[27]

Grade 0: Absence of mucositis.
Grade I: Presence of soreness with erythema.
Grade II: Presence of painful erythema and ulcerations that do not affect the patient food intake.
Grade III: Confluent ulcerations that affect the food intake.
Grade IV: The patient requires parenteral nutrition.

Schedule

- Before the beginning of the therapy, baseline subjective and objective assessments will be recorded for both test and control groups.
- Also subjective and objective assessment will be carried out for both groups at day 1, 5, 9 and 14.

Before radiotherapy

For all the patients, a detailed medical and dental history was taken. A comprehensive intraoral examination was carried out to determine the need for scaling, extractions or removal of any decay or septic focus before starting radiotherapy.

All patients were motivated and educated to perform the following palliative treatment:

- Oral hygiene techniques which were individualized for each patient according to his ability to tolerate soft tissue manipulation.
- Normal saline and mild solution of sodium bicarbonate were recommended as mouth rinses several times daily.
- Lip lubrication was also recommended.
- Saliva substitutes for xerostomia relief, and "sugar-free" chewing gums to enhance oral moistness.

Certain types of food were eliminated from the patient's diet as hard, or spicy foods, acidic juices, nuts and extremely hot foods and liquids.

Study population was randomly divided into two groups:

Group I (test group)

Ten patients gargled with 5ml honey as gargle diluted with water (1:3) for 15 to 30 minutes prior to the treatment, 15 to 30 minutes after treatment and 6 hours after radiation therapy. Topical application with concentrated honey twice daily for 2 weeks on the present lesions,[28] the patients received the conventional treatment mentioned in the control group in addition to Sidr honey.[28, 29]

Group II (control group)

The control group, where oral mucositis was treated using the conventional treatment for oral mucositis.

The conventional treatment included the following:

1. Oracure gel*: to be applied on the mucosal lesion 3 times per day.
2. Sodium bicarbonate mouth washes (ALKamisr sachets: 0.5 sachets in half warm cup of water 3 times per day.
3. Kenacort in orabase: to be applied 3 times per day on the severe painful ulcers.
4. Vaseline: 3 times per day on the lip.
5. Daktarin oral gel**: half measure spoon of gel 3 times a day.
6. B.B.C spray*: to be sprayed 3 times per day on the affected areas before eating.

Clinical evaluation

Oral lesions were evaluated in both groups before and after the treatment. The response of treatment was measured according to reduction in clinical signs and symptoms using:

1- Subjective assessment

Discomfort and pain severity were reported by each patient before treatment and daily till day 14 using Visual Analogue Scale (VAS). The VAS is a simple, reproducible instrument that allows the severity of the pain experienced to be expressed as a numeric value. It is represented as a plain horizontal 10-cm line. The patient is instructed to bisect the line at a point appropriate to their present discomfort. A zero value equates to being pain free, whereas the most severe pain they have experienced is rated at 10.[30, 31]

2- Objective assessment

Mucositis severity was scored by a scale based on clinical features from WHO scale.[27]

3- Photographs

Photographs were taken at base line and at the end of the study.

Statistical analysis

The data was collected and entered into the personal computer. Statistical analysis was done using Statistical Package for Social Sciences (SPSS/ version 15) software.

The statistical test is used as follows:

1- Mean and standard deviation for each measurement.
2- Number and percent of each category.
3- Yates corrected Chi-Square test used to analysis of categorical data.
4- Wilcoxon matched pairs signed ranks test: A nonparametric significant test used to compare paired, ordinal data.
5- Mann Whitney test was used for comparison between unpaired signed ranks test.

Results

A total of 20 patients, 11 males and 9 females, suffering from radiotherapy induced oral mucositis were enrolled in the present study. They were divided into 2 groups. Patients in group I received the conventional treatment in addition to honey while the patients in group II received the conventional treatment.

