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Research Article

Effects of Khat (*Catha Edulis*) on Bronchial Asthma

Abstract

Introduction: Asthma is a chronic inflammatory disorder of the airways. It is always being a health burden across the globe. The active chemical present in Khat could have a bronchodilator effect like that of catecholamine. The present study aims at determining the effect of khat chewing on bronchial asthma and lung function.

Methods: A comparative cross-sectional study was conducted in Jimma University Specialized Hospital (JUSH) Adult Chest Clinic on 170 asthmatic patients with a 1.4 to 1 ratio of non-chewer to chewer. The interviewer-administered questionnaire, patient history and pulmonary function test using Spirometer were used to collect data.

Result: Of 170 asthmatic patients, 72 were khat chewers and 98 were nonchewers. Frequent asthmatic symptoms were seen in 23 (31.9%) of chewers and 43 (43.9%) of nonchewer (χ^2=2.488, p=0.11). A less frequent use of β_2 agonist was observed on 42 (58.3%) of chewers and 53 (54.1%) of nonchewer patients (χ^2=12.678, p=0.12). Less frequent night-time awake and chewing status was found to be positively associated [AOD=2.633, CI (1.778, 3.059)]. The mean predicted personal best of forced expiratory volume in one second (FEV_1%) for chewers and nonchewer was 62% and 46% respectively while their PEFR% was 40% and 26% respectively.

Conclusion: apart from psycho stimulating prosperities, khat has moderate potential benefit for the improvement of episodes of an asthma attack and reduction of asthmatic symptoms. This study showed that chewer asthmatic patients had relatively better PEFR and also relatively lesser recurrent night-time awake due to an asthmatic attack.

Introduction

The National Heart, Lung, and Blood Institute (NHLBI) defined asthma as a chronic inflammatory disorder of the airways, in which bronchial hyper-reactivity causes recurrent episodes of wheezing, breathlessness, chest tightness and cough associated with airflow obstruction [1]. Asthma typically can range from very mild and intermittent symptoms to one of devastating and life-threatening attack [2]. Though the cost of asthma management is high, the inappropriate treatments cost even higher [3]. Of major therapies, corticosteroids have been the prominent drug followed by 5-lipoxygenase inhibitors, anti-IgE, and immunomodulatory drugs in the treatment regime of bronchial asthma [4].

Bronchial asthma is always been a global problem. Among the European member states, UK was the highest in a survey by European Commission where Finland (11%) and Ireland (10.5%) were following. The same study put Germany as the lowest rated asthma prevalent country together with Spain with a total of 4.4% incidence rate [5]. Inter-country prevalence data of asthma and allergies in childhood indicates that prevalence in Ethiopia was 9.1%, Kenya 15.8%, Nigeria 13.0%, South Africa 20.3%, Algeria 8.7%, Morocco 10.4%, and Tunisia 11.9% [6].

As mentioned above, asthma is a continuous challenge to the world without a cure. It is only possible to control it by reducing the symptoms. Unreserved efforts to treat asthma bring Khat to the attention of researchers towards understanding its effect on bronchial asthma and bronchial muscles. Cathinone, an active ingredient in khat, found to have pharmacological resemblances with that of amphetamine by releasing catecholamine from presynaptic storage sites [7]. A study showed possible modulation of bronchial airways or bronchodilation by administering inhaled dopamine to different subjects having different bronchial tones [8]. Thus cathinone might influence the concentration of Dopamine which is a family of catecholamine. Despite it could improve respiratory performance by decreasing oedema formation it may still inherently have unwanted effects [9].

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Despite the existence of the use and consumption of khat by a large size population of Ethiopia especially those countryside known by their khat cultivation [10], very little is known about its effects other than its content of psychoactive ingredients. This knowledge gap implies to researchers due to the lack of classification of the plant as a drug by international and national institutions. As a result, it gets limited attention by the researcher on its effect on specific systems beyond its psychostimulatory property. There have been doubts about its medicinal use and its consumption as a traditional remedy for asthma, influenza, cough and other chest problems is still a mystery [11]. This study is one of its kinds to show a potential effect of khat on bronchial asthma symptoms and lung function. It is also intended to provide information on asthma management practiced in the clinic where the study was conducted.

