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The Effect of Topical Application of Honey on Management of Chemotherapy Induced Oral Stomatitis

Salwa A. Mohamed[1], AmanyShebl[2]and Soheir Mohamed Weheida[3]

[1]Medical Surgical Department, Faculty of Nursing, Fayoum University.[2]Medical Surgical Department, Faculty of Nursing, Mansoura UniversityDepartment of Medical Surgical Nursing3, University of Alexandria
salwaflower@yahoo.com

Abstract: Chemotherapy agents continue to be the mainstay of cancer treatment, but are associated with short and long term side effects. Oral side effects remain a major source of illness despite the use of a variety of agents to prevent them. One of these side effects is oral Stomatitis. These lesions may produce discomfort and pain which interfere with eating, patient compliance to treatment and potential risk of oral infection. The aim of this study is to determine the effect of topical application of honey in the management of stomatitis in patients undergoing chemotherapy.This study was conducted at the medical oncology department and outpatient clinics of El Mansoura University Hospital. The subjects of this study comprised 40 adults of both sexes. Patients were divided into two groups: group 1 (study group) received 20 ml honey and group II (control group) who was left to the routine hospital care. Tool consisted of two parts to collect the study data: patient's Bio socio-demographic data and Medical data; Oral assessment guide (OAG) tool. The main result showed that subjects among the study group had healthier oral cavity and lower degree of oral stomatitis compared to the subjects in the control group following 10 days of chemotherapy administration. The honey group improved better and foster, analysis of data and comparison of means revealed a statistically significant difference between the two studies groups as regarding the improvement of oral condition in honey group foster than control group. The change in weight between the two studied groups was statistically significant, meaning that the improvement of body weight was much more in experimental group than it was in the control group. According to the results, honey caused virtually better recovery of stomatitis among patients compared with routing solution administered at the ward. The study recommended that patients who suffers from stomatitis should encouraged to frequent and regular training programs to keep the oncology nurses updated with the most resent and effective oral hygiene practices.

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Key words: Chemotherapy, Oral stomatitis, Honey.

1. Introduction:

The Cancer is a group of disease characterized by uncontrolled growth and spread of abnormal cells. If the spread is not controlled, it can results in death **(Chan &Ingoffo,2005).** Chemotherapy plays an important role in the treatment of cancer,whether utilized alone or in combination with surgery, radiation therapy, or biotherapy, it can achieve significant improvement in both the cure rate and the length of survival of persons with cancer **(Krakoff, 1991).**

Stomatitis is perhaps one of the most debilitating and painful side effects of cancer therapy. Approximately 40% of all patients receiving chemotherapy endure stomatitis; 80% of all patients receiving radiation for head and neck tumors also are affected**(Sonis*et al.*,1999)**. Seventy-five percent of those with stomatitis complain of acute oral pain. The pain is sometimes so severe that patients receive narcotics to relieve it or they prematurely withdraw from their cancer therapy**(Brown, and Yoder, 2002).**

Oral stomatitis is one of the most debilitating complications following chemotherapy administration. Stomatitis is an inflammation of the oral mucosa accompanied by symptoms such as redness, swelling, and bleeding. Stomatitis can involve the tongue, lips, cheeks, gums, the floor and roof of the mouth **(Epstein & Schubert, 2004;Price & Gwin, 2008 and Kyle, 2008).** It is appeared around days four to five day from starting chemotherapy with a peak on the 7^{th} -14^{th} day after chemotherapy **(Cheng*et al.*, 2001and Hicks, 2003).** Clinical manifestations progress from erythema, cracking, and inflammation, to pain, bleeding and ulceration (**Raber-Durlacher*et al.*, 2000).** It is essential that all members of the healthcare team are aware of the optimum management strategies for oral mucositis.

Honey was used to treat the infected wounds as long ago as 2000 years before the bacteria were discovered to be the cause of infection. More recently, honey has been reported to have an inhibitory effect to around 60 species of bacteria including aerobes and anaerobes, gram-positives and gram-negative microorganisms **(Nettina, 2007)**. Many research works have been done on the

antimicrobial effect of honey on different bacterial isolates. **Molan (1999)** reported that honey is becoming accepted as a reputable and effective therapeutic agent by practitioners of conventional medicine and by the general public. This is because of good clinical results that are being obtained. Honey has been reported to be effective in the healing of infected postoperative wounds (**Al-waili and Saloom, 1999**).

