

The Therapeutic Effect of Honey on Stomatitis Complicating Chemotherapy in Children at Sohag Governorate

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Abstract: Background: Stomatitis is an inflammation of the lining of any of the soft-tissue structures of the mouth. It is usually a painful condition, associated with redness, swelling, and occasional bleeding from the affected area. Stomatitis can result from cancer treatment such as chemotherapy and some of diseases like (herpetic infections, gonorrhea, measles, leukemia, AIDS (Acquired Immune Deficiency Disease), and lack of vitamin C. The role of pediatric nursing care is of great importance in the prevention and treatment of chemotherapy-induced stomatitis. **Aim of the work:** to assess the therapeutic effect of honey on stomatitis complicating chemotherapy as a treatment of malignancy in children in Sohag Governorate. **Subjects and Methods:** The study was carried out in the cancer institute at Sohag Governorate. The research is a quasi-experimental design. This study included 100 children aged 6-12 years complaining of stomatitis complicating chemotherapy. They were divided into two groups each included 50 children: first group (study group) received a honey as a therapy for stomatitis (29 males and 21 females): the second group (control group) received routine medicine for stomatitis (17 males 33 females). **Results:** The manifestations of stomatitis, grades of inflammation and the effect of stomatitis on eat and drink were nearly similar in both groups with no significant differences. Among children of the study group, nearly half of them improved within 4 days (24 of 50) while other half required 5-7 days to improve. On the other hand, 56% of children of the control group (28 out of 50) improved within 7 days, 20% (10 out of 50) required 10 days and more to improve while 25% (11 out of 50) improved within 4 days. The difference was statistically significant. Among children of the study group, half of them required 5-7 days to improve the majority of them (24 out of 26) had moderate and severe forms of stomatitis. No children in the study group required more than 7 days to respond to treatment. On the other hand, 3 children of the control group who had mild stomatitis required 10 days and more to improve. Meanwhile 7 children in the control group who had severe stomatitis required 10 days and more to improve. **Conclusions:** It is concluded that, the use of natural source like pure honey showed excellent results in the treatment of stomatitis complicating chemotherapy in children with rapid healing even in the severe forms of stomatitis. Honey is very useful as a healing agent and compared to pharmaceutical products, has the advantages of being inexpensive, natural and effective within short duration.

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1. Introduction:

Stomatitis is an inflammation of mucus membranes and tissues in the mouth, such as the gums, tongue, roof and floor of the mouth, and tissue inside the lips and cheeks. Stomatitis can result from cancer treatment such as chemotherapy, some diseases like herpetic infections, gonorrhea, measles, leukemia, AIDS (Acquired Immune Deficiency Disease) and vitamin C deficiency (Sonis *et al.*, 2003).

It is characterized by mouth ulcers usually located on the lips, cheeks, gums, roof or floor of the mouth or sores and pain in the mouth. The first symptoms may be sensitivity to spicy foods and reddened mucous membranes. The patient with stomatitis may also experience a dry or swollen tongue, difficult swallowing and an inability to eat or drink, drooling, fever (Lingen, 2009). It is usually a

short-term condition lasting from just a few days to a few weeks (Mark, 2002).

The mouth and digestive tract are lined by rapidly dividing cells making them more sensitive to chemotherapy and stomatitis usually occurs 3 to 10 days post-chemotherapy (Jane *et al.*, 2003).

Diagnosis and management of stomatitis do not usually require laboratory testing. Testing is necessary only in cases in which the cause of the lesion is unclear or the presence of suspected specific virus. Direct fluorescent antibodies testing of vesicle scraping can provide diagnostic confirmation within several hours (Lisa, 2007).

The role of pediatric nursing care is of great importance in the prevention of chemotherapy-induced stomatitis. Although maintaining oral hygiene is an essential part of daily living, considerable attention has been given to improve oral

care practices. There is an important role for the nurse in maintaining good oral hygiene either directly by providing oral care or indirectly by providing advice and opportunities to provide self-care thus contributing to the children over all comfort (Stephen, 2000).

