

Frequent Use of Khat, an Amphetamine-Like Substance, as a Risk Factor for Poor Adherence and Lost to Follow-Up Among Patients New to HIV Care in Ethiopia

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Abstract

Khat, a plant native to East Africa, has amphetamine-like psychoactive constituents, and is a potential risk factor for HIV infection. Chronic use can cause cognitive impairment and other mental disorders, raising concerns about effects on retention and adherence with HIV care. During 2013–2014, 322 Ethiopian patients newly enrolled at HIV clinics in Dire Dawa and Harar were surveyed about khat use and prospectively followed for 1 year; 9% died, 18% transferred care to other clinics, and 22% were lost to follow-up (LTFU) (no clinic visit for >3 months). Of 248 patients who received a 12-month follow-up survey, 37% used khat in the year after enrollment, with a median use of 60 h in a typical month. Those using khat ≥ 60 h/month (median among users) were more likely than others to be LTFU (31% vs. 16%, $p = .014$); those using khat ≥ 150 h/month (upper quartile) had 44% LTFU rates versus 16% for others ($p = .002$). Complete 3-day adherence (taking all doses) of antiretroviral therapy was reported by 77% of those using khat ≥ 60 h/month versus 95% of all others ($p < .001$), and 67% of those using khat ≥ 150 h/month versus 94% of others ($p < .001$). In two East African cities, where khat use is common, frequent use was a significant risk factor for higher 1-year LTFU and lower self-reported antiretroviral therapy adherence among people living with HIV entering HIV care. Where khat is widely utilized, interventions to promote either nonuse or reduced use are important as part of a comprehensive HIV care package and national HIV strategies.

Keywords: HIV, khat, adherence, retention, Ethiopia

Introduction

KHAT, *CATHA EDULIS*, is a flowering plant native to East Africa used for its stimulant effects, most often by chewing leaves and shoots.^{1–5} Although data are limited, it has been estimated there are 5–10 million people chewing khat on a daily basis,⁴ most commonly in Eastern Africa and the Arabian Peninsula. In a nationwide Demographic and Health Survey, 11% of Ethiopian women and 28% of men reported ever chewing khat, with wide geographic disparities; in the Dire Dawa and Harari regions, 27% and 39% of women and 79% and 82% of men, respectively, reported a history of khat use.⁶

Psychoactive constituents of khat, cathinone and cathine, are structurally similar to amphetamine.^{1–5} Acute use of khat causes stimulant and euphorogenic effects; chronic and excessive use can cause psychological dependence, mania, psychosis, cogni-

tive impairment, and other mental disorders.^{1–5,7} Khat use has been associated with impaired working memory and cognitive flexibility.⁸ Ethiopian studies report khat use related to unsafe sexual behavior, including multiple partners, non-regular partners, and exchange of money for sex; khat has been associated with a twofold increase in risk of HIV infection.^{9–11}

Achieving the World Health Organization's 90-90-90 goals for people living with HIV requires maximizing antiretroviral therapy (ART) adherence and reducing lost to follow-up (LTFU) after initiating HIV care.¹² Substance abuse, including use of drugs, such as methamphetamine, has been associated with reduced linkage to care and ART adherence.^{13–17} Given psychological effects of khat, and khat's structural similarity to other amphetamines, there is reason to believe it may have deleterious effects on retention in HIV care and ART adherence. However, this association has not been well studied.

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During 2013–2014, we surveyed 322 patients recently enrolled in HIV clinics in Dire Dawa and Harar (two cities where khat was commonly reported) about their use of khat.¹⁸ Upon entry into the study, 65% of patients reported khat use during the previous year, using khat a median of 5 h/day and 30 days/month. We then attempted to follow these patients for a 12-month period after enrollment in care, to see whether khat use changed, and whether continued khat use was associated with a greater likelihood of LTFU from HIV care. Among those who we were able to contact for a 12-month follow-up interview, we also asked about their recent adherence to ART.

Materials and Methods

Enrollment and baseline assessment

Recruitment procedures for this study have been previously described.¹⁸ In brief, this study was conducted at HIV clinics in Dil Chora Referral Hospital (Dire Dawa) and Hiwot Fana Teaching Hospital (Harar). Inclusion criteria were age ≥ 18 years and being newly enrolled in HIV care within the previous 3 months. Patients who met criteria were identified by HIV clinic staff and sequentially offered enrollment by the project officer assigned to each hospital. Upon entry, all participants received a verbally administered health survey conducted in Amharic or Oromo, which included the following questions: “During the past year, have you used khat?”, “If yes, during the past year, in a typical month, about how many days per month did you use khat?”, and “On a typical day when you used khat, about how many hours did you spend chewing khat?”

Twelve-month follow-up

Participants were asked for their permission to be recontacted 12 months later, at which time the health survey was repeated. This included again asking the same questions about khat use in the past year, representing the 12-month period after enrolling in HIV care. Surveys were typically conducted in person by the project officer at each hospital; however, if the participant had moved or was otherwise unavailable, we attempted to contact participants by cell phone for a phone survey. As part of the follow-up survey, participants on ART were asked how many of their prescribed ART pills they had taken during each of the past 3 days.

