Effect of Honey on Phagocytic Function during Nutritional Rehabilitation in Infants with Protein Energy Malnutrition

THESIS

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Abstract:

Objectives and Design: It has been proven that malnutition is the most common cause of immunodeficiency worldwide; PEM is associated with a significant impairment of cell mediated immunity, phagocytic function and complement.This study was designed to examine the effect of honey in a calculated dose (20 ml/Kg) on phagocytic function in those patients and whether it would improve (and so help nutritional rehabilitation) or not.

Patients: 30 patients suffering from (PEM), as well as 20 healthy infants participated in this study. The patients were divided into 2 equal groups, during nutritional rehabilitation, where one group was rehabilitated using the honey and the other without honey. Phagocytic index was assessed before nutritional rehabilitation and after 2 weeks of nutritional rehabilitation

Results: After nutritional rehabilitation, the phagocytic index was significantly higher in both PEM groups compared to initial values, but was still significantly lower than the control group. However, after nutritional rehabilitation phagocytic index values in the group who received nutritional rehabilitation with honey supplementation was significant higher than those who received nutritional rehabilitation without honey supplementation. Moreover, the rate of change of phagocytic index was significantly higher in honey supplemented group than non honey supplemented group.

Conclusion: Using honey in nutritional rehabilitation program of patients suffering from PEM may have a better immuno-modulatory effect especially on more rapid recovery of their phagocytic function. Longer term follow up is recommended to clear this point

List of Abbreviations

AIDS: Acquired imuno deficiency Syndrome

Alb: Albumin level

ALT: Alanine transaminase

ALK: Alkaline phosphatase

AMP: Adenosine phosphate

AR: Autosomal recessive

AST: Aspartate transaminase

BCG: Bacille Calmette-Guérin

BF: breast feeding

BUN: Blood Urea Nitrogen

C: complement

Ca: Calcium

CBC: Complete Blood Count

CGD: Chronic granulomatous disease

cm: Centimeter

Creat: Creatinine

EGG: Electrogastrography

Gm%: gram percent

G6PD: Glucose-6-phosphate dehydrogenase

Hb: Hemoglobin level

HBSS : Hank's balanced Salt solution

HIV: Human immunodeficiency virus

HC: Head circumference

HC (%): Head circumference percentage of 50th centile of age

Hct: Haematocrit

Ht: height

Ht%: height percentage of 50th centile of age

ICAM: Intercellular adhesion molecule

IQR: Interquartile range

IFN: Interferon

IL: Interleukin

K: Potassium

Kg: kilogram

KWO: Kwashiorkor

MAC: Midarm circumference

MAC (%): Midarm circumference percentage of 50th centile of age

MCV: Mean corpuscular hemoglobin

MCHC: Mean corpuscular hemoglobin concentration

m: Messenger

MKWO: Marasmus Kwashiorkor

mm: millimeter

Na: Sodium

NADPH: Nicotinamide-adenine dinucleotide phosphate

NK: Natural killer

NO: Nitric oxide

NSAIDs: Non steroidal anti-inflammatory drugs

Lymh: Lymphocytes

P: Phosphorus

Phox: Phagocyte oxidase

P.I: Phagocytic index

PEM: Protein Energy Malnutrition

PNL: Polymorphnuclear leucocytes

Plt: Platelet count

SCFA: short chain fatty acid

SCU: Severe childhood undernutrition

SD: Standard deviation

SFT: Skin fold thickness

SFT (%):Skin fold thickness percentage of 50^{th} centile of age

TLC: Total leucocytic count

TLR: Toll-like receptor

WHO: World Health Organization

Wt: weight

Wt (z): weight by z-score

Wt%: weight percentage of 50^{th} centile of age

X: X-linked

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INTRODUCTION AND AIM OF THE WORK

Protein energy malnutrition (PEM) constitutes a major paediatric problem in most of the developing countries. In Egypt, the syndrome is quite common. It stands as a major threat to Infant's health, growth and development **(Gabr et al**, **1984).**

Epidemiologic studies have shown a relationship between nutritional deficiencies and heightened risk of morbidity and mortality due to infectious disease. These observations led to studies that examined the effect of protein-energy malnutrition on immunocompetence. Protein-energy malnutrition is associated with a significant impairment of cell-mediated immunity, phagocyte function, complement system, secretory immunoglobulin A antibody concentrations, and cytokine production **(Chandra, 1992)**.

