

Effect of Honey on Left Ventricular Systolic Function in Children with Idiopathic Dilated Cardiomyopathy

Thesis

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﴿وَقُلْ رَبِّ زِدْنِي عِلْمًا﴾

سورة طه الآية رقم ١١٤

إهداء

إلى....

نور حياتي أمي

عرفاناً لها بالجميل

وأهدي لها هذا الجهد المتواضع

سعاد أبو خزام فرج

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List of Contents

	Page
Acknowledgment	--
List of Abbreviations	i
List of Figures	ii
List of Tables	v
Introduction	1
Aim of The Work	3
Review of Literature	4
Chapter 1 : Cardiomyopathy	4
Chapter 2 : Idiopathic Dilated Cardiomyopathy	11
Chapter 3 : Honey	46
Patients and Methods	67
Results	74
Discussion	87
Summary	92
Conclusion	94
Recommendations	95
References	96
Arabic Summary	--

List of Abbreviations

ARVC	Arrhythmogenic right ventricular cardiomyopathy
AV	Atrio-ventricular
CAPE	Caffeic acid phenethyl ester
CI	Cardiac index
COCM	Congestive cardiomyopathy at diastole
CRP	C-reactive protein
CRT	Cardiothoracic ratio
DCM	Dilated cardiomyopathy
DTPA	Diethylene-triamine pentaacetic acid
ECG	Electrocardiography
EMB	Endomyocardial biopsies
ESC	European Society of Cardiology
HCM	Hypertrophic cardiomyopathy
HMF	Hydroxyl-methylfurfural
HTx	Heart transplantation
IDCM	Idiopathic dilated cardiomyopathy
IHD	Ischemic heart disease
LVEF	Left ventricular ejection fraction
LVH	Left ventricular hypertrophy
MI	Myocardial infarction
PCMR	Pediatric cardiomyopathy registry
RCM	Restrictive cardiomyopathy
ROS	Reactive oxygen species
TDI	Tissue Doppler imaging
TIC	Tachycardia-induced cardiomyopathy
TPR	Transpulmonary resistance
VT	Ventricular tachycardia
WHO	World health organization

List of Figures

Fig.	Title	Page
1	Classification scheme of cardiomyopathies.	6
2	Histological characteristics of hypertrophic cardiomyopathy.	7
3	Difference between normal heart and heart with DCM.	11
4	Diagnostic flowchart of dilated cardiomyopathy.	12
5	Relationships genes associated with cardiomyopathies and related phenotypes.	14
6	A patient with nonspecific intraventricular conduction delay (IVCD).	15
7	Early repolarization	16
8	Possible triggers of idiopathic dilated cardiomyopathy.	19
9	Chest radiograph shows cardiomegally for child with IDCM.	30
10	ECG in Idiopathic dilated cardiomyopathy	31
11	Two-dimensional end-diastolic echocardiogram in a patient with dilated cardiomyopathy.	36
12	M-mode echocardiogram in a patient with dilated cardiomyopathy.	37
13	Honey composition.	47
14	Anti-oxidant compounds in honey.	50
15	The anti-microbial weapons of honey.	51
16	The mechanisms of the anti-inflammatory effects of honey.	52
17	The percent change of the aortic root	83

Fig.	Title	Page
	diameter (AORD) in the honey and the control (no honey) group ($p > 0.05$).	
18	The percent change of the left atrial diameter (LAD) in the honey and the control (no honey) group ($p > 0.05$).	83
19	The percent change of the fraction shortening (FS) in the honey and the control (no honey) group ($p < 0.001$).	84
20	The percent change of the ejection fraction (EF) in the honey and the control (no honey) group ($p < 0.001$).	84
21	The percent change of the septal wall thickness (SWT) in the honey and the control (no honey) group ($p > 0.05$).	85
22	The percent change of the left ventricular end diastolic diameter (LVED) in the honey and the control (no honey) group ($p > 0.05$).	85
23	The percent change of the left ventricular end systolic diameter (LVESD) in the honey and the control (no honey) group ($p > 0.05$).	86

List of Tables

Table	Title	Page
1	Classification of toxic and metabolic cardiomyopathies.	20
2	Diverse etiologies of dilated cardiomyopathy.	24
3	New York Heart Association (NYHA) functional class below IV.	27
4	Physiochemical characters of the honey used in the study.	72
5	Baseline characteristics of patients.	78
6	The echocardiographic findings at the end of the 12th week (end point of the study).	79
7	The echocardiographic findings between baseline and the end point of the study (12th week) in the honey group.	80
8	The echocardiographic findings between baseline and the end point of the study (12th week) in the control group 2.	81
9	Rate of change (%) of echocardiographic findings between baseline and the end point of the study (12th week) in the honey and control groups.	82

Abstract

Despite recent advances in the management of patients with heart failure, morbidity and mortality rates remain high. Common causes of heart failure are ischaemic heart disease, uncontrolled hypertension and valvular disease. However, in up to 50 % of the cases its exact cause remains initially unknown; this condition is called idiopathic dilated cardiomyopathy (DCM).

Honey is one of the most renowned natural foods. Its composition is extremely variable, depending on its botanical and geographical origins, and the abundant presence of functional compounds has contributed to the increased worldwide interest in this foodstuff. In particular, great attention has been paid by the scientific community towards classes of compounds like phenolic compounds, due to their capability to act as markers of unifloral honey origin.

