TOPICAL APPLICATION OF HONEY AND BEE PRODUCTS-OLIVE OIL MIXTURE IN TREATMENT OF CANCER THERAPY-RELATED ORAL MUCOSITIS

Thesis

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تأثير الاستخدام الموضعي للعسل ومزيج من منتجات النحل وزيت الزيتون في علاج التهابات الأغشية المخاطية للفم الناتجة عن علاج السرطان

رسالة

توطئة للحصول على درجة الماجستير في طب الأطفال

مقدمة من

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SUMMARY

This was a random clinical trial aim to compromise between the therapeutic effect of topical honey applied on patients had oral mucositis as an adverse effect of cancer therapy and the uses of traditional treatment in management of oral mucositis. The patients were randomly divided into 3 groups:

Group 1 (n=20): which included: (male=14, female=6), (ALL=13, Neuroblastoma=2, Hodgkin lymphoma =2, Non-Hodgkin lymphoma=3), mean age=8.20 +4.0).

Group 2 (n=20): (male =13, female =7), (ALL= 11, Neuroblastoma =3, Hodgkin lymphoma=2, Non-Hodgkin lymphoma=4), (mean age=7.1±3.7).

Group 3 (n=20): (male= 11, female=9), (ALL=8, AML=2, Hodgkin lymphoma=1, Non-Hodgkin lymphoma= 8, Neuroblastoma=1, mean age=6.90). This group served as a control group and followed the traditional treatment of oral mucositis.

The first group received pure honey, patients rinsed it in oral mucosa than swallowed it 3 times per day.


بسم الله الرحمن الرحيم
وَأَوْحَى رَبُّكَ إِلَى النَّحْلِ
أَنِ اتَّخِذِي مِنَ الْجِبَالِ
بُيُوتًا وَمِنَ الشَّجَرِ
وَمِمَّا يَعْرِشُونَ. ثُمَّ كُلِي
مِن كُلِّ الثَّمَرَاتِ
فَاسْلُكِي سُبُلَ رَبِّكِ ذُلُلاً
يَخْرُجُ مِن بُطُونِهَا
شَرَابٌ مُّخْتَلِفٌ أَلْوَانُهُ
فِيهِ شِفَاءٌ لِلنَّاسِ إِنَّ
فِي ذَلِكَ لآيَةً لِّقَوْمٍ
يَتَفَكَّرُونَ
صدق الله العظيم
سورة النحل آية (٦٨و٦٩)

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Rania Said Ebrahim

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INTRODUCTION

Oral mucositis is a common side effect of cancer therapies, particularly radiation therapy for head and neck cancer. It commonly results in severe oral pain that can compromise the duration and success of cancer management ***(Spencer, 2005).***

Oral cancer management ***(Spencer, 2005)***. Oral mucositis is defined as oral mucosal change secondary to cancer therapy. It manifests first by thinning of oral tissues leading to erythema. As these tissues become to be thinner, eventually ulceration occurs. The primary symptom is severe debilitating oral pain ***(Epstein, 2003).***

Severe mucositis can greatly complicate the management of cancer. It often leads to interruption of cancer treatment, which can compromise cure rates ***(Trotti et al., 2002)***. Hospitalization is common since patients lose the ability of oral intake due to severe pain and must have alimentation support during this period ***(Reddwing et al., 2004)***.

The most commonly used scales for grading of oral mucositis are the World Health Organization (WHO) scales and the National Cancer Institute-Common toxicity Criteria (NCI-CTC) scales ***(Sonis et al., 2004)***. Although, oral mucositis has been studied

for many years, no available treatment has been proved to be reliably effective to prevent or treat mucositis. Studies investigating single anti-microbial agents such as clorhexidine, clindamycin or antibiotic pastilles combining polymyxin, tobramycine and amphotricin given locally with intent of enhancing oral hygiene have shown only variable success in alleviating oral mucositis ***(Cheng et al., 2004)***.

Honey has anti-inflammatory ***(Al-Waili et al., 2003)***, anti-oxidant ,and anti-microbial effects ***(Molan, 1992)***. The anti-inflammatory effect of honey may be due to its effect in lowering plasma prostaglandin concentration ***(Al Waili, 2003)***. The honey antioxidant effect is due to the honey polyphenols ***(Gheldof et al., 2002)***.