Table 1, shows the patients characterization, regarding sex, in group I there was 6 male and 4 females, while in group II there was 5 male and 5 females, on comparing the two studied groups regarding sex it was found that there was no significant difference between the two studied groups regarding sex ($p > 0.05$). The age in group I was ranged from 29-60 years with a mean of 41.8 ± 6.28, and in group II the age ranged from 34 - 58 with a mean of 42.6 ± 5.98, there was no significant difference between the two studied groups regarding age ($p > 0.05$).

	Test Group		Control group		P
	No.	%	No.	%	
Sex					
Male	6	60.0	5	50.0	0.556
Female	4	40.0	5	50.0	
Age					
Range	29 - 60		34 - 58		0.298
Mean	41.8		42.6		
S.D.	6.28		5.98		

Distribution of group I patients regarding sex.

Table 1. Comparison between the two studied groups regarding age and sex showing no significant difference.

Table 2 show the pain score at different period of follow up in group I, at base line the VAS was ranged from 8-10 with a mean of 8.9 ± 0.88, then after 1st day of treatment it was found that there was no change in the VAS it was ranged from 7-10 with a mean of 8.4 ± 1.07, while after 5th day the VAS was decreased but not significant to be 6.8 ± 1.23, after 9th day the VAS was decreased statistically significant from the baseline, to be 4.0 ± 0.67, after 14th day the mean VAS was 2.7 ± 0.82, on comparing with the base line it was found that this decreasing was highly statistically significant, at end of follow up at 14the day.

Table 3 show the pain score at different period of follow up in group I, at base line the VAS was ranged from 8-10 with a mean of 9.1 ± 0.88, then after 1st day of treatment it was found that there was no change in the VAS it was ranged from 8-10 with a mean of 8.9 ± 0.88, while after 5th day the VAS was decreased but not significant to be 7.7 ± 0.82, after 9th day the VAS was decreased statistically significant from the baseline, to be 6.0 ± 1.15, after 14th day the mean VAS was 4.4 ± 1.58, on comparing with the base line it was found that this decreasing was highly statistically significant, at end of follow up at 14the day.

Case No	Baseline	1st day	5th day	9th day	14th day
1	10	8	7	4	2
2	9	8	6	5	2
3	8	7	5	5	2
4	8	8	6	4	3
5	8	8	8	4	3
6	10	10	8	3	2
7	8	7	5	4	2
8	9	9	8	3	4
9	10	10	7	4	4
10	9	9	8	4	3
Min	8	7	5	3	2
Max	10	10	8	5	4
Mean	8.9	8.4	6.8	4	2.7
S.D.	0.88	1.07	1.23	0.67	0.82
P		0.134	0.001*	0.001*	0.001*

Table 2. Comparison between pain score (VAS) at different period of follow up in test group.

Case No	Baseline	1st day	5th day	9th day	14th day
1	10	10	7	5	3
2	10	10	7	6	7
3	10	8	8	8	7
4	8	8	9	8	3
5	9	9	8	6	3
6	8	8	7	6	4
7	9	9	7	5	5
8	9	9	7	5	4
9	10	10	9	6	3
10	8	8	8	5	5
Min	8	8	7	5	3
Max	10	10	9	8	7
Mean	9.1	8.9	7.7	6	4.4
S.D.	0.88	0.88	0.82	1.15	1.58
P		0.293	0.001*	0.001*	0.0001*

Table 3. Comparison between pain score (VAS) at different period of follow up in control group.

Table 4 show the comparison between the two studied groups regarding the pain score at different period of follow up, at the base line and at 1st day the two studied groups show no significant difference regarding the visual analogue scale ($p > 0.05$), while at 5th, 9th and 14th day was found that there was a highly significant decreasing in the VAS in group II than group I ($p = 0.0001$).

Group	Baseline	1st day	5th day	9th day	14th day
Test Group					
Min	8	7	5	3	2
Max	10	10	8	5	4
Mean	8.9	8.4	6.8	4	2.7
S.D.	0.88	1.07	1.23	0.67	0.82
Control Group					
Min	8	8	7	5	3
Max	10	10	9	8	7
Mean	9.1	8.9	7.7	6	4.4
S.D.	0.88	0.88	0.82	1.15	1.58
p	0.308	0.135	0.035*	0.001*	0.004*

Table 4. Comparison between the two studied groups regarding the pain score by using (VAS).