The main nursing goals for children with stomatitis are relief of pain and prevention of spread of infection. The use of analgesics and topical anesthetics is needed to provide relief especially before meals to encourage food and fluid intake. Drinking bland fluids is helpful in avoiding the painful lesions, mouth care is encouraged; the use of very soft bristle tooth brush or disposable foam – tipped toothbrush provides gentle cleaning near ulcerated areas. Careful hand washing is essential when caring of children; children should keep their finger out of the mouth. Very young children may require elbow restraints to ensure compliance (Marilyn, 2006).

Chemotherapy is the mainstay in treatment of malignancy. In most instances, several chemotherapeutic agents are used to cause multiple damage to cells and there by increase the chance that the cells will no longer be able to reproduce (Pillitter, 2007).

The most common oral problems occurring after chemotherapy are stomatitis, infection, pain, and bleeding. Other possible complications might include dehydration, malnutrition, commonly brought on by difficulties in swallowing and dysphagia (Shulman, 2004).

Most patients receive chemotherapy as an outpatient. Some patients stay in the hospital when first beginning chemotherapy, so their doctor can check for any side effects and change the dose if needed. Frequency and duration of chemotherapy treatment depends on the form of cancer, types of drugs, how the patient responds to the treatment, and the patient's health and ability to tolerate the drugs. Chemotherapy administration may take only a few minutes or as long as several hours. Chemotherapy may be given daily, weekly, or monthly (Skeel and Roland, 2003).

Honey has been used from ancient times as a method of accelerating wound healing and is mentioned for healing purposes in the Bible, Torah and Quran (Namias, 2003)). Honey has been suggested as an effective healing agent for various kinds of infected ulcers in both traditional and modern medicine (Vardi *et al.*, 1998).

Honey has therapeutic features; it has potential for the treatment of dental disease, mouth ulcers and other problems of oral health. It has potent-broad-spectrum antibacterial activity that rapidly clears

infection from wounds when applied topically (Jones, 2001).

Honey's therapeutic importance as a known antibacterial agent has been recognized since 1892. Recent research has been conducted on the role of honey in wound management when applied topically. Several properties of honey have been reported that make it an ideal wound dressing material: honey provides a moist healing environment thus healing occurs rapidly with minimal scarring, honey has anti-inflammatory action, it also reduces edema thus improving circulation, reduces pain and exudation, it improves of debridement and reduction of wound malodoit, stimulates angiogenesis, granulation and epithelialization by stimulating the growth of fibroblasts thus it helps skin regeneration. (Dunford *et al.*, 2000).

Honey has several antimicrobial properties: bacteria are mostly made of water, it is sucked dry in the presence of honey because of osmosis, bacteria are further inhibited by honey because honey produces hydrogen peroxide which provides acidic media for bacteria, it activates the immune response by providing glucose for the white blood cells (Paul *et al.*, 2007).

2. Subjects and Methods:

Research design:

The research is a quasi –experimental design that used to fit with the nature of this study and to meet the aim of the study.

Sample and groups:

The study included 100 children aged 6-12 years suffering from stomatitis complicating cancer chemotherapy. They were divided into age and sex matched two groups; first group (study group) included 50 children who received honey as a therapy for stomatitis, second group(control group) included 50 children who received routine medicine to stomatitis. Children with any other diseases that can cause stomatitis were excluded.

Study Setting:

The study was conducted in cancer institute in Sohag Governorate from 15/9/2009 to 22/5/2010.

Tools of the study:

Three tools for collecting data were used in this study.

Tool I:

A structured questionnaire sheet was developed to collect data of this study which included:-

- 1- General assessment sheet includes :- socio demographic data of child such as name, age, sex, birth order, parents' occupation, level of education, address, and number of siblings, educational and occupational status of the family,

knowledge of the mother about the disease such as definition, side effects.

- 2- Current health status (diagnosis, stage of disease, child response to chemotherapy and assessment of the presence of side effect related to chemotherapy such as gastrointestinal tract (nausea and vomiting, stomatitis, diarrhea), central nerves system (convulsion, headache and disturbed consciousness), skin (dermatitis, rash, hair loss) urinary system (impaired kidney function, cystitis) other side effect (brittle nail and recurrent infection) .
- 3- Schedule of chemotherapy (weekly, every two week, others) and regularity of treatment (regular or irregular).
- 4- Assessment of symptoms and signs of stomatitis such as dryness, pain, redness, secretions and lacerations; grade of inflammations (mild, moderate, severe); effect of stomatitis on eating and effect of stomatitis on mood of child.