Patients and Methods

Study setting

A comparative cross-sectional study was conducted in Jimma University Specialized Hospital (JUSH) Adult Chest Clinic on patients who were under follow-up. Jimma is one of the cash crop producing areas in Ethiopia where coffee and khat are grown abundantly as the major source of income. Because of the wide range of vegetation and related environmental reasons, bronchial asthma and other respiratory distresses are common in the area.

Sampling

All asthmatic and COPD patients who have been treated as newcomers and under follow up in Jimma University Specialized hospital adult chest clinic were source populations. The study populations were all asthmatic patients under follow up. In this specific study, no probability sampling technique was done, rather all patients under follow-up in the Jimma University specialized hospital adult chest clinic were included. The data was collected in JUSH adult chest clinic from a total of 170 patients with 1.4 to 1 ratio of non-chewer to chewer asthmatic patients. Data were collected from patients based on the sequence of appearance to the clinic.

Inclusion and exclusion criteria: All asthmatic patients who were diagnosed with bronchial asthma and willing to participate in the study were included. Study subjects who had known problems such as TB, unstable cardiac problems, pneumothorax, haemoptysis and patients who were unable to undergo spirometry or unwilling to provide informed consent were excluded

Measurements and questionnaire: The data were collected using semi-structured questionnaire consisting of age, sex, height, the weight of a patient, the health effect of khat on asthmatic patients and quality of life, information on the use of khat, assessment on their asthmatic episode.

Patient history: The patients' history was read from their cards and the information obtained includes: illness other than asthma, the drug they were using at the time of the test and the type of drug prescribed by their physician for the treatment of asthma.

Pulmonary function test: Pulmonary function test was performed using Datospir digital spirometer. Measurements or calculations were made on forced expiratory volume in one second (FEV1) and peak expiratory flow rate (PEFR). Spirometry test on each patient was made five times and the highest out of the five readings was considered to be personal best of the patient. Adjustments were made on all patients' FEV1 and PEFR since there was a potential leak while performing the test which the machine can not consider.

Data collection technique: The data were collected by a nurse, a pharmacist, and the principal investigators. Prior to data collection, each material used as a source of data for the study was arranged in sequence to avoid confusion and repetition during the data collection.

Operational definitions

Control: Is the degree to which symptoms, impairments, and risks are minimized by treatment. Control is the parameter assessed in patients receiving treatment. Control is classified as

Good control: Symptoms in ≤2 days/wk; Nighttime awakening in ≤2/mo; Use of short-acting β_2-agonist for symptom control for ≤2 days/wk and FEV_1 or peak flow is >60% predicted/personal best

Poor control: Symptoms in >2 days/wk; Nighttime awakening in 1–3/wk; Use of short-acting β_2-agonist for symptom control for >2 days/wk and FEV_1 or peak flow is <60% predicted/personal best

Chewing status: The classification was based on the hypothesis that transient effect of khat on respiratory rate can remain for an about 24-36 hours after chewing and ingestion of the khat juice. This definition only works only while dealing with FEV_1 and PEFR measurements

CHEWING STATUS FREQUENCY OF CHEWING

Heavy chewers: ≥ 2 times per day for the last two days before the test

Light chewers: once per day for the last two days before the taste

Nonchewers: who didn't chew for two or more days before the test

%FEV_1 - percentage predicted personal best of forced expiratory volume in one second

%PEFR - percentage predicted personal best of Peak expiratory flow rate

Data processing and analysis: The data was compiled and analyzed using SPSS version 16 computer program executing different statistical analysis. The principal analysis was descriptive statistical analysis. Chi-square, ANOVA, regression

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analysis models were employed to compare means and non-parametric two independent sample t-tests were also used. A P value <0.05 was considered to be statistically significant. The result was summarized and presented using paragraphs and tables.

Validity and reliability: The validity and reliability of data collection tools, questionnaire and spirometer were assured by undergoing pre-test on few patients who were willing to participate and the spirometer was calibrated as per the need and conditions before the actual study.

Ethical consideration: Ethical clearance was obtained from the ethical review board of Jimma University and consent of patients was assured.

