Khat Chewing Induce Transient Elevation of Blood Pressure: By Using 24-Hour Ambulatory Blood Pressure Monitoring, in Yemen Republic

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Abstract

Background: Khat or *Catha edulis* is an indigenous plant in Yemen, Ethiopia and East Africa, which has sympathomimetic and euphoriant effects. It is chewed habitually by people for its pleasurable effect and it produces stimulant amphetamine-like effects. **Aims:** The main aim is to study the effects of khat chewing on blood pressure and heart rate by using ambulatory blood pressure monitoring (ABPM). **Methods:** This was a cross-sectional, observational study in a group of 255 individuals aged 18 - 70 who visited our cardiac center from May 1, 2021, to January 1, 2023, chewing or non-chewing khat, All individuals underwent 24 hours of ambulatory blood pressure monitoring. **Result:** 255 adults are included, 70.6% of whom were khat chewers and 29.4% of whom were non-chewers. The two groups were comparable in most characteristics, and there were no significant differences between the two groups in terms of age, sex, and body mass index but they were significantly different in smoking. Only automatic BP measurements of 4 hours during khat chewing and 4 hours post-khat chewing show significant differences between khat chewers and non-chewers on both systolic (146.2 ± 8.1) versus (128.9 ± 12.1) $P < 0.001$ and diastolic blood pressure (90.6 ± 6.5) versus (81.8 ± 6.8) $P < 001$, but no significant differences detected on 24-hour systolic blood pressure (24-H SBP), 24-hour diastolic blood pressure (24-H DBP), diurnal and nocturnal systolic and diastolic blood pressure between the two groups. Similarly, the mean 24-hour heart rate per minute was significantly higher among khat chewers, (89 ± 6) versus (74 ± 5) $P < 0.05$. **Conclusion:** Khat chewing is associated with a transient increase in systolic and diastolic blood pressure and a transient increase in heart rate as well. Other clinical factors, such as BMI and smoking were significantly associated with hypertension.

1. Introduction

Khat or *Catha edulis* is an indigenous plant in Yemen, Ethiopia and East Africa, which has sympathomimetic and euphoriant effects. It is chewed habitually by people for its pleasurable effect and it produces stimulant amphetamine-like effects that are attributable to Cathinone, a phenylethylamine that is present in fresh leaves [1].

Khat contains a complex group of alkaloids (including Cathinone, Cathine, Ephedrine, and many others) [2]. It also contains glycosides such as Ampelopsin, Tannins, Choline, inorganic salts such as calcium and iron, and vitamins such as vitamin C and amino acids [3].

The cardiovascular changes, induced by chewing khat, show evidence of a significant rise in arterial systolic and diastolic blood pressure and pulse rate with a peak effect of three hours after starting chewing khat. These changes run parallel with the changes in plasma Cathinone levels during and after khat chewing [4].

Hypertension is a growing public health problem, with a remarkable contribution to cardiovascular disease (CVD) morbidity. Worldwide, an estimated 1 billion individuals have hypertension, and approximately 7.1 million deaths per year are attributable to hypertension. It is estimated that more than 20 million people are affected in the African Region where prevalence ranges from 25 percent to 35 percent in adults aged 25 to 64 years [5].

In Yemen, hypertension is a major public health concern. According to a recent study, nearly 30% of adults in Yemen suffer from hypertension. This is an alarming statistic, as uncontrolled hypertension can lead to heart disease, stroke, and kidney failure [6].

The diagnosis of clinical hypertension is based on office blood pressure (OBP) measurement [7]. However, OBP levels do not always reflect BP in daily life, while diurnal variations and nocturnal dipping, which are important determinants of morbidity and mortality, are not routinely measured [8]. Besides, OBP measurement only provides a momentary BP value, frequently under circumstances that can influence BP level [9]. As a result, many hypertensive patients remain unidentified or untreated [10]. Thus, 24-hour ambulatory blood pressure monitoring (ABPM) has become a valuable tool in the diagnosis and management of patients with hypertension [11]. It has valuable prognostic significance in determining target-organ damage and cardiovascular outcomes [12], since it

provides a large number of accurate BP readings throughout both day and night and is highly reproducible.

Accurate assessment of blood pressure (BP) is essential to the diagnosis, prognosis and treatment of hypertension. In this regard, ambulatory BP monitoring (ABPM) has become a useful tool for therapeutic decision-making in hypertensive patients and other subjects at high risk for cardiovascular disease (CVD). In both untreated and treated hypertensive patients, ABPM offers more accurate prognostic information on cardiovascular outcomes than office readings [13].