Tool II:

Assessment of honey use program: one teaspoon (5 mg) of honey was put locally on oral cavity or stomatitis site three times daily. The response to honey and healing period were assessed every 2 days till complete recovery.

Tool III:

Assessment of routine medications used in children including such as drug name, dose. The response to medications and healing period were assessed every 2 day till complete recovery.

Statistical design:

The data were collected, reviewed, entered to computer program, coded, analyzed with the appropriate statistical methods and tabulated using computer program SPSS" version. 17" Chicago .USA. Data were presented using descriptive statistics in the form of frequency and percentage for qualitative variables, mean and standard deviations for quantative variables. *P* values less than 0.05 were considered statistically significance.

3.Results:

Table (1) showed that, both study and control groups were matched regarding age, sex, father education, mother education, residence, number of family and number of children. Table (2) showed that, no significant differences were found between study and control groups regarding side effects of chemotherapy. Table (3) showed that, no significant differences between study and control groups regarding duration of disease, schedule and regularity of chemotherapy. The percentage of good response to treatment was significantly higher in the study than control groups while moderate response was significantly higher in the control than study

groups. Table (4) showed that, manifestations of stomatitis, grades of inflammation and the effect of stomatitis on eat and drink were nearly similar in both groups with no significant differences. Table (5): Among children of the study group, nearly half of them improved within 4 days (24 of 50) while other half required 5-7 days to improve. On the other hand, 56% of children of the control group (28 out of 50) improved within 7 days, 20% (10 out of 50) required 10 days and more to improve while 25% (11 out of 50) improved within 4 days. The difference was statistically significant. Table (6): Among children of the study group, half of them required 5-7 days to improve the majority of them (24 out of 26) had moderate and severe forms of stomatitis. No children in the study group required more than 7 days to respond to treatment. On the other hand, 3 children of the control group who had mild stomatitis required 10 days and more to improve. Meanwhile 7 children in the control group who had severe stomatitis required 10 days and more to improve.

Table (1): Socio-demographic characteristics of children in study and control groups

Characteristics items	Study Group (n= 50)		Control Group (n= 50)		P value
	No	%	No	%	
Age (in years)					
6 – 8	28	56	35	70	<i>P</i> = 0.199 NS
8 - 10	5	10	10	20	
10 - 12	17	34	5	10	
Mean age (years) ±SD	8.62±2.60		8.06±1.60		
Sex					
Male	29	58.0	17	34	<i>P</i> = 0.268 NS
Female	21	42.0	33	66	
Father education					
Illiterate	7	14.0	5	10	<i>P</i> = 0.407 NS
Read and write	9	18.0	12	24	
Moderate educate	34	68.0	31	62	
University educate	0	0	2	4	
Mother education					
Illiterate	14	28	11	22	<i>P</i> = 0.473 NS
Read and write	6	12	5	10	
Moderate educate	30	60	32	64	
University educate	0	0	2	4	
Father occupation					
Farmer	4	8	13	26	<i>P</i> = 0.062 NS
Worker	37	74	33	66	
Employer	9	18	4	8	
Mother occupation					
House wife	46	92	49	98	<i>P</i> = 0.297 NS
Employer	4	8	1	2	
Residence:					
Urban	40	80	45	90	<i>P</i> = 0.131 NS
Rural	10	20	5	10	
Number of children					
More than 5	32	64	31	62	<i>P</i> = 0.210 NS
Less than 5	48	36	19	38	
N.S.: not significant <i>P</i> >0.05 *Significant at <i>P</i> <0.05 **Significant at <i>P</i> <0.01 ***Significant at <i>P</i> <0.001					