Limitation of the study: Some patients had the difficulty of recalling the frequency of asthmatic episodes. The pulmonary function test had to be done several times due to the wrong maneuver of patients and frequent power cut. Moreover, it was difficult to measure the amount and type of khat they used to chew at a time and before the test.

Results

This study was done on 170 asthmatic patients (98 nonchewers & 72 chewers) who were under follow up in Jimma University adult chest clinic. Of the total, 111 (65.3%) were females; 47 (48.0%) were chewer asthmatic patients aged 35-54. Of nonchewer patients 57 (33.5%) were age ranged 55-82. Out of the total chewer patients, 58 (63.0%) were patients whose asthmatic onset was for more than ten years. 29 (17.1%) were nonchewer patients whose onset of asthma was for more than five years but less than ten years.

The association between all clinical parameters and age was statistically significant. When the model was adjusted for good control, the likelihood of facing once or less than once per week (<1x/wk) frequency of symptom among patients whose age ranges between 35-54 was twice as much as that of patients whose age range between 55-82 (Table 1).The linear regression analysis for the association of age with FEV1 and PEFR was expressed as follows:

FEV_1=62.125-0.285* Age; p=0.010

The increase in age by one year reduced FEV_1 by 0.0285 and also an age increase by one year reduced PEFR by 0.155

PEFR=41.579-0.155* Age; p=0.124

Spirometric mean personal best of FEV1% predicted among men was 52%, while it was 47% for female asthmatic patients (p=0.440). And again mean personal best of PEFR% predicted among men was 38%, while it was 32% for female asthmatic patients (p=0.003).

Of the total male patients, 26 (39%) were having a frequency of symptom for more than once per week (>1x/wk) (χ^2=1.046, p=0.306). Among 111 female asthmatic patients 48 (64.0%) experience frequent night-time awakening in twice or less than twice per month (<2x/month) (χ^2=0.99, p=0.753). There was no any statistically significant association between sexual orientation and frequency of asthmatic attack, the frequency of night-time attack and frequency of β_2 agonist usage.

Out of the total, 30.8% of patients whose onset of asthmatic illness was in less than five years had a frequency of asthmatic symptoms for <1x/wk (χ^2=0.494, p=0.482). Again 27 of patients who suffered from asthma since before five years had a night-time attack for <2x/month (χ^2=15.107, p=0.088).27 (34.0%) of the total asthmatic patients whose onset of illness was in less than 5 years used β_2 agonist for twice or less than twice per week (<2 days/wk) (χ^2=5.897, p =0.435).

Of patients who had experience of asthma symptom in <1x/wk, 49 (68.1%) of them chewers while 55 (56.1%) of them were nonchewers. Out of the total chewer patients, 52 (72.2%) of chewer asthmatic patients and 23 (31.9%) of nonchewer patients had night-time awakening for <2x/month. Of chewer asthmatic patients 42 (58.3) and 53 (54.1%) of nonchewers were found to use short acting β_2 agonis for <2 days/wk (Table 2). A logistic regression model was adjusted for good control (frequency of attack in <2x/month) and other confounding factors were corrected for the model. Accordingly, the probability of experiencing night time attack in <2x/month for chewer patients was 2.633 times than that of non-chewer patients [AOR=2.633, (1.778, 3.059)].

Table 1: Clinical parameter correlates with age among asthmatic patients

	B	S.E.	AOD	95.0% C.I.
Frequency of symptom/age				
55-82	0.00		1.00	(1.016,4.694)
35-54	.781	.390	*2.184	(1.466,10.667)
15-24	1.375	.506	*3.955	
Frequency of night time awake /age				
55-82				
35-54	0.00		1.00	(1.312,8.571)
15-24	1.210	.479	*3.353	(0.924,4.544)
	.718	.406	2.049	
Frequency of β_2 agonist usage /age	0.00		1.00	
55-82	.472	.457	1.603	
35-54	.850	.390	*2.339	(.655,3.922)
15-24				(1.090,5.023)

* indicate significant association.