In order to evaluate the effects of oral honey on the left ventricular systolic function in children and adolescents with Idiopathic Dilated Cardiomyopathy, this study was carried out in the Cardiology Clinic, children hospital, Ain Shams University, Egypt during the period from November to May.

There are limited data on the effectiveness or efficacy of honey on blood pressure, however, it was reported that short-term (3 weeks) administration of honey in streptozotocin-induced diabetic spontaneously hypertensive rats resulted in reduction in systolic blood pressure.

During the 3 month-study period, there was no change in the drug treatment of the patients of both groups.

All patients in the honey group tolerated well the honey intake; no patient developed any adverse effect. At the end of the study, the echocardiographic findings did not also show significant changes between the two groups, but in the honey group, there was a highly significant increase in the fraction shortening (FS) and the ejection fraction (EF), and a significant decrease in the left ventricular end systolic diameter.

Keywords : IDCM: Idiopathic dilated cardiomyopathy; LVEF: Left ventricular ejection fraction.

Introduction

Cardiomyopathy is a chronic disease of the heart muscle (myocardium), in which the muscle is abnormally enlarged, thickened, and/or stiffened. The weakened heart muscle loses the ability to pump blood effectively, resulting in irregular heartbeats (arrhythmias) and possibly even heart failure. Dilated (congestive cardiomyopathy) is the most common form of the disease. The heart cavity is enlarged and stretched (cardiac dilation), which results in weak and slow pumping of the blood, which in turn can result in the formation of blood clots (*San Diego, 2004*).

Common causes of heart failure are ischemic heart disease, uncontrolled hypertension and valvular disease. However, in up to 50 % of the cases, its exact cause remains initially unknown; this condition is called idiopathic dilated cardiomyopathy (*Felker et al., 2000*). It may be the consequence of a wide variety of causes, including virus-mediated disease, immune dysregulation, toxic and metabolic, inherited, and tachycardia-induced conditions (*Watkins et al., 2011*).

The goals of treatment in patients with idiopathic DCM are to improve survival, slow disease progression, minimize risk factors, and alleviate symptoms. A standard heart failure regimen with lifestyle modifications should be initiated in all patients with this cardiac disease, including ACE inhibitors, angiotensin-II receptor antagonists, beta-

blockers, diuretics, aldosterone antagonists, and digitalis (*Dennert et al., 2010*).

Honey is a natural product made when the nectar and sweet deposits from plants are gathered, modified and stored in the honeycomb by honey bees. It is composed primarily of the carbohydrates glucose and fructose which account for about 85% of honey solids. Water is the third greatest component of honey. Honey also contains other types of carbohydrates, as well as acids, proteins, enzymes, vitamins and minerals (*White et al., 1962*).

Honey has many benefits for human and animal nutrition and health (*Bogdanov et al., 2008*) including anti-inflammatory (*Al Waili and Boni, 2003*), anti-oxidant (*Frankel et al., 1998*), anti-microbial (*Molan, 1992*), anti-tumor (*Morales and Haza, 2013*) and immune-modulator effects (*Majtan, 2014*). However, in the case of cardiovascular diseases, most of the previous studies were carried out in animals and mainly focused on honey's effects against cardiovascular risk factors such as dyslipidemia and production of free radicals (*Schramm et al., 2003*).

Aim of the work

To evaluate the effects of oral honey on the left ventricular systolic function in children and adolescents with Idiopathic Dilated Cardiomyopathy.

Cardiomyopathy

Definition:

"Cardiomyopathies are a heterogeneous group of diseases of the myocardium associated with mechanical and/or electrical dysfunction that usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilation and are due to a variety of causes that are frequently genetic. Cardiomyopathies either are confined to the heart or are part of generalized systemic disorders, often leading to cardiovascular death or progressive heart failure-related disability" (*Maron et al., 2006*).

Epidemiology:

Worldwide the estimated prevalence of all types of cardiomyopathies is about 3% in the general population (*Cecchi et al., 2012*). Cardiomyopathies, frequently with a genetic cause, include a variety of myocardial disorders in which the heart muscle is structurally and functionally abnormal (*Elliott et al., 2008*). The incidence of cardiomyopathy in infants and children is difficult to assess, in part because of the variation in diagnostic criteria in different regions of the world and partly because of the heterogeneous etiologies of the disease (*Kay et al., 2001*).

Clinical Picture:

The degree of cardiac dysfunction ranges from lifelong symptomless forms to major health problems, such

as progressive heart failure, arrhythmia, thromboembolism or sudden death (**Franz et al., 2001**). A majority of patients remains undiagnosed or misdiagnosed with more prevalent cardiac conditions (**Cecchi et al., 2012**). Whereas major progress has been made in improving the prognosis of affected patients, cardiomyopathies still remain a considerable challenge in the health care system and an economic burden across Europe and the rest of the world.

Classification:

Since the 1950's several definitions, nomenclatures and classification schemes have been acquired by experts. Cardiomyopathies are currently grouped by the 'European Society of Cardiology Working Group on Myocardial and Pericardial Diseases' into specific morphological and functional characteristics with sub-classifications into familial and non-familial subset (**Elliott et al., 2008**). The four major subtypes of cardiomyopathies are hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), arrhythmogenic right ventricular cardiomyopathy (ARVC) and restrictive cardiomyopathy (RCM). The classification also includes an unclassified group with no typical phenotype. Furthermore, the most recent **WHO/WHF** definition also comprises, among the specific cardiomyopathies, inflammatory cardiomyopathy as a distinct entity, defined as myocarditis in association with cardiac dysfunction (**Asakura and Kitakaze, 2014**).