Table (2): Side effects of chemotherapy in children of study and control groups

Characteristics items	Study Group (n= 50)		Control Group (n= 50)		P value
	No	%	No	%	
GIT:					
Nausea vomiting	48	96	42	84	<i>P</i> = 0.35 NS
Stomatitis	48	96	40	80	
Diarrhea	9	18	16	32	
CNS:					
Convulsion	1	2	0	0	<i>P</i> = 0.421 NS
Headache	5	10	2	4	
Disturbed consciousness	3	6	2	4	
Skin:					
Dermatitis	2	4	2	4	<i>P</i> = 0.266 NS
Rash	25	50	34	68	
Hair loss	11	22	15	30	
Urinary system:					
Impaired Kidney function	1	2	1	2	<i>P</i> = 0.560 NS
Cystitis	2	4	0	0	
Others:					
Brittle nail	11	22	17	34	<i>P</i> = 0.061 NS
Recurrent infection	0	0	1	2	

N.S.: not significant $P > 0.05$ *Significant at $P < 0.05$ **Significant at $P < 0.01$ ***Significant at $P < 0.001$

Table (3) Schedule and response to chemotherapy in study and control groups

Characteristics item	Study Group (n= 50)		Control Group (n= 50)		P value
	No	%	No	%	
Malignancy duration					
Mean (months) \pm SD	8.66 \pm 4.123		8.144 \pm 1.60		<i>P</i> = 0.72 NS
Schedule of chemotherapy					
Weekly	3	6.0	2	4.0	<i>P</i> = 0.785 NS
Every 2 weeks	33	66.0	36	72.0	
Others	14	28.0	12	24.0	
Regular of treatment					
Regular	47	94.0	49	98.0	<i>P</i> = 0.360 NS
Irregular	3	6.0	1	2.0	
Response to chemotherapy					
Good Response	27	54	14	28	<i>P</i> = 0.02*
Moderate Response	23	46	36	72	

N.S.: not significant $P > 0.05$ *Significant at $P < 0.05$ **Significant at $P < 0.01$ ***Significant at $P < 0.001$

Table (4) Characteristics of stomatitis in study and control groups

Characteristics items	Study group (n= 50)		Control Group (n= 50)		P value
	No	%	No	%	
Manifestation of stomatitis					
Dryness	9	18.0	8	16.0	<i>P</i> = 0.508 NS
Redness	30	60.0	35	70.0	
Ulceration	30	60.0	29	58.0	
Pain	40	80.0	47	94.0	
Secretion	20	40.0	18	36.0	
Grade of inflammations					
Mild	14	28.0	16	32.0	<i>P</i> = 0.457 NS
Moderate	29	58.0	24	48.0	
Severe	7	14.0	10	20.0	
Effect on eat and drink					
Yes	12	24.0	10	20.0	<i>P</i> = 0.645 NS
Some	37	74.0	35	70.0	
No	1	2.0	5	10.0	

N.S.: not significant $P > 0.05$ *Significant at $P < 0.05$ **Significant at $P < 0.01$ ***Significant at $P < 0.001$

Table (5) Comparison between study and control groups regarding the duration of response to treatment

Characteristics items	Study group (n=50)		Control Group (n= 50)		P value
	No	%	No	%	
Improvement					P= 0.008**
- 2-4 days	24	48.0	12	24.0	
- 5-7 days	26	52.0	28	56.0	
- 10 days	0	0	6	12.0	
- More than 10	0	0	4	8.0	

N.S.: not significant $P > 0.05$ *Significant at $P < 0.05$ **Significant at $P < 0.01$ ***Significant at $P < 0.001$

Table (6) Relation between grade of stomatitis and duration of treatment in study and control groups

Item	Study group Grades of stomatitis			Control group Grades of stomatitis		
	Mild No (%)	Moderate No (%)	Severe No (%)	Mild No (%)	Moderate No (%)	Severe No (%)
Duration of treatment						
- 2-4 days						
- 5-7days	12(85.7)	11(37.9)	1(14.3)	11(68.8)	1(4.2)	0
- 10 days	2 (14.3)	18(62.1)	6(85.7)	2(12.5)	23(95.8)	3(30)
- >10 days	0	0	0	1(6.2)	0	5(50)
	0	0	0	2(12.5)	0	2(20)
Total	14	29	7	16	24	10
P value	P < 0.000***			P < 0.000***		

N.S.: not significant $P > 0.05$ *Significant at $P < 0.05$ **Significant at $P < 0.01$ ***Significant at $P < 0.001$

4. Discussion:

This study aimed to assess the therapeutic effect of honey on stomatitis complicating chemotherapy in children in Sohag Governorate.

