

Coronary Artery Diseases Pattern in Khat users versus Non Khat Users

Thesis

**Submitted for partial fulfillment of the M.Sc of
cardiology**

By

**Jamal Alddeen Mohammed Mahdi Arraimi
(M.B.B.Ch.)**

Supervised by

Dr. Mohamed Ismail

Professor of Cardiovascular Medicine
Faculty of Medicine -Ain Shams University

Dr. Tamer Abu Arab

Lecturer of Cardiovascular Medicine
Faculty of Medicine - Ain Shams University



**Faculty of Medicine
Ain Shams University**

2016

Abstract

In this study, there is significant positive correlation between Duke modified score, number of vessel affected and duration of khat chewing in hours/day, number of khat chewing in days/week, duration of khat chewing in years and also significant positive correlation between number of vessels affected and duration of khat chewing.

In this study, the occurrence of intracoronary angiographic thrombi was higher in khat chewing group being present in 64 patients (64%) compared to 49 patients (49%) in Non khat chewing group, the difference is statistically highly significant ($p < 0.001$).

Key words: Three vessel disease, Acute coronary, syndrome, Acute myocardial infarction



Acknowledgement

First of all, all gratitude is due to **Allah** almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.

Really I can hardly find the words to express my gratitude to **Dr. Mohamed Ismail**, Professor of Cardiovascular Medicine, Faculty of Medicine, Ain Shams University, for his supervision, continuous help, encouragement throughout this work and tremendous effort he has done in the meticulous revision of the whole work. It is a great honor to work under his guidance and supervision.

I would like also to express my sincere appreciation and gratitude to **Dr. Tamer Abu Arab**, Lecturer of Cardiovascular Medicine, Faculty of Medicine - Ain Shams University, for his continuous directions and support throughout the whole work.

Words fail to express my love, respect and appreciation to **my wife** for her unlimited help and support.

Also I would like to express my sincere gratitude to all doctors in cardiac centre **Al-Thawrah and Saudi Germani Hospitals** Sana'a to support from the initial to the final level enabled me to develop and achieve my subject.

Last but not least, I dedicate this work to my family, whom without their sincere emotional support, pushing me forward this work would not have ever been completed.

Jamal Alddeen Mohammed Mahdi Arraimi



Dedication

*Words will never be able to express
my deepest gratitude to my
parents, wife and my sons
Mohammed & Fatma, those
who helped me during preparation
of this study.*

List of Contents

	Page
Acknowledgment	--
List of Abbreviations	i
List of Figures	ii
List of Tables	v
Introduction	1
Aim of The Study	3
Review of Literature	4
Chapter 1 : The History of Khat	4
Chapter 2 : Chemistry of Khat	8
Chapter 3 : Effect of Khat on the Cardiovascular System	15
Chapter 4 : Khat and other systems	20
Chapter 5 : Coronary artery disease	28
Patients and Methods	64
Results	71
Discussion	92
Summary.....	100
Conclusion	104
Recommendations	105
References	106
Arabic Summary	--

List of Abbreviations

3VD	: Three vessel disease
ACS	: Acute coronary syndrome
AMI	: Acute myocardial infarction
BMI	: Body mass index
CABG	: Coronary artery bypasses graft
CAD	: Coronary artery disease
CK	: Creatine kinase
CMRI	: Cardiac MRI
CNS	: Central nervous system
CRP	: C-reactive protein
CT	: Computed tomography
cTns	: Cardiac Troponins
CVD	: Cardiovascular disease
DM	: Diabetes mellitus
DNA	: Deoxyribonucleic acid
ECG	: Electrocardiography
ECM	: Extracellular matrix
ED	: Emergency department
EF	: Ejection fraction
ESC/ACC	: European Society of Cardiology and the American College of Cardiology
GRACE	: Global Registry of Acute Coronary Events
ICU	: Intensive care unit
IHD	: Ischemic heart diseases
IL-6	: Interleukin-6
LAD	: Left anterior descending
LCx	: Left circumflex
LDL	: Low density lipoprotein
LM	: Left main affection

List of Abbreviations (Cont.)