Table 2: Effect of Khat on clinical parameters among asthmatic patients

		Chewers	Non-chewers	χ^2	p-value
Frequency of symptoms	>1x/wk	23(31.9%)	43(43.9%)	2.488	0.115
	≤1x/wk	49(68.1%)	55(56.1%)		
Frequency night time awakening	>1x/wk	35(48.6%)	0(61.2%)	12.678	*0.012
	≤2x/ month	52(72.2%)	23(31.9%)		
Frequency of short acting β_2 agonist use	>2 days/ wk	30(41.7%)	45(45.9%)	0.304	0.581
	≤2 days /wk	42(58.3%)	3(54.1%)		

* indicate significant association.

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The spirometric test showed the mean FEV_1% predicted of the chewer and non chewer was 62.1% and 40% respectively. The test statistics showed the association between FEV_1% predicted and chewing status was not significant (t=7.463, p=0.999).45.9% and 26.4% was PEFR % predicted mean personal best of the chewer and non chewer asthmatic patients respectively (t=7.311, p=0.000.)

Among chewers who chew khat twice, 5 (71.4%) of them had a frequency of symptom in <1x/wk. And 39 (69.6%) of once every day chewers had a frequency of nighttime attack for <1x/wk. Of chewers who chew khat for more than once per week 4 (44.4%) patients had a frequency of night time attack for >1x/wk. The association was not statistically significant (χ^2=0.748, p=0.688.)

Among twice a day chewers, 4 (57.1%) had a frequency of night time attack in <2x/month. Out of the total once everyday chewers, 33 (58.9%) of them had a frequency of night-time attack for >1x/wk. Only one person had a frequency of night time attack for <2x/month among chewers who chewed khat for more than once per week. This result show the association was statistically significant (χ^2=7.323, p=0.026)

Three (42.5%) of the patients who chew khat twice a day used β_2 agonist for more than two days per week. 35 (62.5%) of chewer patients who chew khat every day were found to use β_2 agonist for more than two days per week. Of chewer patients who chew khat for more than once per week, 3 (33.3%) of them found to use β2 agonist for <2x/wk. The association was not statistically significant (χ^2= 2.718, p=0.257).

Spirometric mean of FEV_1% predicted of chewer's who preferred to chew in the morning was 50.33% +6.1 and among night chewers 62.06% +18.55 (p=0.047). Spirometric mean personal best of PEFR% predicted among chewers who chewed khat within 12 hours before the test was 46.4% +20.8 (Table 3).

According to the modified global initiative for asthma (GINA) level of asthma control criteria, of asthmatic chewers, 43 (59.7%) were in a good asthma control situation and 29 (40.3%) were chewers whose asthma was poorly controlled. While 25 (23.5%) of non chewer asthmatic patients had good asthma control, 75 (76.5%) poorly controlled asthma. The result was statistically significant (χ^2=22.976, p=0.000).

Discussion

The possible influencing factors for the asthmatic onset of illness and frequency of asthma symptoms are age, sex, and comorbid diseases. These factors were potential confounders in assessing the effect of khat on bronchial asthma as well. According to the result of the present study, the frequency of asthma symptom increases as age increases. This was observed in the present study as aged asthmatic patients had a frequent asthmatic symptom i.e. more than once per week. This finding was in line with a research done by Nicola, 2011 where they explain the presence of comorbid diseases makes asthma even worse and difficult for diagnosis and treatment [12]. In the same way, night-time awakening due to asthma attack was also seen frequently in elderly patients. Frequent β_2 agonist use also recorded in patients whose age ranges between 55 and 82. But the use of β_2 agonist was less frequent for a larger number of asthmatic patients whose age range was 15-34. In addition; FEV_1 was significantly decreased as age increased. The possible explanation for this finding could be similar to any other physiologic parameters, normal pulmonary functions and responsiveness to certain medication become reduced as age increase [13,14]. The result was in agreement with previous research done indicating the loss of elastic recoiling of the lung in asthmatic patients is associated with age [15].