According to **Gupta*et al.*,2011)**, there is almost large volume of literature appearing on the effectiveness of honey in treating the infected wounds and skin ulcers describes the features that indicate that honey has potential for the therapy of periodontal disease, oral ulcers, and other problems of oral health. One of the most important features that may be particularly beneficial in promotion of oral wellness is its antibacterial activity**.**

2. Methods

Aim:

The aim of this study is to determine the effect of topical application of honey in the management of stomatitis in patients undergoing chemotherapy.

Research design*:*

A quasi-experimental research design was utilized to conduct this study.

Setting:

The study was carried out in themedical oncology department and outpatient clinics of El Mansoura University Hospital.

Subjects:

A convenience sample of 40 adult cancer patients were selected according to the following criteria both sex (male and female),age ranged from 20 - 60 years and free from any oral lesion, patients who received chemotherapy for first time and were meeting the inclusion criteria of the study were selected. The exclusion criteria were that subjects suffering from head and neck cancer and neutopinc patients were excluded.

Tools of data collection:

This Questionnaire consisting of the following 2 parts was used in this study:

I-Sociodemographic and medical data form, which wasdesigned by the researchers. It was written in simple Arabic language anddivided into the following parts:

- Characteristics of the study subjects namely, age, gender,marital status, income, educational leveland working condition.
- Patients' medical data to identify diagnosis, duration of cancer, onset of treatment, number of cycle, weight, height.

II-Oral Assessment Guide (OAG):

Oral Assessment Guide (OAG) develops by **Eilers*et al.*, (1988)**and utilized by the researchers toassessthe patient's oral cavity and the degree of stomatitis.It included the following: voice; swallow; lips and angle of the mouth; tongue; saliva; mucus membrane; gingiva and teeth.It consists of eight-item,are using a 3-point rating scale,ranging from score (1) illustrate a normal findings and score (3) illustrate severe abnormality with compromise of either mucosal integrityor loss of function. The overall assessment scores were ranging from 8-24. The tools classified the patients into the following category:

- Where a score from 8 or less than 9, denotes healthy oral cavity.
- Where a score ranges from 9-16, denotes moderate stomatitis.
- Where a score ranges from 17-24, denotes severe stomatitis

Ethical considerations:

Informed patients consents were fulfilled before data collection after explaining the purpose and nature of study to them. Confidentiality of obtained data was assured, Subjects were informed about their voluntary right to accept or refuse participation in the study, and confidentiality was assured.

Procedure:

- Permission was obtained from the Director of El-Mansoura university Hospital for conducting the study in the Medical Oncology Department Clinic and Outpatient Clinics.
- Data were collected over 5 month started from the beginning April 2011 till to the end of August 2012.
- At the beginning of the study demographic data were collected by interviewing subjects individually, while medical information was obtained from patients medical records.
- The subjects who fulfill the inclusion criteria were selected randomly and divided alternatively into two equal groups, study group (I) and control group (II), 20 patients for each.
- All participants were interviewed individually at medical oncology department to collect data about sociodemographic and clinical characteristics using tool I.
- The sample was randomly divided into study and control groups. The study group, patients were treated by application of 20cc honey, applied by themselves on three times a day for two weeks only, when they started chemotherapy. They hold it in their mouth for 30-60 seconds and then gulped it down.
- In the control group received routine hospital care of oral hygiene on three times a day for two weeks.

- Oral assessment tool were filled by the researcher to identified changes in oral conditions for each subject before starting chemotherapy and after it and this was repeated around the day 10 of the treatment .i.e., two times of measurements for each subject to determine Oral Assessment Guide (OAG) profile during the period of the study. This was done for both groups. Indeed, a comparison was done between the two groups, for determining the effect of honey on prevention and management of oral stomatitis. It took approximately 20 minutes for each patient to complete the questionnaire.

