Original Article

The habitual use of plant alkaloids and the prevalence of myocardial diseases.

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Summary:

Background: The plant (Khat) contains at least 40 types of alkaloids. It has an adrenergic like effect especially on the heart one of these alkaloid is cathedulins group which has molecular height of 600-1200mm.I/L. it is used frequently mainly at the African horn region (e.g. yemen). This plant alkaloids used by people in form of bands (each band is about 50gm, two bands 100gm and so on).
Patients and methods: Three groups of Patients have been included in this study. Group A: (30) patients with dilated cardiomyopathy, Group B: (50) patients with history of ischemic heart disease with clinical presentation of ischemic cardiomyopathy and Group C: (80) cases (50 cases of ischemic cardiomyopathy, 30 cases dilated cardiomyopathy). Used as control group to see the difference from stopping the Khat without adding any medication during the follow up peroid this was over a year with monthly checkup. The place of this was Yemen-Sannaa general hospital and Sannaa private international clinic.
Results: This study showed that the age range of patients and volunteers was similar, mean age (35-65 years), all were male because this plant is used by most of the males and there was difficulty in discussing this problem with the female these three groups were categorized into two groups according to the amounts of all khat bands consumed.
Group1: people using about 50gm of this plant and did comprise 75% of all the cases.
Group2: people using about 50-150gm of this plant and comprising 25% of all the cases.
This study did not show any significant correlation between the incidence of dilated cardiomyopathy and the chronic use of this plant alkaoild, also there was no correlation between the duration of using this alkaloid and probability of getting these cardiac disorders. Stopping consuming this alkaloid did not change the clinical feature dramatically except reduction of liver enzymes elevation.
Conclusion: No significant correlation between using the plant khat and development of ischemic and non ischemic dilated cardiomyopathy.
Keywords: Khat, Myocardial Disease.

Introduction:

The consumption of khat is a very common social habit (with happiness or unhappiness Yemen and parts of southeast Africa. The main active substance in that plant is the cathediulin which has adrenergic like effect leading to increased heart rate, increased blood pressure, increased activity, sweating, euphoria, followed by depression and not rarly ventricular arrhythmia. These changes could be detected in normal people and in patients with ischemic or dilated cardiomyopathy. It has been proved in literature that cardiomyopathy could be induced by direct toxic effect of different substances like alcohol, cytotoxic, catecholamine and allied substance-the effect of catecholamine could be by direct toxic effect, increased metabolic demand relative tissue hypoxia and increased oxidation products (free radicals) with more damaging effect. Also catecholamine's, enhances lipid metabolizem, because calcium overload, increase sarcolemmal permeability and induce vasospasm. From this explanation to the effect of catecholamines like substances, it is understood that this alkaloid is able to attack the myocardial cell directly through its effect on its intracellular function or through its vasospastic effect on the coronary circulation inducing more ischemia in both ischemic cardiomyopathy and dialted cardiomyopathy another problem which is facing most of the khat consumer is the economic problem as most of their finances go to buy it instead of buying foods rich in supplements like vitamins and minerals and the best example of this is thiamine deficiency which may enhance the development of dilated cardiomyoathy. Also it was reported in the literature that patients with dilated cardiomyopathy who were having endocrine disorders associated with release of adrenalin like substance improved after removing that cause by 3-6 months which mean some reversibility in their medical status.

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Patients and methods:

Three types of cases have been admitted in this study:
Group A→ (30) patients proved to be having dilated cardiomyopothy.
Group B→ (50) patient proved to be having ischemic cardiomyopathy by clinical history ECG and coronary angiography.
Group C→ (80) Cases (50 cases of ischemic cardiomyopathy, 30 cases dilated cardiomyopathy).

This group used a comparison group who stopped Khat consumption only without added medication.
All three groups went through the some protocol from history taking (i.e. shortness of breath, activity, chest pain, palpitation, oedema, chest X ray (size of heart, pleural effusion, pulmonary congestions) electrocardiography (New ECG, arrhythmia, heart block), echocardiography left ventricular wall thickness 2-13mm, end diastolic volume 35-56mm, ejection fraction 50-85% Dyskinesia or akinesia, left atrial size,19-40mm,(E/A12-2), blood tests (cardiac enzymes, B-sugar, urea, serum creatinen, complete blood picture, lipid profile, liver functions test). The drugs used by the patients were frusemide 40-80mg/daily ACE inhibitor 6.5-25mg/daily. Angiotension receptor blocker (ARB) (autcard 4-8mg/daily), glycerin trinitrate 0-5mg.s/l on need, isorbide dinatrate 10-40 mg/daily, α and β blocker carviadlol 3.½-25mg/daily, calcium channel blocker 60-120mg/daily, Digoxin 0.125mg-0.25mg/daily Dopamine & dobutamine 5-20microgram/Kg/h. all groups patient were during abuser of Khat for at least 10-15 years or more.