Ulceration of the oral mucosa is caused by the damage insulted by chemotherapy or radiotherapy on the basal epithelial cells of the mucosa which decreases the replacement of these cells by new cells. Deprivation of new cell replacement, the mucosa becomes narrow, atrophied and ulcerated (Gerpen, 2005; Dorothy *et al.*, 2008; Lalla *et al.*, 2008).

The side effects and complications of cancer drugs include stomatitis, delay in cure, severe pain, nutritional deficiencies, systematic infection, and the increased duration of illness and mortality (Giles *et al.*, 2004). Mucositis causes nutritional deficiencies, dehydration and severe indigestion (Brown and Wingard, 2004 ; Bruce, 2004).

Chemotherapy does not distinguish between healthy and malignant cells, attacking all that reproduce rapidly including epithelial cells. Cancer patients receiving intensive chemotherapy suffer from stomatitis. Open sores in cancer patients suffering from mucositis and stomatitis leave them susceptible to infection (English *et al.*, 2004).

Honey is a viscous, supersaturated sugar solution derived from nectar gathered and modified

by the honeybee. Honey contains approximately 30% glucose, 40% fructose, 5% sucrose, and 20% water as well as many other substances such as amino acids, vitamins, minerals and enzymes (Sato and Miyata, 2000).

Honey and honey-based products are used as sources of energy and nutrition. Also, it is important in human health care and disease treatment (Evans and Flavin, 2008). Honey was used to treat infected wounds as long ago as 2000 years before bacteria were discovered to be the cause of infection (Chancho, 2009).

In the current study, all children in the study group and 80% of those in the control group responded to treatment within 7 days and 20% of children in the control group required 10 days and more to improve. This is consistent with the study of MacDonald (2002) who reported that, oral lesions usually resolve within a week to ten days, less commonly.

The present study showed that the response of stomatitis to honey application is significantly higher than to traditional therapy ($P = 0.008$).

These results are in agreement with Lusby *et al.* (2002) who found that mucosal healing was stimulated in rats by honey application as the high sugar content of honey inhibits bacterial growth.

Slow and low level production of hydrogen peroxide within wounds kills bacteria without causing tissue damage and also aids in debridement of wounds. Therapeutic honey application also produces a moist wound environment and also help in healing of wounds (**Shaw et al., 2000**).

Lusby et al. (2002) and Cooper et al. (2002) found that, honey can promote faster healing of wounds, reduce hospital stays, minimize scarring, remove infections, remove malodors, and alleviate pain and more acceptable to patients. It was also found to be particularly effective in wound healing and reducing infections and inflammations in cancer patients.

Jull et al. (2009), found that honey is effective in wound healing of both acute wounds as burns and lacerations and chronic wounds as venous leg ulcers and pressure ulcers in addition to shortening the healing time.

Annpoorna and Vipin (2010), found that honey reduces inflammation and has an anti-inflammatory action on stomatitis following radiotherapy and chemotherapy for cancer.

Lay-Flurrie (2008) mentioned that, the honey works differently from antibiotics which attack the bacteria's cell wall and inhibit intracellular metabolic pathways. Honey is hygroscopic, draws moisture out of the environment and thus dehydrates bacteria. Its sugar content is also high enough to hinder the growth of microbes, and inhibits the growth of many different bacterial species that cause wound infections.

Stomatitis is considered as a devastating side effect of chemotherapy for several reasons. Patients with stomatitis may have symptoms like painful ingestion leading to nutrition deficiency, dehydration, bacterial and fungal infections, and disturbed mood and sleep (**Brown and Wingard, 2004**).

Conclusions:

Based on findings of the present study, it is concluded that, the use of natural source like pure honey showed excellent results in the treatment of stomatitis complicating chemotherapy in children with rapid healing even in the severe forms of stomatitis. Honey is very useful as a healing agent and compared to pharmaceutical products, has the advantages of being inexpensive, natural and effective within short duration.

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