To the best of our knowledge, it is the first study that used 24-H ABPM for evaluation of the effect of khat chewing on systolic and diastolic blood pressure.

Purpose:

1) To study the impact of khat chewing on systolic and diastolic blood pressure and heart rate by using 24-H ABPM.

2) To examine the association of age, gender, BMI, smoking, and khat chewing with the presence of transient elevation of blood pressure in Yemen republic.

2. Methods

2.1. Study Participants

This was a cross-sectional, observational study in a group of 255 individuals visited our cardiac center from May 1, 2021 to January 1, 2023 were analyzed, khat chewers or non-khat chewers, observed or referred to our cardiac center and from apparently healthy individuals recruited from center staff or their relatives. The inclusion criteria were men and women aged ≥ 18 years with valid ABPM data (at least 85% successful recordings). Exclusion criteria were arm circumference > 41 cm or atrial fibrillation or other arrhythmias that could interfere with ABPM recordings, and pregnant women were excluded from the study due to the possible confounding effect of pregnancy on the weight and blood pressure. Subjects doing shift work were assessed only during a work period consisting of daytime activity and resting at night.

The study was approved by the local scientific ethics committee. The included individuals were informed about the study and asked for their participation, taking the consent of those who agreed to be included in this study.

2.2. Blood Pressure Measurement

BP was measured at the office with a calibrated mercury sphygmomanometer, after 5-minute rest in a sitting position. The OBP value was taken as the mean of three readings taken 2 min apart. Thereafter, 24-hour ABPM with appropriate cuff sizes was performed using the space Labs 90,207 (Redmond, WA, USA) automated noninvasive oscillometric device, programmed to register BP readings automatically at 20-min intervals during the waking (daytime) period (between 7 am and 11 pm) and at 30-min intervals during sleep (nocturnal) periods (be-

tween 11:30 pm and 6:30 am). ABPM registries were performed on working days, and the patients were instructed to engage in their normal daily activities, but to avoid strenuous exercise and to keep the arm immobile and stop moving and talking at the time of cuff inflation, return the following morning for device removal. Valid registries had to fulfill a series of pre-established criteria, including ≥80% of SBP and DBP successful recordings during the daytime and nighttime periods, 24-hour duration, and ≥1 BP measurement per hour.

2.3. Khat Chewing

Individuals participated in the study were informed to chew the same amounts and types of khat that they used to chew daily and time of chewing khat are standardized to be from 2 PM to 6 PM.

2.4. Study Variables

All individual data including age, gender, DM and BMI were collected at the time of ABPM. Variables collected for each patient based on the interviews and physical examination at the time of visit and on data drawn from clinical records were defined and measured in accordance with national and international guidelines [14] [15]. These included age, gender, weight, height, body mass index (BMI), known cardiovascular risk factors (e.g., smoking habit, dyslipidemia, and diabetes mellitus).

Height in stocking feet and weight in light clothing were measured, and body mass index (BMI) was calculated as weight (kilograms)/height (meters squared). Casual systolic and diastolic BPs were measured using a standard mercury sphygmomanometer on the right arm of seated participants after at least a 5-minute rest. Readings were made to the nearest 2 mm Hg, and diastolic BP was taken as the phase V Korotkoff sound. Serum total cholesterol was measured and Diabetes mellitus was defined as a fasting glucose level of ≥126 mg/dL (7.0 mmol/L), a nonfasting glucose level of ≥200 mg/dL (11.1 mmol/L), and/or use of medication for diabetes mellitus.

2.5. Statistical Analysis

Data are shown as mean ± standard deviation if normally distributed or as a percentage otherwise. Continuous variables in patient groups were compared by analysis of variance. Categorical variables were compared by the Chi-square test. The Student's t test was used for continuous variables and Pearson's test for linear correlations. A value of $P < 0.05$ was accepted as statistically significant. Bivariate and multiple linear regression and binary logistic regression analysis were performed in order to identify determinants of SBP and DBP and to estimate their corresponding coefficients of variability. Odds ratio (OR) was used to measure association of dependent and independent variables where 95% confidence interval (CI) and P-value were utilized to determine statistical significance. The statistical analysis was performed using SPSS version 22.0 (IBM SPSS Inc., Chicago, IL, USA).

3. Results

A total of 255 adults who met the eligibility criteria were participated, 70.6% were khat chewers and 29.4% were non-chewers. Of the khat chewers, 63.9% were males and 36.1% were female. Table 1, show that the two groups were comparable in most characteristics, and there were no significant differences between the two groups in terms of age, sex, body mass index but they were significantly different in smoking.