Data analysis:

The collected data were coded as per variables and entered in SPSS data sheet and analyzed using the SPSS-PC statistical software (SPSS for Windows, version 10.0). Pearson's chi- square tests were used to determine the relationship between the use drugs and patient demographics. Chi square, t-test, Pearson's correlation coefficients (r) were also performed to evaluate the association between the variables. Statistical significance was considered at *p*-value < 0.05.

3. Results

Table (1): Describes sociodemographic characteristics of patients in the study and control groups. It shows that (50%) of patientsin the study group have age range between 35 to 45 years compared with (40%) of patients in the control group, with no statistically significant difference between both groups (p>0.05). As regard to sex, (50%) males and (50%) females in both groups. Regarding maritalstatus, this table revealed that (45%) in the study group and (60%) in the control group were married. While (35%) in the study group and (25%) in the control group were widowed. There was no statistically significant difference between both groups (*p*>0.05).Regarding educational level, it was observed from this table that the highest frequencies (65%) of studied control subjects, while 60 % in control group were literate. In relation to the residence, most of the studied subjects were from rural areas while lower in both groups were from urban areas.

Table (2)presents distribution of the studied sample according to their clinical data. As regard diagnosis 40 % of patient in study group suffered from cancer breast but 45 % in control group had the same diagnosis. While 10% in study group and 5% in control group suffered from cancer cervix. There was no statistically significant difference between both groups (*p*>0.05). As the number treatment cycle, the most of the patient in both group had 3-6 cycle. As regards to weight mean duration was higher in study group after 10 day (73.45+16.033). There are no statistically significant differences among the patients in the study and control groups.

Table (3) showed thatmean score of oral assessment categories in both groups at the basic assessment. It points that there was no statistically significant difference was existed between the study and control group respectively (*p*>0.05).

Table (4)shows themean score of oral assessment in both groups after implementation of the program. It points that no statistically significant difference regarding teeth, gingivitis (*p*>0.05). While there was highly statistically significant difference existed between patients in the both groups under study as regard to the patients' voice, swallow, lips, tongue, mucus membranes, and TOAG respectively(*p*<0.01).

Table (5): describes the correlation between total oral assessment categories and some variables of the studied groups at 10 days post of chemotherapy. It points a positive statistically significant correlation between post honey intervention score and education level (r=0.467, *p*<001), which means that teaching patients lead to improved scores of oral wellness. While there was no significant statistically difference between total oral assessment score and age, sex at 10 days post of chemotherapy (*p*>0.05).

4.Discussion:

Although chemotherapy is an important treatment modality, it brings various side effects to cancer patients because it can cause fast-dividing normal cells as well as tumor. The most distressing side effects of chemotherapy are nausea, vomiting, and mucosal ulceration (**Vokurka*et al.*,2005**).

The present study revealed that the majority of patient age ranged from 35- 45 years old. This result supported by the work of the **American Cancer Society (2009)** who concluded that the risk of begin diagnosed with cancer increases as individuals aged, most cases occur in adults in the middle aged or older. In the same line study by (**Nettina, 1996**) stated that it is worth mentioning that 55% of cancer occurs in people over 65 years of age.

The present study revealed that more than half of the study and control groups were female. This result agrees with **Smyth (1999)** reported that cancer is three times as common in women as in men. On the other hand; **Smeltzer and Bare (2004)** explained that men experience a higher incidence of cancer than do women.

Table (I): Distribution of the studied sample according to their sociodemographic characteristics

Items	Study G. (n=30)		Control G (n =30)		X2	*P*- value
	No	%	No	%		
Sex :						
Male	20	50%	20	50%	0.00	N.S
Female	20	50%	20	50%		
Age (years) :						
<25	5	25%	2	10%	4.61	N.S
25-34	2	10%	6	30%		
35-45	10	50%	8	40%		
> 45	3	15%	4	20%		
Marital status :						
Single	4	20%	3	15 %	0.17	N.S
Married	9	45. %	12	60%		
Widowed	7	35%	5	25.%		
Education :						
Literate	12	60%	13	65%	3.56	N.S
Illiterate	8	40%	7	35%		
Work :						
Work	10	50. %	12	60%	3.53	N.S
Not work	10	50%	8	40%		
Residence:						
Rural	13	65%	15	75%	3.33	N.S
Urban	7	35%	5	25%		

N.S:Not significant

Table (2): Distribution of the studied sample according to their clinical data.