Results:
The numbers of cases admitted in this study were 120 cases distributed into three groups. Group A (30 cases) of dilated cardiomyopathy, (50 cases) of ischemic cardiomyopathy, (90 cases) as comparison group. Their ages range was between (35-65years). All of them are chronic consumers of khat for at least period of 10-15 years. The amount of khat consumed daily ranged between 50-150gm daily sixty five cases from the 160 cases (40.6%) were consuming about 50gm of khat daily the remaining 30 cases (25%) were consuming khat more than l00gm over a period about of 12 hrs daily.
The above groups were distributed according to the amount taken daily as show in table I.

Table I: Distribution of cases according to the amount consumed daily:

Type of cases	50gm	50-100gm	100-150gm
Dilated cardiomyopathy	20cases	5cases	5cases
Ischemic cardiomyopathy	25cases	10cases	15cases
Comparison group	10cases	50cases	20cases
Total	50cases	35cases	35cases

Patients groups were put into two categories according New York heart association classification as in table II

Table II: Distribution of the study patients according to / NYHA classification:

Type of cases	I-II classes	III-IV classes
Dilated cardiomyopathy	20	10
Ischemic cardiomyopathy	30	20
Comparison group	60	20
Total	110	50

This table showed that the majority of cases in both groups were in class I, II New York heart association classification. Drugs given to the patients before and after stopping the use of khat were nearly similar in both groups (A&B) as shown in table III.

Table III: effect of change of dos on measurement of cardiac parameters patients with dileted cardiomyopathy/ischemic cardiomyopathy:

	Protocol of drugs management	Signs & symptom	Ejection Fraction	End-diastolic volume
1st Month	Frusemide 20/daily ACE inhibitor 12.5mg/daily carvidalol 3.5mg/daily	shortness of breath leg oedema	28-39%	62.59mm
3rd month	Frusemide40mg /daily ACE inhibitor 25mg/daily carvidalol 6.5mg/daily	↓shortness of breath ↓leg oedema walking around two blocks	34-83%	55.11mm
6th month	Frusemide 80/daily ACE inhibitor 37.5mg/daily carvidalol 12.5mg/daily	Breathing is easy walking better and doing shopping	57-54%	54.49mm

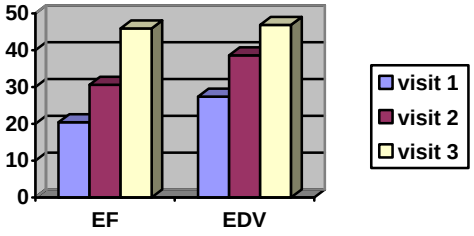
Regarding the control (comparison group) table IV showing the follow up with no clinical improvement as shown in table IV.

Table IV: The result of parameters in the assessment of comparison (control) group:

Parameter	1st month review	3rd month review	6th month review	After one year
Clinical feature	Shortness of breath Chest pain	No change	Increased Dyspnea III-IV NYHA classification	Same
ChestX-ray	Cardiomealy pulmonary plethora	Same	Same + 20% of cases have right pleural effusion	Same
Electrocardiography	Lowvoltage ECG ST↓ T↓ LBBB	Same	30% strain pattern at the left chest tests	Same
Echocardiography	EF 34.5% EDV58.24	EF 36.04 48.40	%35.61 58.32	P-value< 0.005 P-value> 0.005
Blood testes	SGOT↑ SGPT↑	Same	SGOT→ SGPT↑↑	Same

Table V, VI summarize the descriptive statistical analysis concerning both patient and control group. Analyzing these result it was found the within the control group there was significant difference between 1st and 2nd visit by measuring Ejection

fraction but there was No significant difference with the measurement of End-diastolic volume. Regarding the patient group (A, B) there was significant difference between Ejection and End-diastolic volume (EDV) all over the successive visits. Considering both patient (group A, B) and control (group C) for there was significant difference between Ejection Fraction & End-diastolic volume but there is not such difference at the 2nd visit. Regarding Ejection fraction while EDV is significantly different. This also to the 6th month visit. Figer.1 demonstrable theses result.



Figer1: patient group-comparison between first, second and third visits

Table V: the results of parameters in assessment of dilated cardiomyopathy patients.