Table 5 show the lesion size score in group I at different period of follow up, at base line it was found that the lesion size score ranged from 2-4 with a mean of 2.9 ± 0.88, while immediately after 1st day the lesion size in score was unchanged with range from 2-4 with a mean of 2.7 ± 0.82, after 5 days the lesion size was ranged from 1-3 with a mean of 1.3 ± 0.67, the change was a significant, also after 9 days it was found that there was significant change in the size lesion, it was 1.3 ± 0.67, after 14 days the lesion size in score was significantly decreased to be 1.30 ± 0.48 ($p = 0.001$).

Case No	Baseline	1st day	5th day	9th day	14th day
1	2	3	3	1	1
2	3	2	1	3	1
3	4	2	1	1	1
4	2	2	1	1	2
5	2	2	1	2	1
6	4	3	1	1	1
7	3	2	1	1	2
8	4	4	3	1	1
9	2	3	3	1	1
10	3	4	2	1	2
Min	2	2	1	1	1
Max	4	4	3	3	2
Mean	2.9	2.7	1.7	1.3	1.3
S.D.	0.88	0.82	0.95	0.67	0.48
P		0.204	0.008	0.001*	0.000*

Table 5. Mucositis severity in tested group at different period of follow up.

Table 6 show the lesion size score in group I at different period of follow up, at base

line it was found that the lesion size score ranged from 2-4 with a mean of 3.3 ± 0.67, while immediately after 1st day the lesion size in score was unchanged with range from 2-4 with a mean of 3.0 ± 0.67, after 5 days the lesion size was ranged from 1-3 with a mean of 2.6 ± 0.70, the change was significant, also after 9 days it was found that there was significant change in the size lesion, it was 2.2 ± 0.92, after 14 days the lesion size in score was significantly decreased to be 2.2 ± 0.63 (p = 0.001).

Table 7 show the comparison between group I and II regarding lesion size in score at different period of follow up, it was found that at base line and immediately after treatment there was no significant difference between the two groups regarding lesion size, after 1, 5, 9 and 14 weeks it was found that there was a highly significant decreasing in mean lesion size in score in group II than group I.

Case No	Baseline	1st day	5th day	9th day	14th day
1	4	3	3	2	3
2	3	2	3	3	2
3	4	3	2	3	2
4	2	3	3	1	3
5	3	2	2	2	2
6	3	3	1	3	2
7	3	4	3	3	2
8	3	4	3	3	1
9	4	3	3	1	2
10	4	3	3	1	3
Min	2	2	1	1	1
Max	4	4	3	3	3
Mean	3.3	3	2.6	2.2	2.2
S.D.	0.67	0.67	0.70	0.92	0.63
P		0.251	0.030	0.013	0.001*

Table 6. Mucositis severity in control group at different period of follow up.

Group	Baseline	1st day	5th day	9th day	14th day
Group I					
Min	2	2	1	1	1
Max	4	4	3	3	2
Mean	2.9	2.7	1.7	1.3	1.3
S.D.	0.88	0.82	0.95	0.67	0.48
Group II					
Min	2	2	1	1	1
Max	4	4	3	3	3
Mean	3.3	3	2.6	2.2	2.2
S.D.	0.67	0.67	0.70	0.92	0.63
p	0.134	0.091	0.013	0.011	0.001*

Table 7. Comparison between the two studied groups regarding the Mucositis severity score.

Table 8 show the percent of improvement in patients in the two studied groups, it was found that there was a significant increase in improvement in tested group than control group (p < 0.05).

	Tested group		Control group	
	No.	%	No.	%
Improved	8	80.0	4	40.0
Not improved	2	20.0	6	60.0
X2	3.36			
p	0.046*			

Table 8. Comparison between the two studied groups regarding the number of improved cases.

