

THE SUBJECTIVE EFFECTS OF CHEWING QAT LEAVES IN HUMAN VOLUNTEERS

Nageeb A.G.M. Hassan, MBBS, PhD; Abdallah A. Gunaid, MBBS, MD;
Fouad M.Y. El Khally, MBBS, PhD; Iain M. Murray-Lyon, MBBS, MD, FRCP

Background: Chewing the leaves of the Qat plant (*Catha edulis*) for their pleasurable central stimulant effect is a habit that is widespread in Yemen and certain areas of East Africa. The use of the Qat leaves is believed to cause a variety of gastrointestinal and genito-urinary symptoms as well as sleep disturbance. We studied the subjective effects of chewing Qat leaves in human volunteers.

Subjects and Methods: This prospective study included 1600 healthy adult male subjects who chewed Qat, and a similar number of 1600 subjects who never chewed Qat serving as control. Subjects in the Qat group chewed Qat for at least four hours daily for three successive days before answering a questionnaire.

Results: The study revealed that the prevalence of gastrointestinal (GI) symptoms (epigastric bloating, belching and abdominal distension) and genito-urinary symptoms (weak stream of micturition, post-chewing urethral discharge) were significantly higher ($P < 0.0001$) among Qat-chewing subjects than controls. Similarly, central nervous system (CNS) symptoms such as anorexia, insomnia (delayed bedtime), late wake-up the next morning and low work performance the next day, were significantly higher in Qat chewers ($P < 0.0001$). Stepwise multivariate logistic regression analysis revealed that GI symptoms which were significant in univariate analysis were no longer significant, whereas CNS and genito-urinary symptoms remained significant ($P < 0.0001$).

Conclusion: This study confirms that Qat chewing induces anorexia, weak stream of micturition, post-chewing urethral discharge and insomnia (delayed bedtime), which result in late wake-up next morning and low work performance the next day. These effects are believed to be caused by the central and peripheral actions of cathinone and cathine in the Qat leaves.

Ann Saudi Med 2002;21(1-2):34-37.

Key Words: Qat, *Catha edulis*, cathinone, cathine.

The Qat plant (*Catha edulis*) is cultivated in the Republic of Yemen and certain areas of East Africa. Its leaves are widely chewed, especially among men, for their central nervous system-stimulating properties.¹ In the Yemen, the habit of Qat chewing is widespread as a deep-rooted socio-cultural tradition. Since fresh leaves possess the desired stimulant effect, their use previously remained virtually unknown beyond the areas of plantation.² However, in recent years, the advent of air transport has facilitated the distribution of fresh Qat to many places including European capitals.³

Qat leaves contain a variety of substances, including phenylalkylamine compounds (alkaloids), such as nor-

pseudoephedrine (cathine) and alpha-aminopropiophenone (cathinone).² They are responsible for the stimulating effects, with the latter alkaloid being more potent than the former one.⁴ The popularity of Qat chewing derives from stimulation of the central nervous system by cathinone, which is structurally and functionally closely similar to amphetamine. There are also peripheral actions of a sympathomimetic type. Both central and peripheral actions resemble those of amphetamine,⁴ with differences being quantitative rather than qualitative.⁵ Qat leaves also contain considerable amounts of tannins (7% - 14% in dried material) and flavonoids.¹⁻⁶ Genito-urinary symptoms may be attributable to the sympathomimetic effect of cathinone on smooth muscle.⁶ Gastrointestinal symptoms may be related to the astringent properties of Qat tannins,⁷ and/or the sympathomimetic effect of cathinone.⁶

This study was carried out because physicians had observed that Qat chewing was associated with complaints related to the gastrointestinal and genito-urinary systems, as well as sleep disturbance among a substantial number of individuals in Yemeni society. The aim was, therefore, to explore subjective symptoms related to chewing Qat leaves among healthy adult Yemeni males.

From the Departments of Pharmacology and Therapeutics (Dr. Hassan), Internal Medicine (Dr. Gunaid), and Physiology (Dr. El-Khally), Faculty of Medicine and Health Sciences, University of Sana'a, Sana'a, Republic of Yemen, and the Department of Gastroenterology (Dr. Murray-Lyon), Chelsea and Westminster Hospital, London, U.K.