3.1. Khat Chewing Status of the Chewers

The reported reasons for chewing khat include, to practice habit of chewing, to pass time, to accompany or socialize with family members, to stay awake or due to family pressure and to get more concentration at work or study.

3.2. Blood Pressure

Clinic blood pressure and heart rate Table 2 show no significant difference between khat chewers and non-chewers on office systolic and diastolic blood pressure also no significant differences detected between the two groups on heart rate as well on office measurement

3.3. ABPM

As shown in Table 2, Among all the ABPM parameters only automatic measurements of 4 hours during khat chewing and 4 hours post-khat chewing show significant differences between khat chewers and non-chewers on both systolic (146.2 ± 8.1) versus (128.9 ± 12.1) P < 0.001 and diastolic blood pressure (90.6 ± 6.5) versus (81.8 ± 6.8) P < 001. The mean systolic and diastolic BP were higher on khat chewers group in compare to the non-showers, but no significant differences detected on 24-hour systolic blood pressure (24-H SBP), 24-hour

Table 1. Characteristics of study population.

	Khat chewers 180 (70.6%)	Non-khat chewers 75 (29.4%)	P. value
Age (years)	40.69 ± 10.34	44.20 ± 13.73	0.323
Sex			
Male no (%)	115 (63.9)	45 (60)	0.794
Female no (%)	65 (36.1)	30 (40)	
Height (cm)	165.27 ± 9.05	166.86 ± 8.47	0.564
Weight (kg)	66.63 ± 10.98	67.86 ± 4.98	0.586
BMI (kg/m^2)	24.5833 ± 4.58	24.64 ± 3.01	0.965
Smoking no (%)	40 (22.2)	5 (6.7)	<0.05
Hypercholesterolemia no (%)	30 (16.7)	15 (20)	0.776

Abbreviations: BMI: body mass index; p < 0.05 indicates statistically significant.

Table 2. Clinic and ambulatory blood pressure parameters and heart rate between the khat chewers and non-chewers.

	Khat chewers 180 (70.6%)	Non-khat chewers 75 (29.4%)	P. value
OSBP mmHg	136.25 ± 9.20	125.33 ± 22.94	0.211
ODBP mmHg	86.11 ± 7.37	82.33 ± 9.42	0.050
Office HR bpm	75 ± 6.4	74 ± 7.1	0.418
24-Hour SBP mmHg	130.56 ± 15.54	125.13 ± 12.81	0.239
24-Hour DBP mmHg	81.25 ± 6.9	79.17 ± 6.79	0.329
24-Hour MAP mmHg	97.17 ± 9.24	94.49 ± 8.58	0.256
Daytime SBP mmHg	134.39 ± 9.87	128.76 ± 12.57	0.094
Daytime DBP mmHg	84.57 ± 6.36	81.92 ± 6.90	0.191
Daytime MAP mmHg	101.89 ± 9.33	97.51 ± 8.53	0.125
Nighttime SBP mmHg	116.07 ± 14.10	116.44 ± 13.77	0.931
Nightime DBP mmHg	73.19 ± 9.74	72.50 ± 8.28	0.812
Nighttime MAP mmHg	87.48 ± 10.94	87.15 ± 9.61	0.919
Khat chewing and 4-H post-chewing time SBP mmHg	146.24 ± 8.13	128.9 ± 12.11	0.001
Khat chewing and 4-H post-chewing time DBP mmHg	90.57 ± 6.46	81.84 ± 6.82	0.001
Khat chewing and 4-H post-chewing time HR bpm	93.30 ± 6.32	79.40 ± 5.32	0.001
24-hour HR bpm	80.40 ± 9.61	78.22 ± 8.27	0.418

Abbreviations: OSBP: office systolic blood pressure; ODBP: office diastolic blood pressure; office HR: office heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; bpm: beat per minute; $p < 0.05$: statistically significant.

diastolic blood pressure (24-H DBP), diurnal and nocturnal systolic and diastolic blood pressure among the two groups. Similarly, the mean 24-hour heart rate per minute was significantly higher among khat chewers, (89 ± 6) versus (74 ± 5) $P < 0.05$.

3.4. Association of Khat Chewing and Other Predictors with Blood Pressure

Table 3 and Table 4 show that in simple linear regression analysis, age, BMI, and smoking were significantly associated with both systolic and diastolic blood pressure. These variables with significant association on bivariate analysis were further analyzed using multiple linear regression models to identify independent predictors of systolic and diastolic blood pressure. After adjusting for these variables; BMI and smoking remained significantly associated with systolic and diastolic hypertension.