Propolis is a natural product derived from plant resins collected by honeybees. It is used by bees as a glue, a general-purpose sealer, and as draught-extruder for beehives. Propolis has been used in folk medicine for centuries. It is known that propolis possesses anti-microbial, antioxidative, anti-ulcer and anti-tumor activities ***(Khalil, 2006)***. The main active components of olive oil include oleic acid, phenolic constituents, and squalene. The main phenolics include hydroxytyrosol, tyrosol, and oleuropein, which occur in highest levels in virgin olive oil and have demonstrated

antioxidant and antimicrobial activities ***(Waterman et al., 2007)***.

In the cancer setting, honey may be used for radiation-induced mucositis, radiotherapy-induced skin reactions, hand and foot skin reactions in chemotherapy patients and for oral cavity and external surgical wounds ***(Bardy et al., 2007)***.

The large volume of literature reporting its effectiveness indicates that honey has potential for treatment of periodontal disease, mouth ulcers, and other problems of oral health ***(Molan, 00)***.

AIM OF THE STUDY

Evaluation of the effect of topical application of a 4:2:1 mixture of honey, olive oil propolis extract and bees wax as natural products in treatment of cancer therapy-related oral mucositis in children.

CANCER IN CHILDHOOD

Although the incidence of childhood cancer increased slightly in the early 1980s, there has been no substantial change in the incidence of major pediatric malignancies since the mid-1980s. Mortality rates for childhood malignancies have declined significantly as a result of improvements in supportive care and therapy ***(Linet et al., 1999)***.

The most common childhood malignancies are acute lymphoblastic leukemia (ALL), central nervous system (CNS) tumors and lymphomas. Together, these cancers account for 63% of cases ***(Gloeckler Ries et al., 2003)***.

Table (1): Incidence of childhood cancers:

Cancer	Incidence (%)
Leukemia	30.2
Central nervous system tumors	21.7
Lymphoma	10.9
Neuroblastoma	8.2
Soft tissue sarcomas	7.0
Renal tumors	6.3
Bone tumors	4.7
Other types	11.0

(Linet et al., 1999)

In Egypt, there has been a changing pattern in the prevalence of childhood malignancies, with increasing incidence of acute lymphoblastic leukemia, neuroblastoma and non-Hodgkin's lymphoma (NHL).

Table (2): The relative frequency of pediatric cancers in Egypt (1993-1997).

Cancer	Egypt NCI (1997)
Leukemia	36.7%
Central nervous system tumors	1.6%
Lymphoma	32%
Neuroblastoma	1.6%
Wilm's tumor	3.7%
Soft tissue sarcomas	9.2%
Bone tumors	8.8%
Liver tumors	0.2%
Retinoblastoma	1.3%
Other	5%

(National Cancer Institute of Egypt, 2006)

Table (3): Adverse effect of radiotherapy.

Organ system	Sequelae
All tissues	Second malignancies, functional and cosmetic problems
Teeth and salivary glands	Dry mouth, dental developmental abnormalities, periodontal disease, tooth decay cosmetic problems, oral mucositis
Muscles and soft tissues	Atrophy or hypoplasia, fibrosis and contracture, lymphedema
Eye	Cataract, retinopathy, dry eye, vision loss, photophobia
Ear	Chronic cerumen impaction
Heart	Pericardial effusion, constrictive pericarditis, early-onset coronary artery disease
Chest	Pulmonary fibrosis, restrictive lung disease, recurrent pneumothorax, breast cancer
Central nervous system	Neurocognitive deficits, chronic seizure disorder, cerebrovascular accident (stroke), imaging changes: cerebral atrophy encephalomalacia, lacunes, and ventriculomegaly
Kidneys	Hypertension, renal insufficiency
Bladder and collecting system	Bladder fibrosis, dysfunctional voiding, urinary incontinence, urinary tract obstruction
Pituitary gland	Reduced growth or growth failure, early or delayed puberty, other hypothalamic-pituitary endocrinopathies
Thyroid gland	Hypothyroidism, hyperthyroidism, thyroid nodules
Gonads	Males: sterility, Leydig's cell dysfunction. Females: ovarian failure, early menopause
Gastrointestinal tract	Malabsorption, intestinal stricture hepatic dysfunction, chronic enterocolitis

(Castellino and Hudson, 2002)