Address reprint requests and correspondence to Dr. Hassan: Department of Pharmacology and Therapeutics, Faculty of Medicine and Health Sciences, University of Sana'a, PO Box 14315 (MAAIN), Sana'a, Republic of Yemen.

Accepted for publication 21 January 2002. Received 23 August 2001.

TABLE 1. Univariate analysis of gastrointestinal, genito-urinary and central nervous system symptoms in Qat chewers and non-Qat chewers.

Symptoms	Qat chewers n=1600 (%)	Control subjects n=1600 (%)	Odds ratio (95% CI)	Chi-square value	P-value
Gastrointestinal symptoms					
Epigastric bloating	592 (37.0)	130 (8.1)	6.64 (5.40, 8.16)	381.8	<0.0001
Epigastric belching	310 (19.4)	64 (4.0)	5.77 (4.36, 7.62)	183.2	<0.0001
Abdominal distension	581 (36.3)	79 (4.9)	10.98 (8.57, 14.07)	481.0	<0.0001
Genito-urinary symptoms					
Weak stream of micturition	359 (22.4)	57 (3.6)	7.83 (5.86, 10.46)	252.0	<0.0001
Post-chewing urethra discharge	680 (42.5)	15 (0.9)	78.10 (46.52, 131.11)	812.8	<0.0001
Central nervous system symptoms					
Poor appetite (anorexia)	906 (56.6)	36 (2.3)	56.72 (40.17, 80.07)	1138.7	<0.0001
Insomnia (delayed bedtime)	1265 (79.1)	404 (25.3)	11.18 (9.48, 13.18)	928.4	<0.0001
Late wake-up next morning	896 (56.0)	41 (2.6)	48.39 (34.95, 67.01)	1103.2	<0.0001
Low work performance next day	843 (52.7)	33 (2.1)	52.88 (36.95, 75.68)	1031.3	<0.0001

TABLE 2. Stepwise multivariate logistic regression analysis of subjective symptoms of central nervous system and genito-urinary system related to Qat chewers as compared to non-Qat chewers.

Symptoms	Odds ratio (OR)	95%CI	P-value
Central nervous system symptoms			
Poor appetite (anorexia)	51.77	30.93 to 86.67	<0.0001
Insomnia (delayed bedtime)	2.32	1.75 to 3.10	<0.0001
Late wake-up time next morning	10.24	6.76 to 15.5	<0.0001
Low work performance next day	10.06	6.42 to 15.77	<0.0001
Genito-urinary symptoms			
Weak stream of micturition	2.37	1.41 to 3.98	<0.001
Post-chewing urethral discharge	43.83	24.74 to 77.64	<0.0001

Subjects and Methods

A total of 1600 healthy adult male subjects aged 20-32 years were recruited as Qat subjects, while a similar number aged 19-33 years were recruited as control subjects over a three-year period. Both groups were from the same environment except that one group chewed Qat and the other group did not. The Qat chewers attended Qat chewing sessions at the same time on three successive days. They were not regular Qat chewers. All subjects denied any history of pre-existing disease of the central nervous system (CNS), gastrointestinal tract or genito-urinary tract. None was taking any drugs during the study period. All volunteers were told not to take tea, coffee or soft drinks containing caffeine during the study, and were also told to avoid smoking. The participants were informed about the study and each gave informed consent. Ethical clearance was also obtained. They were subjected to clinical assessment, including height and weight measurement and the body mass index (BMI: kg/m²) was calculated.

During the Qat-chewing session, each participant chewed a fresh bundle of the same type of Qat leaves for at least four hours on each of the three study days, and then spat out the leaves. The control subjects spent the same time in the same environment.

Subjects were asked to fill in a questionnaire at the end of the third Qat-chewing session inquiring about: 1)

appetite (poor or normal); 2) epigastric symptoms such as bloating, belching (yes or no); 3) abdominal distension (yes or no); 4) stream of micturition (weak or easy), urethral discharge (yes or no); 5) sleep pattern (delayed or normal); 6) waking-up next morning (late or normal); and 7) work performance next day (low or normal). The same procedure was followed for the control subjects.