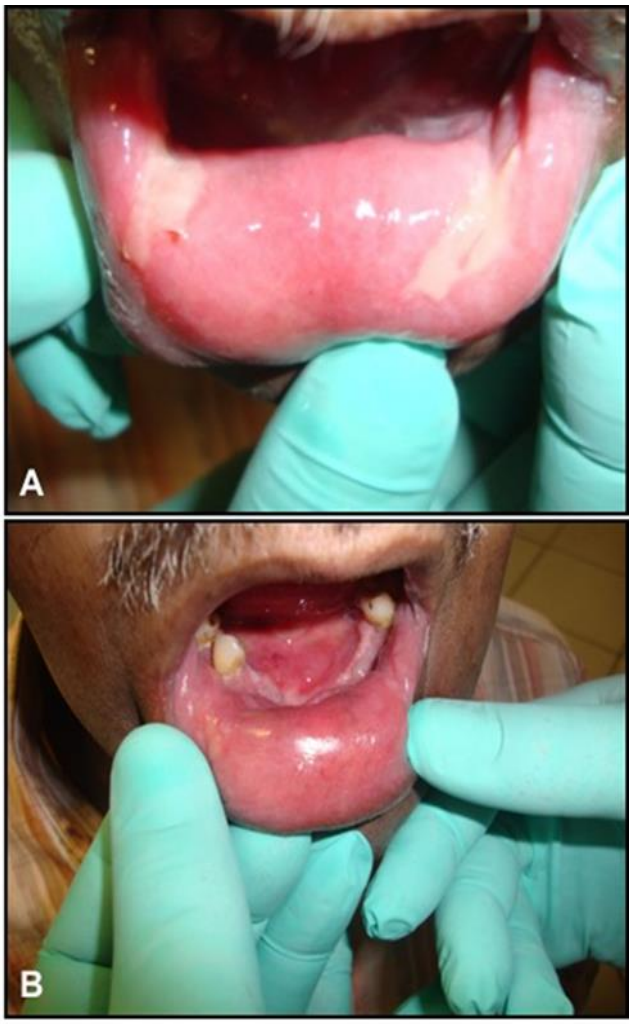

Figure 1. Oral mucositis grade II on lower lip. A. Pretreatment photograph, B. Post treatment photograph showing healing of the oral mucositis after 2 weeks.

Figure 2. Oral mucositis grade IV involving tongue, buccal mucosa. A. Pretreatment photograph, B. Post treatment photograph showing enhancing of oral mucositis to grade III after 4 days, C. Post treatment photograph showing enhancing of oral mucositis to grade I after 2 weeks.