In addition to the health survey, at the 12-month follow-up, we also collected data from the participant’s HIV clinic record concerning whether they were still attending the original HIV clinic of enrollment; this included abstraction of dates of all clinic visits since enrollment.

Informed consent was obtained from participants, who received 50 birr (~\$2.50 U.S.) for the baseline survey and 100 birr for follow-up. Ethical approval was obtained from the University of Minnesota Institutional Review Board and the Haramaya University College of Health and Medical Sciences Institutional Review Board.

Analyses

For those who reported khat use in the previous year, we quantified khat use as the product of (number of days used in a typical month) \times (number of hours used in a typical day), or number of hours of khat use in a typical month. On the adherence questions, those who reported taking all ART pills

every day for the past 3 days were defined as having complete (100%) self-reported 3-day ART adherence.

Based on follow-up data from the HIV clinic record, participants at 12 months were classified into one of four follow-up categories. If the participant was known to have died in the past year, they were classified as “dead.” If the participant was known to have transferred HIV care to another clinic in the past year, they were classified as “transferred.” If there was no record at the 12-month follow-up of the participant having attended the HIV clinic for at least the previous 90 days, and if they were not known to be dead or to have transferred, they were classified as “LTFU.” For 17 participants considered by their clinic as LTFU, we were able to ascertain by telephone follow-up that they had transferred care to other clinics, and they were reclassified as “transferred.” Finally, if the participant was still attending their clinic visits and had been seen one or more times in the previous 90 days, they were classified as “retained” in care.

Predictors of LTFU and 3-day adherence were evaluated using chi-square for categorical variables, and the Kolmogorov–Smirnov nonparametric test to compare median values for continuous variables. Data were double entered; discrepancies between entries were reconciled by checking the original data forms. Analyses were conducted using SAS version 9.3 (SAS Institute, Inc., Cary, NC).

Results

Baseline characteristics

Of 322 participants enrolled in this study, 55% were female; the mean age was 34 years. Thirty-six percent were day laborers, 20% civil servants or in business (e.g., merchants), 15% unemployed, 13% housewives, and 16% other occupations. The median CD4⁺ count at enrollment was 179 cells/mm³; 35% were WHO Stage III or IV. As previously reported,¹⁷ in the year before entry, 209 (65%) respondents reported using khat, with a median of 30 days of use in a typical month, and median of 5 h of use per day; the median use of khat in a typical month among these users was 120 h [interquartile range (IQR) = 45–180].

Twelve-month follow-up

After 12 months of follow-up, 30 (9%) participants were classified “dead,” 58 (18%) were considered “transferred,” and 70 (22%) were considered LTFU. Therefore, 164 (51%) participants were classified as retained in care. LTFU rates did not significantly differ by gender, age, marital status, education level, or alcohol use in the past year ($p > .10$) (data not shown).

Two hundred forty-eight (77%) persons participated in the 12-month follow-up health survey. This included 42 patients identified as transfers, 46 who were classified as LTFU, and 160 classified as retained in care. Ninety-one (37%) respondents reported using khat one or more times in the year after enrolling in care, with a median of 15 days of use in a typical month, and 5 h of use per day; the median use of khat in a typical month among these users was 60 h (IQR = 20–150). Forty-five (18%) of all persons with complete data reported using khat ≥ 60 h in a typical month (approximating the median among current users), and 25 (10%) reported using khat ≥ 150 h in a typical month. Among the 248 participants who

were seen at both time periods, 162 (65%) reported any use of khat in the year before enrollment, compared with 91 (37%) who used any khat in the year after enrollment ($p < .001$). Among those participants who continued to use khat during both time periods, the median calculated amount of use in a typical month decreased by 35 h.

Khat use and LTFU

Of 91 persons who reported any khat use in the year after enrollment in care, 21% were classified as LTFU, 16% as transferred, and 63% retained in care; rates of LTFU compared with retention in care did not differ significantly between those who did and did not use khat ($p > .10$) (Table 1). However, when we looked at those who used khat ≥ 60 h in a typical month (approximating the median), those who used khat this amount were more likely to be LTFU than retained in care ($p = .014$); differences were even more pronounced when we looked at who used khat ≥ 150 h in a typical month (representing the top quartile of use) ($p = .002$). Among those who used khat during the year after enrollment, those who were LTFU reported a median use of 150 h in a typical month, compared with a median use of 40 h in a typical month among those who were retained ($p = .013$).

Khat use and 3-day adherence

Of 210 persons who responded to questions during the 12-month survey about their ART adherence, 16 (8%) reported missing one or more doses of ART during the previous 3 days, for a 92% self-reported rate of complete 3-day adherence. Complete 3-day adherence was reported by 89% of those who used any khat in the year after enrollment compared with 94% of others ($p = .17$), by 77% of those who used khat ≥ 60 h in a typical month compared with 95% of all others ($p < .001$), and 67% of those who used khat ≥ 150 h in a typical month compared with 94% of all others ($p < .001$). Among those who used khat in the year after enrollment, those who did not have complete 3-day adherence reported a median use of 150 h in a typical month compared with 40.0 h

for those with complete 3-day adherence ($p = .011$). Complete 3-day adherence rates did not significantly differ by gender, age, marital status, education level, or alcohol use in the past year ($p > .10$) (data not shown).