Statistical Analysis

Statistical analysis of data was performed using the Statistical Package for Social Sciences (SPSS software package). Results were analyzed using Student's (unpaired) *t*-test of significance for continuous variables and Pearson's chi-square for categorical data (comparing proportions). Odds ratio (OR) with 95% confidence interval (CI) was calculated from 2x2 tables to assess the degree of association. Significance was taken as less than 0.05. Stepwise multivariate logistic regression analysis was computed using the SPSS package.

Results

The mean age (mean±SEM) (26±0.34 vs. 25±0.30) and BMI (20.3±0.41 vs. 21.2±0.36) for the Qat chewers and controls were comparable (*P*>0.05). Univariate analysis of symptoms induced by Qat chewing as compared to controls is shown in Table 1. The gastrointestinal symptoms were

significantly higher among Qat-chewers as compared to the control. They included epigastric bloating (OR=6.64; 95% CI: 5.40 to 8.16; χ^2 : $P<0.0001$), belching (OR=5.77; 95% CI: 4.36 to 7.62; χ^2 : $P<0.0001$), and abdominal distension (OR=10.98; 95% CI: 8.57 to 14.07; χ^2 : $P<0.0001$).

Similarly, genito-urinary symptoms were significantly higher among Qat chewers than the controls. They included weak stream of micturition (OR=7.83; 95% CI: 5.86 to 10.46; χ^2 : $P<0.0001$) and post-chewing urethral discharge (OR=78.10; 95% CI: 46.52 to 131.11; χ^2 : $P<0.0001$). Qat-induced central nervous system manifestations were the most prominent symptoms and were highly significant as compared to the controls. They included same-day dinner-time anorexia (OR=56.72; 95% CI: 40.17 to 80.07; χ^2 : $P<0.0001$); same-day insomnia (delayed bedtime) (OR=11.18; 95% CI: 9.48 to 13.18; χ^2 : $P<0.0001$); late wake-up next morning (OR=48.39; 95% CI: 34.39 to 67.01; χ^2 : $P<0.0001$); and low work performance next day (OR=52.88; 95% CI: 36.95 to 75.68; χ^2 : $P<0.0001$).

Stepwise multivariate logistic regression analysis was also conducted to rank the Qat-induced subjective symptoms in the order of their power to discriminate (Table 2). This analysis was computed using the SPSS software statistical package in two steps; the first included stepwise discriminate analysis, and the second included the stepwise logistic regression. Epigastric bloating, belching and abdominal distension which were statistically significant in univariate analysis were no longer statistically significant, whereas CNS symptoms anorexia, delayed bedtime (insomnia), late wake-up the next morning, low work performance the next day and genito-urinary symptoms (post-chewing urethral discharge, weak stream of micturition) remained highly significant.

Same-day dinner-time anorexia was the strongest Qat-induced symptom (exposure coefficient =51.77; 95% CI: 30.93 to 86.67), followed by post-chewing urethral discharge (exposure coefficient =43.83; 95% CI: 24.74 to 77.64); late wake-up time next morning (exposure coefficient =10.24; 95% CI: 6.76 to 15.51); low work performance next day (exposure coefficient =10.06; 95% CI: 6.42 to 15.77); same-day delayed bedtime form of insomnia (exposure coefficient =2.32; 95% CI: 1.75 to 3.10); and ultimately weak stream of micturition (exposure coefficient = 2.37; 95% CI: 1.41 to 3.98).

Discussion

In this study, we have shown that chewing Qat for three days was associated with significant CNS and genitourinary symptoms, such as anorexia, delayed bedtime insomnia which results in late wake-up next morning and low work performance next day, as well as weak stream of micturition and post-chewing urethral discharge. However, gastrointestinal symptoms were mild.

It seems likely that these effects resulted from one or more of the chemical constituents of the Qat leaves, which

are known to contain a variety of alkaloids including cathinone and cathine, flavonoids, tannins, aminoacids, essential oils and vitamin C.⁷ The sympathomimetic effects of Qat consumption are thought to be due to the concurrent action of cathinone and cathine, whereas its central nervous system effects are almost entirely due to cathinone.⁴

Cathinone is a biosynthetic precursor that accumulates in young leaves, and is absorbed rapidly by the buccal mucosa and after swallowing the juice of the leaves.^{4,7} In adult Qat leaves, it undergoes enzymatic reduction to the less active compounds, cathine and norephedrine. Cathine undergoes little buccal absorption and is taken up rather slowly from the gastrointestinal tract.⁴ Cathinone and cathine exert their amphetamine-like actions by the release of catecholamines from pre-synaptic storage sites.²