In this study, bronchial asthma is more prevalent among females than in males. The result obtained was in line with an earlier study that revealed asthma is more common in boys than girls before puberty but more common in females than males after puberty [16]. The hormonal fluctuation throughout the life of a woman might be the reason for the different immunological response of the body towards allergy [17]. However, in other finding sexual orientation did not show any significant effect on patient's frequency of symptom, night-time awake and $\beta_2$agonist usage. Opposite to this finding, a study done on asthma and rhinitis showed that females are prone to develop asthmatic symptoms moderate to severe than males [16]. Perhaps significant variation was recorded on PEFR between male and females. Mean of both measurements were higher in males than in females. This is true as pulmonary volumes are lower in females than in males due to high thoracic dimension or the presence of larger number of bronchioles [18,19].

Another study also disclosed that females are more likely to develop late-onset and persistent wheeze [20]. Regarding onset of illness, the frequent asthmatic attack was seen among patients whose onset of asthma was for more than ten years. The poor immunological response to diseases and reduced physiological function of respiratory apparatuses could be the cause of more frequent asthma attack [21]. Frequent night-time awake was observed on patients whose onset of asthma was for more than ten years. But for the same patients, use of β_2 agonist was less frequent than the rest of patients. The result was close to the fact that regardless of the duration of illness patients could suffer from the disease equally. A study also shows that severe asthma could develop through time or once the disease is developed [22].

Clinical parameters are the key guidelines for the assessment of asthma. Although the association between experience of symptoms (coughing, sneezing, dyspnoea) and chewing status was found statistically not significant (p>0.05), the majority of chewers were the one who experienced symptoms in less than

Table 3: FEV_1 and PEFR among khat chewer asthmatic patients within a specified period of time before spirometry.

Specified time of chewing	FEV_1 % predicted predicted	PEFR %
within 12 hours	62.66%±19.47	46.4%±20.8
with in 24 hour	61.4% ±18.86	44.6%±19.7
within 36 hours	62%±8	51%±7.8

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two times per month (68%). Concerning night time awake, chewing status and frequency of night-time awake were found to be significantly associated (p=0.012). The high statistical significance association could be due to the majority of chewers prefer to chew khat at night. Accordingly, its effect might yet exist until pulmonary function test performed.

FEV_1 and PEFR are the best pulmonary parameters which have been used for the assessment of obstructive and restrictive airway diseases. According to British Thoracic Society classification, 1997; FEV_1 of 60-79% is a sign of the mild attack, FEV1 = 40-59% for moderate attack and FEV_1 <40% for the severe attack. Hence, chewer patients seem to have improved pulmonary function while nonchewers were attacked moderately or severely. These could be due to the difference in airway diameters among chewers and nonchewers. It might be possible to predict that Khat might have an effect on the release of dopamine which in turn has bronchodilating property by modulating airway smooth muscle contraction [8].

A large number of everyday chewer patients used salbutamol ($\beta 2$ agonist) in less than two days per week. The reason might be as they used to chew khat every day; it can be expected that khat has been a replacement or an option for their attack over a short-acting β_2 agonist. This phenomenon was described by a group of researchers in 2008 as khat is taken as a traditional remedy to treat respiratory illnesses by locales in those areas known by their high khat plantation [23]. The relatively high percentage means of both PEFR and FEV_1 for chewers who practiced khat chewing in 12 hours before the test presumably related to the half-life of khat ingredients (cathine and cathinone). Literature shows amphetamine and metabolites of amphetamine have plasma half-life approximately 2hrs whereas cathinone and cathine average 5.2+3.2 hr hours [24]. Predictably, the shorter the time gap between chewing and spirometric test the better will be the measurement outcomes. Therefore, regardless of the amount and the type of khat chewed, the presence of those active ingredients in the plasma could cause many physiologic changes including airway dilation.

The hypothetical rationale for why chewers had relatively well-managed asthma and intermittent asthmatic episodes in this study could be the effect of khat through its constituents upon activation of α_2 and $5HT_7$ receptors and also inhibition of ACh thereby modulating airway smooth muscle contraction [25].

The above mentioned statistical and patients' personal sound verdicts support the possibility of khat's effect on bronchial asthma through manipulating airways and their smooth muscles. In conclusion, apart from psychostimulating prosperities, khat might have moderate potential benefit in the improvement of episodes of an asthma attack and reduction of asthmatic symptoms. This study showed that chewer asthmatic patients had relatively better PEFR and also relatively lesser recurrent nighttime awake due to an asthmatic attack.

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