Table 3. Simple and multiple linear regression model examining the association between different variables with systolic blood pressure among khat chewers.

	Simple linear regression				Multiple linear regression			
	Beta coefficient	SE	95% (CI) for beta coefficient	p. value	Beta coefficient	SE	95% (CI) for beta coefficient	p. value
Age	0.334	0.127	0.004, 0.521	0.047	0.420	0.163	−0.004, 0.664	0.060
Sex	−0.084	2.853	−7.200, 4.396	0.626	−0.066	2.781	−6.800, 4.594	0.695
BMI	0.440	0.273	0.226, 1.335	0.007	0.501	0.485	−0.106, 1.881	0.028
Smoking	−0.050	3.304	−7.673, 5.756	0.034	−0.056	3.234	−7.709, 5.539	0.040
Obesity	0.383	2.557	0.981, 11.373	0.071	−0.059	4.125	−9.399, 7.499	0.820
Hypercholostolemia	0.290	3.532	−0.939, 13.416	0.086	−0.155	4.733	−13.030, 6.362	0.487
DM	0.283	3.814	−1.184, 14.318	0.094	0.139	4.349	−5.681, 12.134	0.464

Abbreviations: BMI: body mass index; DM: diabetes mellitus; SE: standard error: CI: confidence interval; A p-value < 0.05 was considered statistically significant.

Table 4. Simple and multiple linear regression model examining the association between different variables with diastolic blood pressure among khat chewers.

	Simple linear regression				Multiple linear regression			
	Beta	SE	95% (CI)	p. value	Beta	SE	95% (CI)	p. value
Age	0.337	0.101	0.005, 0.416	0.045	0.364	0.128	−0.035, 0.490	0.087
Sex	0.009	2.277	−4.512, 4.744	0.960	0.036	2.189	−4.008, 4.958	0.830
BMI	0.433	0.218	0.167, 1.053	0.008	0.436	0.382	−0.167, 1.397	0.030
Smoking	−0.062	2.626	−6.290, 4.385	0.019	−0.032	2.545	−6.321, 4.104	0.046
Obesity	0.388	2.029	0.863, 9.108	0.079	−0.051	3.246	−7.302, 5.997	0.842
Hypercholestolemia	0.347	2.753	0.350, 11.539	0.068	−0.072	3.725	−8.861, 6.399	0.743
DM	0.375	2.932	0.962, 12.879	0.094	0.223	3.422	−2.901, 11.119	0.240

Abbreviations: BMI: body mass index; DM: diabetes mellitus; SE: standard error: CI: confidence interval; A p-value < 0.05 was considered statistically significant

4. Discussion

The number of khat chewers is increasing and its consumption has become popular in all parts of Yemen's population. As the consumption of khat is continuing to increase markedly in Yemen, more studies are needed to assess the association and adverse effects of khat consumption on blood pressure in detail. This study aimed to investigate the association of khat chewing on systolic and diastolic blood pressure, heart rate and predictors of hypertension

We evaluate the association of khat chewing with the elevation of both systolic and diastolic blood pressure, either above the defined level of the upper normal range (hypertension) or even above the baseline level measured just before chewing khat although less than the range of hypertension. Earlier studies have

suggested that chronic use of khat predisposes to high blood pressure and other cardiovascular morbidity [16] [17]. All the previous studies used manual methods for blood pressure measurements during khat chewing, but Blood pressure (BP) varies according to many internal and external factors. In addition to the awake and sleep cycle, many behavioral factors, such as mental stress, exercise, food consumption, changes in body weight, dietary intake of sodium and other electrolytes, drinking and smoking habits, consumption of coffee and tea, and bathing, influence both the level and variation in BP, and nowadays, ambulatory BP monitoring (ABPM) has become a useful tool for diagnostic and therapeutic decision making in hypertensive patients and other subjects at high risk for cardiovascular disease [18]. So, in our present study, we used the ambulatory 24-hour blood pressure monitoring for measurement of blood pressure throughout 24 hours including khat chewing periods.