Failure to retain the statistical significance of gastrointestinal symptoms in multivariate model may suggest that the acute effects of Qat on gastrointestinal tract were comparatively less than on the CNS and genito-urinary systems. Marked loss of appetite (anorexia) after Qat chewing in our study may be attributed to a combination of a central amphetamine-like effect and delay in gastric emptying.^{6,8} Insomnia with delayed bedtime is believed to be due to central release of noradrenergic neurotransmitters by cathinone,⁸ and results in late wake-up and low performance the next day.⁹

The weak stream of micturition among Qat chewers has been attributed to a sympathomimetic effect on α -adrenoceptors, which are predominant in the bladder neck and proximal urethra.¹⁰ Post-chewing urethral discharge induced among Qat chewers has been described previously and the mechanism operating is not yet understood.^{1,11} Other Qat-induced sexual manifestations including increased libido, spermatorrhea and erectile dysfunction have been also described.^{1,8,11,12}

This study has shown that Qat consumption has many adverse effects, particularly on the CNS which, given the widespread use of Qat in Yemen, may have a serious impact on the productivity of labor in the country. The adverse effects on micturition may be particularly troublesome in elderly patients with prostatic hypertrophy. We have shown elsewhere that Qat chewing raises blood pressure,¹³ and may be linked to gastrointestinal cancer.¹⁴ These adverse biosocial effects lend support to those who call for limitations to be placed on Qat consumption.

Acknowledgements

We are very grateful to all participants involved in this study and to Mr. Mohamed Al-Qubati for his statistical assistance.

References

1. Luqman W, Danowski T. The use of khat (*Catha edulis*) in Yemen. Social and medical observations Ann Intern Med 1976;85: 246-9.
2. Kalix P. Cathinone: a natural amphetamine. Pharmacol Toxicol 1992;70:77-86.

3. Yousef G, Hug Z, Lambert T. Khat chewing as a cause of psychosis. *Br J Hosp Med* 1995;54:322-6.
4. Kalix P. Pharmacological properties of the stimulant khat. *Pharmacol Ther* 1990;48:397-416.
5. Eddy N, Halbach H, Isbell H, Seevers M. Drug dependence: its significance and characteristics. *Bull WHO* 1965;32:721-33.
6. Heymann TD, Bhupulan A, Zureikat NEK, Bomanj J, Drinkwater C, Giles P, Murray-Lyon IM. Khat chewing delays gastric emptying of a semi-solid meal. *Aliment Pharmacol Ther* 1995;9:81-3.
7. Kalix P, Braeden O. Pharmacological aspects of the chewing of khat leaves. *Pharmacol Rev* 1985;37:149-64.
8. Halbach H. Medical aspects of the chewing of khat leaves. *Bull WHO* 1972;47:21-9.
9. Giannini AJ, Burge H, Shaheen JM, Price WA. Khat: another drug of abuse? *J Psychoactive Drugs* 1986;18:155-8.
10. Nasher AA, Qirbi AA, Ghafoor MA, Catterall A, Thompson A, Ramsay JWA, Murray-Lyon IM. Khat chewing and neck bladder dysfunction.: a randomised controlled trial of α_1 adrenergic blockade. *Br J Urol* 1995;75:597-8.
11. Le Bars M, Fretillere Y. Les aspects medicaux de la consommation habituelle du cath. *Med Trop* 1965;25:720-32.
12. Elmi A. The chewing of khat in Somalia. *J Ethnopharmacol* 1983;8: 163-76.
13. Hassan NAGM, Gunaid AA, Abdo-Rabbo AA, Abdel-Kader ZY, Al-Mansoob MAK, Awad AY, Murray-Lyon IM. The effect of Qat chewing on blood pressure and heart rate in healthy volunteers. *Trop Doct* 2000;30:107-8.
14. Gunaid AA, Sumairi AA, Shidrawi RG, Al-Hanaki A, Al-Haimi M, Al-Absi S, et al. Oesophageal and gastric carcinoma in the Republic of Yemen. *Br J Cancer* 1995;71:409-10.