

Khat Chewing among Male Patients with Acute Cerebral Infarction in Hadhramout

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Abstract:

Background and Objectives: The habit of Khat (*Catha edulis*) chewing for its amphetamine-like effects is highly prevalent in Yemen and East Africa, and expanded to USA and Europe. The aim of this study is to determine the frequency of khat chewing among male patients with acute cerebral infarction (ACI) and its effects.

Materials and Methods: A retrospective cohort hospital-based study. Medical record files of all male patients admitted in Ibn-seena General Hospital in the period 2011-2015, with the diagnosis of ACI to estimate the frequency of khat chewing among them and its effects.

Results: Male patients with ACI were 774 patients and with hemorrhagic stroke (HS) were 194 patients. Chewing khat among ACI patients was significantly higher than HS (OR 1.78, 95% CI 1.24-2.57, $p = 0.0017$). Khat chewers were significantly younger than non-chewers (59.1 ± 11.8 and 68.9 ± 15.3 , respectively, $p = 0.001$). Hypertension was significantly higher among chewers than non-chewers (OR 1.44, 95% CI 1.07-1.94, $p = 0.016$). Smoking was higher among chewing patients, while diabetes was higher in non-chewing patients but both were not significant. Insignificant differences between chewers and non-chewers regarding to previous stroke attacks, transient ischemic attacks, and atrial fibrillation. Clinical presentation of stroke, as well as in-hospital mortality did not show any statistical significance between chewer and non-chewer male stroke patients.

Conclusion: Chewing khat was a risk factor for ACI more than HS. ACI attacks khat chewing victims in a younger age Hypertension was associated with khat chewing more than with non-chewers. No difference in clinical presentation and in-hospital mortality between chewing and non-chewing patients.

Keywords: Khat chewing, Stroke, Cerebral infarction, Hadhramout, Yemen.

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مضغ القات بين المرضى بالإحتشاء الدماغى الحاد الذكور في حضرموت

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الخلفية والأهداف: تنتشر كثيرا عادة مضغ القات في اليمن وشرق افريقيا، نظرا لتأثير المشابه لمادة الأمفيتامين، وامتدت هذه العادة الى الولايات المتحدة الأمريكية و أوروبا. الهدف من هذه الدراسة هو تحديد نسبة متعاطي القات بين المرضى الذكور بالإحتشاء الدماغى الحاد وتأثيره.

المنهجية: دراسة استرجاعية ، حيث تم تجميع المعلومات من الملفات الطبية للمرضى الذكور في مستشفى ابن سينا العام خلال الفترة بين 2011-2015، والذين تم تشخيصهم بالاحتشاء الدماغى الحاد.

النتائج: كان المرضى الذكور المصابين بالإحتشاء الدماغى الحاد 774، بينما المصابين بالنزيف الدماغى 194 مريض، و مضغ القات بين المصابين بالإحتشاء الدماغى الحاد كان أعلى و ذا دلالة إحصائية عنه بين المصابين بالنزيف الدماغى ($p = 0.0017$). و بدلالة إحصائية كان سن ماضغي القات اقل من غير الماضغين (59.1 ± 11.8 و 68.9 ± 15.3 عاما على الترتيب $p = 0.0017$). ارتفاع ضغط الدم كان أعلى بدلالة إحصائية عند متعاطي القات عن غير المتعاطين ($p = 0.016$). التدخين كان أعلى وداء السكري كان اقل نسبة عند المتعاطين و لكن بدون اهمية إحصائية. لا يوجد فروقا بين المجموعتين في الإصابة السابقة بالمرض والرجفان الأذيني والنوبة الإفقارية العابرة. العرض المرضى والوفيات داخل المستشفى لم يوجد اي اهمية إحصائية بين متعاطي القات عن المتعاطين

الاستنتاج: مضغ القات كان عامل خطورة عند مرضى الإحتشاء الدماغى الحاد عنه عند مرضى النزيف الدماغى. الإحتشاء الدماغى الحاد عند الذكور يصيب الضحية في سن اقل عند متعاطي القات عن غير المتعاطين. ارتفاع ضغط الدم اكثر ارتباطا عند المتعاطين عن غير المتعاطين. لا فروق بين المجموعتين في العرض المرضى و لا نسبة الوفيات.