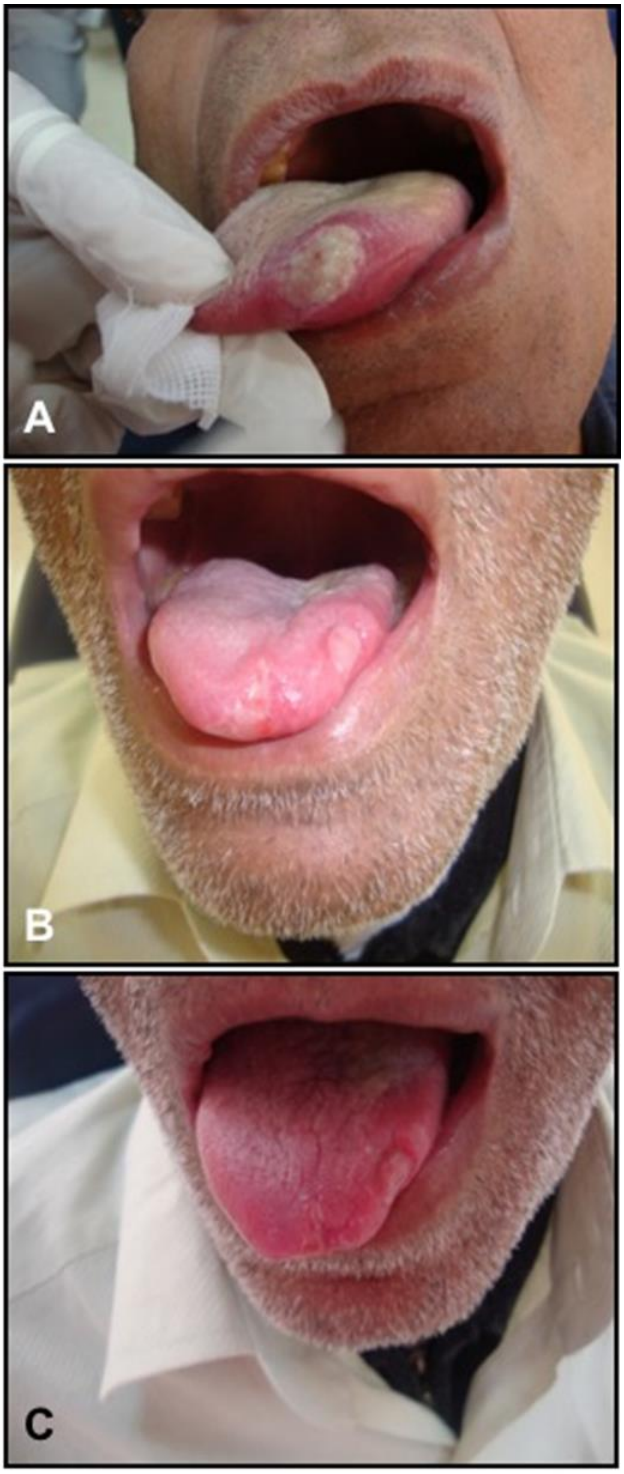

Figure 3. A head and neck cancer patients having oral mucositis grade IV on the tongue. A. A Pretreatment photograph, B. A post treatment photograph of the same patient showing improvement of the oral lesion after 1 week, C. A post treatment photograph showing improvement of the lesion to grade I after 2 weeks.

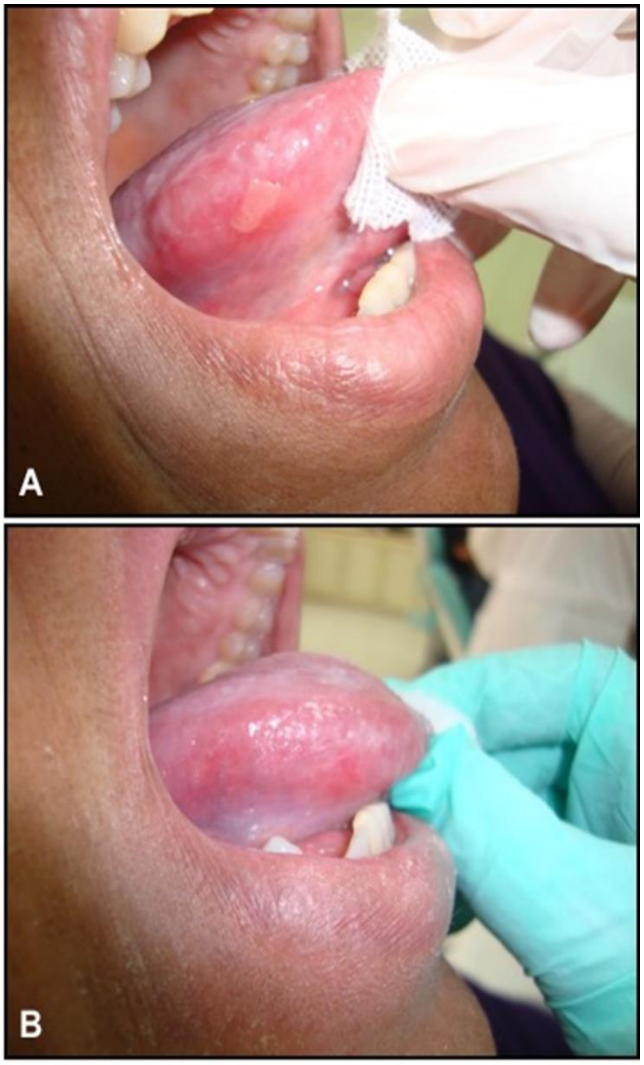

Figure 4. Oral mucositis grade II on the lateral border of tongue. A. Pretreatment photograph, B. Post treatment photograph showing healing of the oral mucositis after 2 weeks.