Type	Visit		EF	EDV
Control	1.00	Mean	34.05	58.2400
		N	22	25
		Std. Deviation	3.031	3.07246
	2.00	Mean	36.04	58.4074
		N	27	27
		Std. Deviation	2.103	3.58693
	Total	Mean	35.14	58.3269
		N	49	52
		Std. Deviation	2.723	3.31793
Patient	1.00	Mean	28.39	62.5926
		N	28	27
		Std. Deviation	3.348	3.62957
	2.00	Mean	34.83	55.1111
		N	23	27
		Std. Deviation	2.980	2.29269
	3.00	Mean	57.54	47.3636
		N	28	33
		Std. Deviation	6449	6.61352
	Total	Mean	40.59	54.4943
		N	79	87
		Std. Deviation	13.677	7.87825

Table VI: the results of parameters in assessment of ischemic cardiomyopathy:

Dependent Variable	(I) Visit	(J) Visit	Mean Deference (I-J)	Std. Error
EF	1.00	2.00	6.433	1.300
		3.00	29.143	1.234
	2.00	1.00	6.433	1.300
		3.00	22.710	1.300
	3.00	1.00	29.143	1.234
		2.00	22.710	1.300
EDV	1.00	2.00	7.48148	1.28717
		3.00	15.22896	1.22727
	2.00	1.00	7.48148	1.28717
		3.00	7.74747	1.22727
	3.00	1.00	15.22869	1.22727
		2.00	7.74747	1.22727

Discussion:

Reviewing the follow up of the two types of patients in this study (dilated and ischemic cardiomyopathy) over a period of a year did not show any real improvement on group C patients who stopped consuming Khat only without added medical treatment. However there was clinical improvement in patient GA&B who were having increases their medical treatment anin table VII, IV. As reported in literature that adrenergic like effect drug cardiomyopathy but this study showed that the result of consumption of khat (cathedulin alkaloid) is not the only factor in the development of dilated cardiomyopathy. This his been supported by two things first thing is that many people were addict to khat alkaloid but wherever having dilated or ischemic cardiomyopathy but some of them showed elevated liver enzymes which returned back to the normal levels after stopping the consumption of khat [1,2]. The second thing is that some chronic consumer of this plant alkaloid had ischemic heart disese [3] but not dilated cardiomyopathy or the other way around [4, 5] which means clearly that khat was not the primary cause in having ischemic or dilated cardiomyopathy. it has been found that some cases of dilated cardiomyopathy were reversible after removing the cause of its, development like (catecholamine induced cardiomyopathy) over period of about 6 months but in the group A (khat alkaloids consumers) never returned back to normal after stopping consuming khat even after a period of more than one year [6].This mean that there are other documented causes of dilated cardiomyopathy like viral infection, connective tissue disorders, nutritional causes (deficiency & alcholism) which can precipitate abnormal metabolic process, also certain endocrine disorders with high catecholamine like effect (Thyrotoxicosis , pheochromocytoma) all these examples may be associated with other factor which could predispose to the development of cardiomyopathy as gentic factor leading to DNA mutation or alteration in immune system function [7,8]. To analyse the khat catecholamine-like effect followed by development of dilated cardiomyopathy in order to make comparison between its effect and other medical catacholomices associated disorders it was found that there must be a certain toxic effect level (concentration) to induce direct toxic damage Also the metablic demand in myocardial cell in khat consumers did not reach the stage in which there was abnormal tissue hypoxia which can lead to abnormal lipid metabolizem and transcellular shift of calcium or decreased concentration of phosphate at the myocardial membrane which may lead to increased permeability [9] increased. Catacholamine level in blood may lead to sever vasospasm associated with abnormal myocardial cell function [1,2] .but it looks that in patients of khat consumers did not have a concentration level of catecholamine like Substances to lead to this pathological process [4]. Some international studies of dilated cardiomyopthy confirmed the presence of increased

level of (G protein) [4] (the contractile apparatus of myocardial cells) in the form of increased α subunit of the inhibitory guanine-Nucleotide binding protein at myocardial cell membrane (in dilated cardimyopathy) leading to reduction of basal adenylate cyclase which is important in the in inotropic effect of myocardial cell with less response to adrenergic like drug [6, 9, 10].

Conclusion:

This study did not show any correlation between khat consumption & dilated and development of myocardial disorders.

This study showed that there may be more then one single cause to have cardiac disease, people in some parts of the world expence their money on buying khat rather than buying good elements of food. Leading to deficiency of essential nutritional element which could be primary or seconding factor to have cardiac disorder process.

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