A study was done to evaluate of polymorphonuclear neutrophils in moderate malnutrition, it showed a decrease in the process of ingestion and digestion during phagocytosis occurs in malnourished patients **(Forte et al, 1999).**

Honey is a source of "natural" sugars. There are several reports of the effectiveness of honey in gastrointestinal disorders, wound healing and as an antibacterial, anti-inflammatory and antitussive agent. The composition of a particular sample of natural honey will

depend upon the composition of the nectars and where it originates. Honey is composed mainly of fructose, dextrose, maltose, sucrose and moisture with other trace components. The main sugars in honey, fructose and glucose are absorbed directly into the blood; provide a rapid source of energy without the need of digestion **(Naguib et al, 2001).**

A study was done on effects of honey compared with sucrose and a sugar-free diet on neutrophil phagocytosis and lymphocyte numbers after long-term Feeding in rats, it concluded that honey may have a beneficial effect on immune activity **(Chepulis, 2007)**.

Limited research has demonstrated that honey can stimulate the release of tumour necrosis factor-α and cytokines in monocyte cells **(Tonks et al., 2001, 2003),** and increase proliferation of B- and T- lymphocytes and neutrophils in vitro **(Abuharfeil et al. 1999).** In addition, honey has been demonstrated to stimulate antibody production during primary and secondary immune responses against thymus-dependent and thymus-independent antigens **(Al-Waili and Haq, 2004).**

This study was designed to evaluate the beneficial effect of honey intake during the nutritional rehabilitation of patients with PEM on their phagocytic function.

Protein Energy Malnutrition

Introduction:

The World Health Organization defines malnutrition as "***the cellular imbalance between supply of nutrients and energy and the body's demand for them to ensure growth, maintenance, and specific functions***." Malnutrition is globally the most important risk factor for illness and death, contributing to more than half of deaths in children worldwide. Protein-energy malnutrition (PEM), first described in the 1920s, is observed most frequently in developing countries **(Grigsby, 2006).**

The long-term effects of nutritional deficiencies in early life depend on the severity and duration of the deficiency, the stage of the children's development, the biological condition of the children and the socio-cultural context **(Grantham-McGregor et al., 2000).**

Definition:

Deficiency of a single nutrient is an example of undernutrition or malnutrition, but deficiency of a single nutrient usually is accompanied by a deficiency of several other nutrients. Protein-energy malnutrition (PEM) is manifested primarily by inadequate dietary intakes of protein and energy, either because the dietary intakes of these 2 nutrients are less than required for normal growth or because the needs for growth are greater than can be supplied by what otherwise would be adequate intakes. However, PEM is almost always accompanied by deficiencies of other nutrients. For this reason, the term **severe childhood undernutrition** (SCU), which more accurately describes the condition, is preferred **(Heird, 2008).**

The terms primary malnutrition and secondary malnutrition refer, respectively, to malnutrition resulting from inadequate food intake and malnutrition resulting from increased nutrient needs, decreased nutrient absorption, and/or increased nutrient losses. Both primary and secondary malnutrition occur in developing as well as developed countries; malnourished children often present with gastroenteritis or pneumonia **(Heird, 2008).**

Types of PEM

Primary PEM results from a diet that lacks sufficient sources of protein and/or energy. Secondary PEM is more common in United States, where it usually occurs as a complication of AIDS, cancer, chronic kidney failure, inflammatory bowel disease, and other illnesses that impair the body's ability to absorb or use nutrients or to compensate for nutrient losses. PEM can develop gradually in a patient who has a chronic illness or experiences chronic semi-starvation. It may appear suddenly in a patient who has an acute illness **(Gale Research, 1999).**

PEM applies to a group of related disorders that include marasmus, Kwashiorkor (KWO), and intermediate states of marasmus Kwashiorkor (MKWO) **(Lin et al., 2003).**

Marasmus (Non-edematous Form of PEM):

The term marasmus is derived from the Greek word marasmos, which means withering or wasting. Marasmus involves inadequate intake of protein and calories and is characterized by emaciation **(Lin et al., 2003).**

A child is defined as suffering from Marasmus if his weight is below 60% of the expected weight (fiftieth centile)

for his age **(Axton, 1990).** Marasmus is the most common form of PEM. It is due to severe caloric depletion and is diagnosed in the presence of clinical muscle wasting, loss of subcutaneous fat and absence of edema **(Gernaat and Voorhoeve, 2000).**

Kwashiorkor (KWO) (Edematous Form of PEM):

The term KWO is taken from the Ga language of Ghana and means "the sickness of the weaning" **(Lin et al., 2003).**

KWO is defined as weight between 60 and 80% of that expected for age, together with the presence of edema **(Axton, 1990).** It is a clinical syndrome which results from acute deficiency of proteins and inadequate caloric intake, and is diagnosed in the presence of edema, mental apathy and one or more symptoms or signs (hepatomegaly, diarrhea, hair discoloration, skin changes and muscle wasting) **(Gernaat and Voorhoeve, 2000).** According to the **WHO, (1999),** KWO is a common severe form of PEM characterized by edema, dermatosis and irritability.