LV	: Left ventricular
MHC	: Major histocompatibility complex
MI	: Myocardial infarction
MSCT	: Multislice computed tomography
NO	: Nitric oxide
NSTEMI	: Non ST elevation myocardial infarction
PAI-1	: Plasminogen activator inhibitor-1
PCI	: Percutaneous coronary intervention
PPV	: Positive predictive value
RAO	: Right anterior oblique
RCA	: Right coronary artery
ROS	: Reactive oxygen species
SCEs	: Sister chromatid exchanges
SR	: Scavenger Receptor
SD	: Standard deviation
SPSS	: Statistical Program for Social Science
STEMI	: ST-elevation myocardial infarction
TB	: Tuberculosis
TXA ₂	: Thromboxane A ₂
UA	: Unstable angina
VCAM-1	: Vascular-cell adhesion molecule-1
VLDL	: Very low density lipoprotein
VSMCs	: Vascular smooth muscle cells
VWF	: von Willebrand factor
WHO	: The World Health Organization

List of Figures

Fig.	Title	Page
Review of Literature		
1	Khat (<i>Catha edulis</i>) plant.	5
2	The social khat session (Majlis Al-khat).	7
3	Chemical structure of the phenylpropylamine alkaloid from khat (<i>Catha edulis</i> Forsk)cathinone, norephedrine,norpseudoephedrine (cathine) compared with amine and noradrenaline.	9
4	Chemical structure of the phenylpentenylamine and catheduline alkaloids from khat (<i>Catha edulis</i> Forsk).	10
5	Activating effect of LDL infiltration on inflammation in the artery.	33
6	Role of macrophge in inflmmation of the artery.	35
7	Antithrombotic properties of healthy vascular endothelium.	38
8	Diagram of platelet, coagulation, and vessel-related mechanisms involved in platelet adhesion, activation and further aggregation.	40
9	Differentiation between MI types 1 and 2 according to the condition of the coronary arteries.	54
Results		
1	Comparison between the two groups according to the age.	72
2	Comparison between the two groups according to the gender.	72

Fig.	Title	Page
3	Comparison between groups as regard risk factor for CAD	74
4	Severity of khat chewing among the study group	75
5	Comparison between groups as regard mode of presentation to catheter Lab.	77
6	Comparison between groups as regard vital data	78
7	Comparison between groups as regard EF%.	79
8	Comparison between groups as regard Duke modified score	82
9	Comparison between both groups as regards angiographic intracoronary thrombi	85
10	Sensitivity and specificity Duke modified score in Discrimination of groups	91

List of Tables

Table	Title	Page
Review of Literature		
1	Braunwald Clinical Classification of UA/NSTEMI.	50
2	Criteria for diagnosis of acute myocardial infarction.	52
3	Elevation of cardiac troponin in myocardial injury in absence of overt heart disease.	58
Results		
1	Comparison between groups as regard to age and sex.	71
2	Comparison between groups as regard risk factor for CAD	73
3	Pattern of khat chewing	75
4	Severity of khat chewing among the study group	75
5	Comparison between both groups as regard reason for coronary angiography	76
6	Comparison between groups as regard vital data	78
7	Comparison between both groups as regard EF%	79
8	Comparison between groups as regarding C.A	81
9	Comparison between groups as regards Duke modified score	82
10	Correlation between EF% and other parameters, using Pearson Correlation Coefficient, in Khat chewing group	83
11	Correlation between Duke modified score,	84