Clinical data	Study (20)	Control (20)	X2	*P*-value
Type of cancer:	No (%)	No (%)		
Breast	8(40)	9(45)	3.45	NS
Hodgkin'slymphoma	6(30)	6(30)		
Non hodgkin'slymphoma	4(20)	4(20)		
Cervix	2(10)	1(5)		
Treatment cycle :				
3- 6	14(70)	16(80)	4.03	NS
7 - 10	5(25)	4(20)		
11-14	1(5)	0(0)		
Body weight :				
Weight pre of therapy	70.12+16.08	70.01+16.05	t=0.870	NS
Weight 10 days apost therapy	73.45+16.033	71.34+15.083		

*N.S: Not significant

Table (3): Mean score of patient's oral assessment categories in the studies group atthe beforechemotherapy

Items	Study (*Mean* ± *S.*D)	Control (*Mean* ± *S.*D)	t-test	Remarks
Voice	0.0034±(0.1719)	0.0034± (0.1719)	0.000	NS
Swallow	0.2666± (.0478)	0.276 ± (.0479)	0.159	NS
Lips	1.210± (0.402)	1.564± (0.378)	0.331	NS
Tongue	1.100±(0.2981)	1.0667± (0.252)	0.451	NS
Saliva	1.000± (0.000)	1.000± (0.000)	-	-
Mucous membrane	0.138(0.335)	1.0654(0.2436)	0.581	NS
Gingival	0.137(0.333)	1.133(0.298)	0.165	NS
Teeth	1.675(0.726)	1.543(0.658)	0.183	NS
TOAG	6.000(2.419)	6.485(2.278)	0.975	NS

NS: Not significant ; TOAG: total oral assessment guide

Table (4): Mean score of patient's oral assessment categories in the studies group 10 days of post chemotherapy

Items	Study	Control	t-test	Remarks
Voice	0.583 ± (0.753)	0.781± (0.745)	5.182	*P*<0.05
Swallow	0.410±(0.0581)	0.576 ± (.0479)	5.10	*P*<0.05
Lips	1.210±(0.402)	1.904± (0.607)	5.24	P<0.05
Tongue	1.560(0.685)	1.056(0.591)	2.65	P<0.05
Saliva	0.000(0.000)	0.000(0.000)	-	-
Mucous membrane	0.1345(0.433)	0.543(0.657)	8.43	P<0.05
Gingival	1.032(0.1816)	1.1673(0.388)	1.735	p>0.05
Teeth	1.465±(0.725)	1.643± (0.698)	1.760	p>0.05
TOAG	6.3945± (3.218)	7.670± (4.165)	2.334	P<0.05

P<0.05: Significant statistically; P>0.05: Not significant statistically; TOAG: total oral assessment guide

Table (5): Correlation between total oral assessment categories and some variables of the studied groups post 10 days of chemotherapy

Research variable	Total t scores of oral assessment guide (OAG)	
	Day 1	Day 10
Age		
r- value	.175	.166
p- value	.233	.132
Sex		
r- value	.086	.035
p- value	.276	.405
Education level		
r- value	.004	.481
p- value	.467	.000*

In relation to type of cancer, slightly half of the patients (50%) were breast cancer in study group and 45% in control group. This result was in agreement with **Beiki*et al.*,2012)** who stated that breast cancer is the most common tumor among women worldwide. While **El Hadaad (2000),** emphasized that non-Hodgkin's lymphomas represent a major health problem throughout the World. It is already a common malignancy and is, unfortunately, continuing to increase rapidly in incidence.