Interestingly, a study conducted in Yemen, suggested that khat would reduce blood pressure significantly. To the best of our knowledge, this is the only report that suggests such findings [19]. This study did not explain the underlying mechanism, but instead, correlated reduced cognitive function and blood pressure to khat usage. Other previous study reported no evidence of an increase in systolic or diastolic blood pressure among khat chewers [20], but many previous studies demonstrated that there is a significant positive association between chronic khat chewing and both systolic and diastolic blood pressure [21] [22]. This is consistent with our findings which show significant transient elevation of both systolic and diastolic blood pressure among khat chewers in comparison to non-chewers. Beyond the transient rise in blood pressure due to the acute effect of khat, persistent vasoconstriction may develop secondary to the prolonged effect of cathinone. However, the difference in the findings may be due to differences in duration, amount and frequency of khat chewing and differences in the study populations studied.

Our findings suggest a transient rise of both systolic and diastolic blood pressure and heart rate that occurs during khat chewing and may extend up to 4 hours post-chewing but gradually declined to normal values over time throughout 24-hour. That goes with what has been demonstrated in experimental studies [23], although it was contrary to other studies which show the sustained elevation effect of chronic khat chewing on blood pressure [24].

This study also demonstrated that there was a significant association between BMI with systolic and diastolic blood pressure. This finding was consistent with another study which reported that there was a significant positive correlation among BMI, systolic and diastolic hypertension. Furthermore, it showed that overweight/obese subjects were more likely to have hypertension than those with normal BMI [25].

The current study has also shown that khat chewing was significantly associated with cigarette smoking. This result is in line with other studies that have shown that cigarette smoking was significantly associated with the chronic use of khat [26] [27].

The mean systolic and diastolic blood pressure among khat chewers was significantly higher than that of the non-chewers, by 18 mmHg 8.7 mmHg sequentially. Such a range of blood pressure variation may appear insignificant at an individual level but can be regarded as an important difference at a population level and may have a significant contribution to increasing the risk of morbidity and mortality related to cardiovascular diseases at the population level.

In our study, we found that both systolic and diastolic blood pressure are significantly elevated in khat chewers in compare to non-chewers during the khat chewing period and 4-hour post chewing but no significant differences were detected in mean 24-hour, mean diurnal and mean nocturnal measurements. In addition to that, heart rate is also markedly elevated in khat chewers in comparison to non-chewers and maximum elevation occurs in khat chewing and 4-hour post chewing period. This is in line with other several studies which showed that elevation of blood pressure occurs during khat chewing, reaches the peak within 3 hours and reverses to the normal range 2 - 3 hours after chewing [28] [29] [30].

The mechanism of blood pressure elevation by khat chewing can be explained by cathinone effects. Cathinone appears to be the main ingredient of khat responsible for elevated blood pressure, by increasing sympathetic activity, increasing heart rate and increasing myocardial contractility and causing prolonged vasoconstriction, all those activities increase systolic and diastolic blood pressure [31] [32].

As noted in the aforementioned studies, khat, or its active alkaloid cathinone, influences both heart rate and contractility, and therefore, increases cardiac output, which is a major determinant of mean systolic blood pressure. Khat-induced hypertension is associated with ß1-adrenoceptor-mediated tachycardia. Increases in sympathetic activity after khat, or cathinone, the administration probably could be elucidated by an increase in renin secretion from the kidney, and an increase in the activity of the renin-angiotensin-aldosterone system (RAAS). The RAAS activation might cause an increase in blood volume and this might increase the peripheral vascular resistance reflected in elevated diastolic blood pressure [33] [34]. On the other hand, it was postulated that khat-induced vasoconstriction is not mediated via a1-adrenoceptors or indirect-acting sympathomimetic action, but could be related to the release of endogenous vasoconstrictors like endothelin and angiotensin, although the mechanism was unclear. This suggests the possibility that the khat-induced vasopressor effect could be mediated by an endothelin-induced release of prostaglandin and thromboxane A2 (vasoconstriction effects) [35]. Further pharmacologic and in vivo studies will be needed to verify this hypothesis [36].

5. Limitations

First, it is not known whether the association of chronic chewing with systolic and diastolic blood pressure is due to cathinone or other khat constituents. Khat

contains many different compounds and we did not identify the specific compounds in this study.

Second, we could not assist the effects of different types and amounts of khat on blood pressure separately, since that needs a specific study

6. Conclusions

The current study has shown that khat chewing is associated with a transient increase in systolic and diastolic blood pressure and a transient increase in heart rate as well. Other clinical factors such as BMI and smoking were significantly associated with hypertension.

Programs for the prevention and control of high blood pressure in the population need to devise strategies to counter the expansion of khat chewing and other substance use behaviors.

Conflicts of Interest

The authors declare no conflicts of interest.

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