الكلمات المفتاحية: مضغ القات، الصدمة الدماغية، الإحتشاء الدماغى، حضرموت، اليمن

Introduction:

Khat (*Catha Edulis*) is an evergreen tree or large shrub. Users chew this stimulant habitually for its euphoric effect and as a recreational drug that also improve performance.^[1-3] Cathinone and cathine are the main ingredients of the plant. These compounds are structurally related to amphetamine, noradrenaline and ecstasy.^[4,5] The sympathomimetic and central nervous system stimulating effect produced by khat chewing are mainly due to cathinone.^[6]

The mucosa of the oral cavity is considered to be the first absorption segment, thus the pharmacokinetics of the khat alkaloid in humans explains why chewing is the preferred form of khat ingestion.^[6]

Khat grows and is widely used in the region extending from Eastern to Southern Africa, as well as on the Arabian Peninsula, mainly in Ethiopia, Somalia, Yemen, Kenya, Malawi, Uganda, Tanzania, the Congo, Zambia, Zimbabwe, Madagascar and South Africa.^[7,8] In these countries, social parties have a long history as a part of formal social customs, for example, to encourage discussion of community issues.^[2] A khat quantity of 100-200 grams is usually consumed in each session,^[9] which is equivalent to an oral dose of 5 mg of amphetamine.^[10]

Khat chewing is currently legal in United Kingdom, however cathinone and cathine are controlled drugs, but, it is illegal in United States as well as in Canada, Norway and Sweden, it is more prevalent among immigrants from Somalia, Ethiopia and Yemen.^[11]

The growing research evidence shows that different cardio-vascular disorders such as hypertension, ischemic heart diseases and stroke, were associated to khat chewing.^[12,13] Although, Yemen is one of the countries in which khat chewing is a common social habit, in Hadhramout it was forbidden, until 1990, and there was no published study from Hadhramout about it, this study was conducted to report the association between Khat and acute cerebral infarction (ACI) among males in Hadhramout.

Material and Methods:

This was a retrospective hospital-based cohort study of male patients with ACI admitted at Ibn-seena General Hospital (ISGH), Mukalla, Hadhramout, Republic of Yemen during the period between January 1st. 2011 and December 31st. 2015. The hospital is a tertiary referral and is the biggest hospital in Hadhramout Province in which medical and health institute students get their training and it serves about

3,000,000 inhabitants. Data were collected from patients' medical records based on the World Health Organization (WHO) stepwise approach to stroke surveillance (STEPS-stroke) protocol,^[14] involving age, sex, risk factors, khat chewing, clinical presentation, and in-hospital mortality.

Stroke was diagnosed according to World health Organization (WHO),^[15] ACI and hemorrhagic stroke (HS) were diagnosed based on CT neuro-imaging.

Chewing khat at least once weekly regularly was considered as khat chewer, occasional chewers were not considered.

Statistical Analysis:

Data were processed by the Statistical Package for Social Sciences (SPSS) software version 20.0 (IBM Corporation, Armonk, NY, USA). The paired "t" test was applied to compare mean age and Pearson's chi-square test to compare risk factors and clinical presentation. We estimated odds ratio (OR) and the resulting confidence interval (95% CI) for risk factors. All statistical hypothesis tests were 2-sided, and *p* values <0.05 were considered statistically significant.

Results:

Male stroke patients documented in ISGH patients' medical record files between 2011 and 2015 were 968 patients, from them, 774 (80%) diagnosed as ACI and 194 patients (20%), as HS. Khat chewers among Male ACI patients were 271/774 (35%) and significantly higher than male HS patients; 45/194 (22.1%), (OR 1.78, 95%CI 1.24-2.57, *p* = 0.0017) (Table 1).

Patients chewing khat were significantly younger than those who were not (59.1 ± 11.8 and 68.9 ± 15.3 , respectively, *p* = 0.001). Hypertension was significantly higher among chewers than non-chewers within CI male patients (OR 1.44, 95% CI 1.07-1.94, *p* = 0.016). Smoking was high among chewers comparing to non-chewers, with no significance (OR 1.15, 95% CI 0.79-1.69, *p* = 0.49). Diabetes was less among chewing patients than non-chewers with no significance (OR 0.75, 95% CI 0.56-1.01, *p* = 0.056). There were insignificant differences between chewing and non-chewing patients regarding to previous stroke attacks, transient ischemic attacks and atrial fibrillation (Table 2).

Clinical presentation of stroke, including headache, vomiting, motor deficit, dysphasia, and impaired consciousness, as well as in-hospital mortality did not show any statistical significance between chewers and non-chewers (Table 3).

Discussion:

To our knowledge, there are no published studies compared khat chewing between CI and HS, this work revealed that the frequency of khat chewers among CI male patients was significantly higher than in those with HS.

Cathinone action on CNS includes catecholamine release from postsynaptic storage, and leads to tachycardia, vasoconstriction, and increase in blood pressure, respiratory rate, and body temperature. Catecholamines also induce platelet aggregation and increase the risk of cardio-vascular events including stroke.^[16] Miranda and O'Neill reported stroke-like complications following amphetamine abuse.^[17] Since khat is similar to amphetamine, complications arising due to abuse can be assumed to be similar.