The result of the present study revealed that the majority of patients were from rural area in both groups. On contrary to the finding, **Higginbotham (2001)** found that there is evidence to suggest rural populations are diagnosed at a more advanced stage of cancer**.**This finding raises questions regarding availability and utilization of preventive, screening, and diagnostic services in rural areas as well as the existence of unique social and behavioral barriers. According to **(Monroe*et al.*, 1992)**the majority of data available indicate there are no differences between rural and urban populations with regard to cancer incidence and mortality, but a number of studies find cancer incidence increases with population density, which is a characteristic of relatively more urban settings.

In the present study, no statistically significant relations were detected between OAGL scores at start chemotherapy in the study and control group (p > 0.05).The current study showed improvement in oral assessment scores in patients who apply herbal than patients who apply pharmacology agent.

In the recent past honey has been used for the treatment of burn wounds, infected surgical wounds, pressure ulcers, and postoperative wound infections. Important factors which influence the effectiveness of honey are as follows: antibacterial, anti-inflammation, highly tissue nutrition minerals and vitamins that help repair tissue directly. This finding is congruent with that of **Rashad*et al.*,(2009)** which aimed to evaluate the efficacy of pure natural honey as prophylaxis against radiochemotherapy induced mucositis in head and neck cancer among forty patients. They found that prophylactic use of pure natural honey was effective in reducing mucositis resulting from radiochemotherapy in patients with head and neck cancer.

Regarding moisturizing and healing enhancement properties are explaining the rapid improvement in the condition of voice, swallow, lips, tongue, and mucus membranes of the study group more than the control group after 10 days of application of topical honey, these results were

congruent with the result of **Solomon(1986)** evaluated 18 patients with chemotherapy-induced mucositis during sucralfate treatment. After 7 days of treatment 10 patients were considered to have objective improvement and 11 subjective improvements.

Results of the current study showed a statistically significant improvement in the total oral assessment among patients over time ($p< 0.010$). This result was further supported by **Barahimi*et al.*, (2006)** showed that honey caused virtually better recovery of stomatitis among patients compared with routing solution administered at the ward among 70 patients with acute myeloid leukemia and lymphoid leukemia under chemotherapy. Also **Aldouri (2003)** found that experimental study quicker ulcer healing observed in honey treated rate than untreated. In the same line in **Mohamed & Al-Douri (2008)** noted that Honey has an obvious influence on the rate of healing process of the oral ulcers.

In the present study, showed a positive statistically significant correlation between post honey intervention score and education level ($r=0.467, p<001$), which means that educated patients lead to improved scores of oral wellness. The significant correlation mentioned above is illustrated graphically. While there was no significant statistically difference between total oral assessment score and age, sex post 10 days of chemotherapy ($p>0.05$).

Conclusion:

Based on the findings of the present study, it was concluded that honey was an effective preventing and decreasing oral stomatits and gingivitis in patients receiving chemotherapy. Analysis of data and comparison of means revealed a statistically significant difference between the two study groups as regard improvement in oral pain in the study groups faster than control group and body weight in two studied group following 10 days of chemotherapy administration and significant differences were illustrated.

Recommendations:

Based on the findings of the present study the following recommendations are suggested:

- Health education programs for patients receiving chemotherapy about the oral hygiene.
- Continuous visiting for dental physician to avoid oral complication
- Creating an oral care plan to patient with honey is an important recommendation in preventing oral complications and decreasing severity of oral stomasitis.
- Regular training programs to keep nurses in oncology unit updated with the most recent strategy for oral hygiene that promote oral wellness.
- Replication of the current study on a larger probability sample from different geographical areas, to achieve generalizable results.

Implications

The results implicated that:

Nurses providing care to cancer patients should be prepared to manage the toxicities of the chemotherapy. This includes careful assessment, providing patients with essential information and assistance with behavioral and physical nursing interventions that prevent and alleviate patient's side effects of pharmacological treatment.

The educational care plan must encompass the entire process of chemotherapy, the purpose and side effects of the medication prescribed, intervention to alleviate stomatitis and instruction about oral hygiene in order reduce pain in mouth and promotes oral wellness**.**

Corresponding author:
SalwaAttia, Medical Surgical Department, Faculty of Nursing,Fayoum University, Egypt
Salwaflower@yahoo.com

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