Discussion

Among HIV patients newly enrolled in care in eastern Ethiopia, we found that frequent use of khat after enrollment in care was associated with lower retention and poorer ART adherence. Although any use of khat was not associated with either outcome, use of khat at least 60 h in a typical month was associated with poorer outcomes, with even greater differences when we looked at those with ≥ 150 h of use per month. Our cut-points of 60 and 150 h of use in a typical month were based upon the median and upper quartile values among users, so we cannot say what the threshold is for harmful effects; however, our data does indicate that the more one uses khat, the greater are the negative consequences.

Achieving the World Health Organization’s 90-90-90 goals for people living with HIV requires maximizing adherence and reducing LTFU after initiating HIV care. Our results suggest that khat, an amphetamine-like substance, may represent a potential barrier to meeting these goals. Our results are consistent with studies of methamphetamine and other drugs as factors associated with poorer ART adherence and retention in care.¹³⁻¹⁷

For those evaluated at both time periods, it is encouraging that any use of khat in the previous year decreased after enrollment in HIV care. Our analysis of khat use before and after entry into care must be interpreted with caution, since some of those using khat at baseline were not in the follow-up survey because of death, transfer, or LTFU. However, our results comparing baseline and follow-up results suggest some patients are motivated to stop their drug use.

Among those who continued to use khat during both time periods, some respondents reported a decrease in hours of use/month. Our findings suggest that for those continuing to use drugs, a harm reduction approach that discourages heavy khat use may be a reasonable option for some individuals. In certain communities, khat has social and cultural significance and acceptance^{3,19}; for these individuals, encouraging moderation in use rather than promoting total nonuse may be more favorably received.¹⁹ Various personal, clinic-related, or social factors may have motivated decreases in khat use among some participants. We recommend additional systematic qualitative or quantitative evaluation to determine which factors might have the greatest impact to encourage decreased use, and could be incorporated into harm reduction interventions.

There are several other limitations to this analysis. First, we surveyed people living with HIV (PLWH) entering HIV care in two cities where khat use is common⁶; results may differ in other populations and geographic areas. Second, because khat use and adherence were self-reported, some persons may have underreported frequency of khat use or overestimated their ART adherence. Although overreporting of self-reported 3-day ART adherence is documented,²⁰ our finding that khat users had poorer adherence is consistent with reports of other amphetamine-like derivatives and poorer ART adherence.^{13,17} Our other outcome, retention in care, was validated by reviewing clinic records from HIV clinics of enrollment. For 17 participants initially considered by their clinic as LTFU, we

TABLE 1. ONE-YEAR OUTCOMES AMONG HIV PATIENTS NEWLY ENROLLED IN CARE BY KHAT USE DURING A 12-MONTH PERIOD AFTER STUDY ENTRY: DIRE DAWA AND HARAR, ETHIOPIA, 2013–2014

	Transfer	Lost to follow-up	Retained	p ^a
Frequency of khat use ^b				
Any khat use, n (%)				
Yes (N=91)	15 (16)	19 (21)	57 (63)	>.10
No (N=157)	27 (17)	27 (17)	103 (66)	
≥ 60 Hours/month, n (%)				
Yes (N=45)	8 (18)	14 (31)	23 (51)	.014
No (N=199)	32 (16)	32 (16)	135 (68)	
≥ 150 Hours/month, n (%)				
Yes (N=25)	2 (8)	11 (44)	12 (48)	.002
No (N=219)	38 (17)	35 (16)	146 (67)	

Transfer=known to have transferred HIV care to another clinic; retained=attended HIV clinic one or more times in previous 90 days; lost to follow-up=no record of attending the HIV clinic for previous 90 days, and not known to have transferred or died.

^aComparing lost to follow-up with those who were retained.

^bHours/month missing data for four participants.

were able to ascertain by telephone follow-up that they had self-transferred care to other clinics; other participants who could not be located may have also transferred. Unaccounted transfers among patients initially classified as LTFU is also reported in other studies.^{21,22} Finally, relationships between khat use and poorer HIV treatment outcomes may be confounded by other factors, such as mental health, food insecurity, or socioeconomic status. However, even if this relationship is not causal, our analysis identifies an at-risk population for whom targeted programs could be beneficial. We recommend that future intervention trials to reduce khat use in PLWH should include in their outcomes retention in care, as well as changes in ART adherence, HIV clinical status, and laboratory measures such as CD4⁺ count and HIV viral load.

In summary, in two East African cities where khat use is common, frequent use was a significant risk factor for higher 1-year LTFU and lower self-reported ART adherence among PLWH entering HIV care. In settings where khat is widely utilized, interventions to promote either nonuse or reduced use are important as part of a comprehensive HIV care package and should be included as part of national HIV strategies to achieve 90-90-90 goals for PLWH.

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Author Disclosure Statement

No competing financial interests exist.

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