Discussion

Cancer is a malignant disease which is characterized by a series of cellular changes that lead to abnormal cell proliferation with the potential to invade surrounding tissues and metastasize to distant locations. Cancer cells can originate from many areas of the body and cause symptoms specific to the region where the tumor manifests.[32, 33]

The incidence of head and neck cancer varies around the world. Yarbro et al.[34] in 2004, reported that head and neck cancer accounts for between three and five percent of all cancers. In 2010, cancer of the head and neck region accounts for approximately ten percent of malignant tumors worldwide.[35] The main treatment options are surgery, chemotherapy, radiation therapy or a combination of these.[36-38]

The head and neck are important regions of the body because they are essential for many physiological functions and are critical for a person's appearance, expression and social interactions. Cancer within the head and neck region can cause structural deformities and disrupt the functions of this region which can lead to a significant decrease in patients' quality of life.[36]

The National Institutes of Health (NIH) consensus conference (1989) states that before the start of cancer treatment, patients who receive head and neck radiation or chemotherapy must be evaluated for potential risk factors for oral complications, by a thorough oral and dental evaluation.[39]

Radiotherapy to the head and neck region puts a number of organs at risk. Some sensitive head and neck structures have relatively low tolerance doses and excess dose to these structures may result in chronic side effects for the patient. These structures are dose-limiting and include spinal cord (myelopathy), brain (necrosis), retina (blindness), ear (deafness), thyroid and pituitary glands (hormonal imbalance) and oral cavity (mucositis) which disrupt the function and integrity of the mouth.[37,38,40]

Oral mucositis is the most common side effect of radiation therapy to the head and neck region. It occurs in 40% of patients receiving chemotherapy and 100% of those receiving head and neck radiotherapy.[38] Mucositis-associated oral pain results from the loss of the epithelial lining, ulceration and the associated edema. The pain is often poorly controlled with standard analgesics or topical anesthetics. When the pharyngeal mucosa is affected, the pain and burning sensations are more intense with swallowing or speaking.[13]

The study sample was selected from patients having head and neck cancer receiving radiotherapy from the department of clinical Oncology, Faculty of Medicine, Alexandria University. Patients having other type of malignancies than head and neck cancer were excluded, as oral mucositis in these conditions may be induced by chemotherapeutic agents. Patients having hepatitis B or C were also excluded to allow for proper infection control measures during the examination and follow up

sessions. Smokers were also excluded from the study as smoking impairs wound healing.

The current study involved twenty patients, nine females and eleven males, age ranging between 20 and 60 supporting the concept that oral mucositis in females occurred at the same rate as in men.[41] Drunkards were also excluded from the studied sample because alcohol causes irritation to an already damaged mucosa, increasing mucosal damage and pain levels.[42]

Removal of all sources of irritations and oral care protocol were recommended for both groups in order to avoid any exacerbating factor for oral lesions.[26]

Many interventions have been used in OM management, but only few of them have sufficient support from positive results in controlled clinical trials to be recommended in treatment guidelines.[8] There is increased evidences that support topical application of honey can reduce the severity of mucositis associated with chemotherapy or radiation therapy.[37] Thus, this study was conducted to evaluate clinically the effectiveness of honey in the management of radiotherapy induced oral mucositis and to compare it with the conventional treatment In the current study, the test group experienced downward shift in the VAS score throughout the treatment period and at the end of the treatment there was a significant decrease in the VAS. On the other hand, the studied patients in the control group show slight decrease in the VAS.

As regarding the lesion size for the patients in the test group, eight of the ten patients experienced improvement of the lesion while the patients in the control group only four patients out of ten that show improvement of the oral mucositis lesion.

The detected possible role of honey in the management of oral mucositis may be due to its nature. Honey has a valued place in traditional medicine for centuries.