Three case of stroke were reported to be complications of long-term of khat chewing. Vanwalleghe et al,^[18] in Belgium, presented a 41-year-old male of Somalian origin, who had chewed khat regularly since the age of 30 and continued this habit after moving to Belgium, he developed stroke 2 hours after khat chewing. Kulkarni et al,^[19] in Yemen, reported a 47-year-old who was a regular khat chewer for 30 years. Meulman et al,^[20] in Netherland, it was documented a 33-year-old Somalian man with a 10-year history of khat chewing. All the three cases had no any other risk factors for atherosclerosis or hypercoagulability.

In Yemen, A case-control study by Mujilli et al,^[21] showed the link between khat chewing and CI. Furthermore, a Gulf group studied the association of khat chewing and the risk of stroke by using a multinational prospective design of hospitalized acute coronary syndrome (ACS) patients from 6 adjacent countries including Yemen, and found that khat chewers were more likely to develop post-ACS.^[22]

This work showed that the male CI patients who were khat chewers were younger than those who were not. Although a the case-control in Sanaa, Yemen,^[21] reported the opposite, this contradiction can be explained that khat chewing is a habit in Sanaa and surrounding area for hundreds of years, while it was illegal in Hadhramout until 1990, and the elderly had not accepted this habit in Hadhramout. However, ages of the aforementioned cases supported our finding.^[18-20]

Hypertension remains a common risk factors for stroke, it more frequent among HS than CI patients,^[23-26] other studies showed the opposite.^[27,28] Furthermore, we found that the frequency of hyper-

tensive patients among khat chewers was higher than non-chewers, which was agreed by other studies.^[12,21,29-31] Khat chewing may lead to a cathinone-induced hypertensive encephalopathy 'khatatonia', a 45-year-old Somalian man with a background of hypertension and chronic kidney disease, was presented by Bede et al, in Ireland, as a case of khatatonia.^[32]

The sympathomimetic effect of cathinone is considered.^[6] In a pharmacokinetic study, diastolic and systolic blood pressures were elevated for about 3 hours after chewing.^[33] The rise of blood pressure started before the rise of alkaloid plasma concentrations. The dose used was about 0.6 g/kg of a traditional khat session dose and chewing was for 1 hour. In another study, diastolic and systolic blood pressure, mean arterial blood pressure, and heart rate were raised during the 3 hours of khat chewing and during the following hour.^[34]

Discussion:

We reported that, younger age, hypertension and smoking were more frequent among HS than IS patients, while older age, diabetes, AF and TIA were more related to IS than HS. Sex and alcohol intake did not favor either stroke type. Impaired consciousness including coma and in-hospital mortality were more among HS than in IS victims.

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Conflicts of interest and disclosure

The authors had no conflicts of interest to disclose.

Table 1: Comparison of khat chewing between stroke types.

	ACI (n=774)		HS (n=194)		OR (95% CI)	p value
	n	%	n	%		
Khat chewing						
Yes	271	35	45	22.1	1.78 (1.24-2.57)	0.0017*
No	503	65	149	77.9		

ACI: Acute cerebral infarction, HS: Hemorrhagic stroke. OR: Odds ratio, CI: Confidence interval.

*Statistically significant.

Table 2: Characteristics and risk factors distribution of ACI patients according to khat chewing.

	Chewers [n(%)]	Non-chewers [n (%)]	OR (95% CI)	Pvalue
Age, years, mean±SD	59.1±11.8	68.9±15.3	-----	<0.001*
Hypertension	157 (57.9)	246 (48.8)	1.44 (1.07-1.94)	0.016**
Diabetes mellitus	111 (41)	242 (48.1)	0.75 (0.56-1.01)	0.056**
Smoking	52 (19.2%)	86 (17.1)	1.15 (0.79-1.69)	0.49**
Previous strokes	25 (9.2)	36 (7.2)	1.32 (0.77-2.25)	0.31**
TIA	57 (21)	87 (17.3)	1.27 (0.88-1.85)	0.20**
Atrial fibrillation	24 (8.9)	43 (8.5)	1.04 (0.62-1.75)	0.88**

Table 3: Characteristics and risk factors distribution of ACI patients according to khat chewing.

	Khat chewers [n (%)]	Khat non-chewers [n (%)]	Pvalue*
Headache	65 (24)	96 (19.1)	0.11
Vomiting	40 (14.8)	79 (15.7)	0.73
Motor deficit	264 (97.4)	491 (97.6)	0.87
Dysphasia	69 (25.5)	121 (24.1)	0.66
Impaired consciousness	97 (35.8)	156 (31)	0.18
In-hospital mortality	68 (25.1)	137 (27.2)	0.52

* Statistically significant when p <0.05.

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