Table	Title	Page
	no. of vessel affected and duration of khat chewing in hours /day, duration of khat chewing in days /week and duration of khat chewing in years	
12	Comparison between both groups regards to thrombus lesion	85
13	Multivariate analyses identifying the factors affecting EF% in khat chewing group	86
14	Multivariate analysis identifying the predictors of Three vessel disease (3VD) in the whole study population	87
15	Multivariate analysis identifying predictors of LM affection the whole study population	88
16	Multivariate analysis identifying the predictors of Duke Modified Score in the whole study population	89
17	Multivariate analysis identifying the predictors of the presence of angiographic intracoronary thrombi in the whole study population	90
18	Diagnostic Performance of Duke modified score in Discrimination of Khat chewing and non Khat chewing	91

Introduction

Fresh leaves from khat trees (*Catha edulis Celestrasae*) are chewed daily by over 20 million people in Yemen and East African countries.. Chewing khat (qat) is a popular social habit which has spread to Yemeni (**Griffiths., 1998**).

The main active substances in fresh khat leaves are cathinone, cathine and norephedrine. Cathinone, the chief active ingredient of khat, bears high structural and functional similarity to amphetamine (**Kalix., 1992**). Acting as an indirect sympathomimetic, it induces catecholamine release in central dopaminergic and serotonergic synapses, as well as from peripheral noradrenalin storage nerve endings. Centrally, cathinone causes hyperactivity, excitability, euphoria and restlessness (**Pehek et al., 1990**).

Cathinone increases blood pressure and heart rate through noradrenalin release from peripheral neurons similar to amphetamine (**Kalix, 1992**).

In each session (party), about 100–200 mg of khat is consumed by a person. Such an amount is equivalent to an oral dose of 5 mg of amphetamine (**Al-Motarreb et al., 2010**).

Catecholaminergic actions of amphetamines include inotropic and chronotropic effects on the heart, which can lead to arrhythmias, hypertension, and myocardial infarction (MI). Amphetamines produce feelings of euphoria, relieve

fatigue, improve performance on simple tasks, increase activity levels, and suppress the appetite. The abuse potential of amphetamines primarily stems from their euphorigenic effects. Prolonged use of amphetamines may lead to drug dependence and tolerance, in which case higher doses are required to achieve the desired effects. An acute overdose of an amphetamine may result in seizure, hypertension, tachycardia, hyperthermia, psychosis, hallucination, stroke, or death (*Derlet, 1989*).

Cathinone produces vasoconstriction of the coronary arteries (*Al-Motarreb et al., 2003*). These findings are strong evidence to support the clinical observation that khat can produce acute myocardial infarction through coronary spasm. Cathinone has minimal positive chronotropic activity. However, there was pronounced negative inotropy presumably due to impaired coronary perfusion.

Aim of The Study

The aim of study is to compare the effects of chronic khat use on the coronary artery diseases pattern in comparison to non khat users using coronary angiography.

Chapter 1

The History of Khat

Catha edulis, ordinarily known as khat, qat, visit or miraa, **C**(*Beckerleg, 2010*) is a bush or little to medium sized evergreen tree that has a place with the Celastraceae family. It develops as a shrub or little tree, principally in Yemen and East African Countries (*Zewdneh and Ephrem, 2014*).

The chewing of khat leaves is common in some countries of east Africa and the Arabian Peninsula. It has a depth-rooted social and cultural tradition in some Muslim, Somali and Yemeni societies. In some Muslim nations in which liquor is denied, khat is normally utilized as a part of social circumstances, in spite of the fact that it is regularly denounced on religious grounds (*Basker, 2013*).

The Khat plant is known by an a variety of names by the general population of the areas where it is originated from. All these names portray *Catha edulis* Forsk, the khat tree. In Yemen and Somalia, the expression "Qat" or 'Qaat and Jaad' is generally known. In Ethiopia, the term 'Talk or Jat' is normally perceived, while in Kenya it is known as "Miraa" or 'Murungi'. In any case, among these names the term khat is being the most mainstream name given to the plant and this shows up for the most part from the universal market and studies directed on this territory (*Apps et al., 2011; Andersson and Carrier, 2009; Favrod-Coune and Broers, 2010*).