It may be due to:[43]

1- Anti-inflammatory effect: honey contains enzymes which produce peroxide which provides antimicrobial properties.
2- The sugar content in honey which is high enough to hinder the growth of the microbes.
3- The acidic ph of honey and this acidity is low enough to inhibit the growth of most microorganisms.

Honey's anti-inflammatory action and stimulatory effects on granulation and epithelialisation, help in rapidly reducing pain and edema.[36] By providing moist healing, it can minimize hypertrophic scarring.[40] Honey also stimulates the angiogenesis, granulation and epithelialisation, which helps speed up the healing process. Honey can trigger the sequence of events to enhance angiogenesis and proliferation of fibroblasts and epithelial cells by producing certain growth factors like Tumor Necrosis Factor (TNF-alpha).[33]

As the mechanisms by which honey facilitate wound healing have become better understood, Several studies have shown that topical application of honey significantly enhances the wound healing process.[37]

In a study on diabetic foot leg ulcers, the patients applied honey for six times for 3 weeks. There was fast and great reduction in the dimensions of ulcers following honey application.[33]

Patients participated in this study were aged from 25 to 60 yrs. the wide age range was because of the difficulty to collect 20 head and neck cancer patients having oral mucositis.

Concerning group I, the results of this study revealed improvement in the severity of the oral mucositis. The possible explanation of these results might be related to the effectiveness of the different therapeutic agents combination used in this treatment modality. The present protocol was largely based on oral decontamination, palliative measures and pain control. This protocol followed the guidelines of the MASCC and ISOO that are widely accepted in the clinical practice.[20]

Oral decontamination was achieved in this study through the antimicrobial agents such as oracure gel, as well as the antifungal therapy, the analgesic effect was through the use of B.B.C spray.

The antifungal effect in this study was obtained through topical application of Dactarin oral gel and systemic antifungal agents used when the condition was indicated. According to Helmick et al.[44] the antifungal activity of imidazole groups such as miconazole, clortimazole which attributed to their inhibitory effect on nitrous oxide metabolism by yeast and bacteria. Helmick's findings showed that imidazoles had antibacterial activity in addition to its antifungal effect. The kenakort in orabase

used would also promote the healing process.[45,46]

The significant improvement in the honey group may be due to the patient's compliance to apply Honey, its taste is sweet and well tolerated by patients, furthermore, the antibacterial, antioxidant and wound healing effects of honey.

The results of this study were not in agreement with the study conducted on treatment of oral lichen planus by sidr honey, as Sanathkhani et al.[28] found that there was no significant difference between the honey and the conventional treatment of oral lichen planus.

According to Hawley et al.[47] the results were also not in agreement with the current study, this may be due to the patient intolerance for the manuka honey used in that study, also the patients participated in the study were treated with radiotherapy and chemotherapy.

Bardy et al.[48] found that there was no significant difference between the topical application of honey and the conventional treatment which is different than the current study, but this might be due to patient's compliance was problem in the study due to the intolerable taste of Manuka honey, the long period of the follow up and greater number of the patients.

However, Motallebnejad et al.[29] concluded that the topical application of honey is safe and effective for the treatment of radiation induced mucositis, which is in agreement with the current study.

Based on the results of the present study, the topical application of honey may be useful in decreasing the severity of radiotherapy induced mucositis. However, during the clinical application of the study, some limitations have been encountered. The patients are immune-compromised and psychologically disturbed, most of them found difficulty to comply with the appointment schedules. So, the clinical examination and the follow up were done in the same place of the radiotherapy treatment.

Conclusion

1- Sidr honey may be effective in reducing the severity & pain of radio therapy induced oral mucositis.
2- Significant differences were found between both treatment modalities concerning their effects on reducing the symptoms of oral mucositis.
3- Regular, systemic oral care protocol has to be implemented for all patients to reduce inflammation, prevent infections and alleviate mucosal symptoms.
4- Sidr honey was well tolerated and there were no side effects noted in the study.

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