Marasmic Kwashiorkor (MKWO):

The combined form of PEM is called marasmic kwashiorkor. Children with this form have some edema and more body fat than those with marasmus **(Beers and Berkow, 1999).**

Epidemiology:

Internationally: In 2000, the world health organization (WHO) estimated that malnourished children numbered 181.9 million (32%) in developing countries. Also, an estimated 149.6 million children younger than 5

years are malnourished when measured in terms of weight for age. In south central Asia and Eastern Africa, about one half of children have growth retardation due to PEM. This figure is 5 times the prevalence in the western world **(Lin et al., 2003).**

In Egypt, a cross-section nutritional survey of children aged 6-24 months attending health-care centers in Alexandria governorate throughout one year was done by **Mortada et al., (1990).** The results of the study revealed a prevalence rate of under nutrition of 25% which was mostly of the first degree as expressed by Gomez categories. When expressed using Waterlow classification, a prevalence of stunting of 29.7% was observed. Further, **Galal (2002),** has report that rates of early childhood malnutrition remain stubbornly stable and relatively high in Egypt.

Marasmus is the predominant form of PEM in most developing countries. It is associated with the early abandonment or failure of breast feeding and with consequent infections, most notably those causing infantile gastroenteritis. These infections result from improper hygiene and inadequate knowledge of infant rearing that are prevalent in the rapidly growing slums of developing countries. While KWO is less common and is usually manifested as MKWO. It tends to be confined to parts of the world (rural Africa, the Caribbean and Pacific islands) where staple and weaning foods such as yam, cassava, sweet potato, and green banana are protein deficient and excessively starchy **(Beers and Berkow, 1999).**

Classification of PEM

1- Classifications based on weight

a- Gomez classification **(Gomez, 1956).**
b- Garrow classification **(Garrow, 1966).**
c- Jelliffe classification **(Jellife, 1966).**
d- Wellcome classification **(wellcome, 1970).**
e- Buzina classification **(Buzina, 1980).**

2- Classifications based on length

a- Modified Jelliffe classification **(Jelliffe, 1968).**
b- Waterlow classification **(Waterlow, 1972).**
c- McLaren and Read classification **(McLaren and Read, 1975).**

Body measurements give reasonably accurate estimates of body wasting.

Children more than 3SD below the median reference weight-for-height can be said with some certainly to be severely malnourished, while those between 2 and 3SD below the median are moderately malnourished. However, of the children not yet below 2SD, some may also be malnourished in reality, particularly in communities where more than 15% of the population have weight-for-height value less than 2SD below the reference median **(WHO, 2000).**

3- Classification based on clinical signs

McLaren et al. (1967) introduced a simple system known as McLaren's scoring system and in **1980, Thanangkul et al.,** modified the McLaren system.

4- Classification of PEM based on the Z-scoring:

Z score or standard deviation score:

A drawback of the **Wellcome** classification is that it requires age to be precisely known which is often not the case in rural areas with limited standerds of health care and

education. It has also become clear that weight for age is in fact a compound parameter of two virtually independent processes, namely stunting (low height for age due to past or chronic mild growth retardation) and wasting (low weight for height due to acute severe growth retardation only the later is one of the key pathological processes the various clinical manifestations of acute PEM **(Gernaat and Voorhoeve, 2000).**

It was recommended by **Gernaat and Voorhoeve, (2000)** to use the weight for height Z score (as an indicator for wasting) and the presence or absence of edema to classify acute PEM as shown in (table 1).

Z score (or standard deviation score) is the difference between the actual measurement and the median age and sex matched reference population divided by the standard deviation of the reference population **(Shann, 1993).**

$$\text{Z score} = \frac{\text{Individual's wt} - \text{median value of reference population}}{\text{SD value of reference population}}$$

Here, wasting is defined as Z score of weight for height < -2 in a normally distributed reference population.

Table (1): Classification of acute PEM by Z-score

Weight for height	Edema	No edema
> -2 Z score (no wasting)	Kwashiorkor	No acute PEM
< -2 Z score (wasting)	Marasmic kwashiorkor	Marasmus

(Gernaat and Voorhoeve, 2000).