

Effects of khat use on response to antipsychotic medications in patients with newly diagnosed schizophrenia: a retrospective study

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Abstract

Background: Khat contains the amphetamine-like cathinone, and can trigger onset of schizophrenia and exacerbate pre-existing psychosis. However, it remains unknown whether the use of khat complicates the outcome of schizophrenia treatment.

Aims: We tested the hypothesis that patients with schizophrenia who are using khat will fail to respond to standard antipsychotic treatment.

Methods: We retrospectively studied a consecutive series of patients who presented to an adult psychiatric clinic in Al-Amal Psychiatric Hospital in Jazan, Saudi Arabia, between January 1, 2013 and December 31, 2016. Patients with newly diagnosed schizophrenia on antipsychotic monotherapy ($n = 1007$, 817 men) were included and categorized into khat and non-khat users. A khat chewing index was developed to further categorize low, mild, moderate and heavy khat users. Antipsychotic medications were reviewed to determine their potential and the cause of substitution in association with khat use.

Results: There were 483 (48%) khat users. Olanzapine, haloperidol and aripiprazole were the most frequently used drugs (46.3%, 15.6% and 10%, respectively). The retention rate of the initial drug differed between the khat users and nonusers (53.8% and 78.4%, respectively). The proportion of moderate and heavy users (55% and 49%, respectively) who changed their initial drug was greater than that of low and mild users (35.6% and 44.7%, respectively). Lack of drug efficacy was the most appealing reason for switching the initial drug among moderate (51.7%) and heavy khat users (48.4%).

Conclusions: Khat use hinders an individual's response to initial antipsychotic drug treatment for schizophrenia. Further studies are warranted to investigate the treatment decisions for this group of patients.

Keywords: antipsychotics, drug response, khat, schizophrenia, treatment outcome

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Introduction

Khat is a commonly used drug in the Eastern Mediterranean Region, which is becoming more prevalent in some countries, including Saudi Arabia (1). In Jazan, which lies in Southwest Saudi Arabia, khat use has been a traditional practice and the current pattern of use is becoming more excessive (2). Khat is consumed by chewing, which continuously produces pharmacokinetic properties (3,4). The fresh leaves and twigs of the khat shrub contain high concentrations of cathinone, an amphetamine analogue that produces euphoric effects (3,4). The other desired effects reported by khat users include increased energy, empathy, openness, and increased libido (5,6). Although limited use may not be accompanied by serious consequences, prolonged exposure can lead to dependence, psychosis and mood disturbances (7–10). The World Health Organization (WHO) has stated that khat causes psychological but not physical dependence among moderate users who consume the drug on a daily basis (11).

Schizophrenia is a complex neurodevelopmental disorder with high heritability (12). Epidemiological studies from the United States of America, Europe,

and Australia have consistently demonstrated that half of patients with a first episode of psychosis have co-occurring substance use disorders (in particular, alcohol, cannabis and stimulants), which is at least 3 times higher than that in the general population (13–15). Co-occurrence may result in more psychotic symptoms (hyperactivity, mood liability, impulsivity, hostility and uncooperativeness), depressive symptoms, and greater perceived stigma (7–10). By contrast, only a few studies have shown that khat has a particular propensity to induce or aggravate psychiatric symptoms in countries where the chewing of khat leaves is common (8,16,17). Little is known about the association between khat use and response to antipsychotic treatment in schizophrenia patients. Importantly, clinicians in our region have the impression that khat use has a higher propensity to induce or aggravate psychiatric symptoms and complicate the outcome of schizophrenia treatment in some patients.

This clinical observation was one of the primary motivations to initiate this study. We retrospectively studied a consecutive series of patients who presented over a 4-year period to an adult psychiatric clinic for assessment with a potential first episode of

schizophrenia. We included all patients with newly diagnosed schizophrenia on antipsychotic monotherapy. The antipsychotic medications were reviewed to determine their potential and the cause of substitution in association with khat use. We aimed to test the hypothesis that patients with newly diagnosed schizophrenia who are classified as khat users fail to respond to standard antipsychotic monotherapy. Failure was defined as the need to change the initial antipsychotic drug due to lack of efficacy in controlling the symptoms of schizophrenia and/or intolerable adverse effects.

Methods

Study design

We retrospectively assessed a consecutive series of patients with newly diagnosed schizophrenia who attended an adult psychiatric clinic in Al-Amal Psychiatric Hospital in Jazan, Saudi Arabia, between January 1, 2013 and December 31, 2016. The study hospital is the only government mental health facility in the region.

Patients

We included all adults with newly diagnosed schizophrenia on antipsychotic monotherapy. The term newly diagnosed was defined as having no previous diagnosis of schizophrenia and no history of antipsychotic medication 12 months before their first presentation to the adult psychiatric clinic. Patients' data were collected from the Al-Amal Psychiatric Hospital database. The records were assessed thoroughly by 3 psychiatrists, and the following data were entered on a pre-prepared electronic data collection sheet on the survey monkey database: sex, age, detailed description of symptoms, clinical presentation, investigations, antipsychotic medication, drug combination with other central nervous system (CNS) stimulants or depressants, khat chewing behaviour (duration, frequency and amount), and screening tests for other CNS stimulants. We excluded patients with a history of substance abuse including amphetamines, alcohol and cannabis, and history of medication that could affect dopaminergic neurotransmission within 3 months before the first presentation.

Adult psychiatric clinic: routine investigation and diagnosis

Each patient was assessed thoroughly by a consultant psychiatrist. This included a detailed description of events of interest as well as associated symptoms. Screening tests to detect the presence of amphetamines or cannabinoids were routinely requested. Since chewing khat is more prevalent in this region than in other areas of the country, questioning patients regarding khat use is part of the daily practice in the clinics, and precise information is always obtained. Diagnosis of schizophrenia was established by a consultant psychiatrist according to International Classification of Diseases, 10th Revision.

Khat chewing index

A simple index was developed to measure the degree of khat use according to the data available. The index was also used to categorize khat users into groups. The idea was based on the smoking severity index with some modifications to measure khat use.

Khat chewing index = amount of khat usually used/session × number of days usually using khat/week during the last year × number of years of using khat

The amount of khat used was calculated and expressed in piles (~1 kg). We did not multiply the number of days per week by 48 weeks, as the same number was used to calculate the amount of khat consumed by all users, and doing so would have increased the result for no reason. Hence, all khat users were categorized into quartile bases in order to develop the following 5 categories: 1- non-khat users; 2- low users, comprising khat users with an index < 25%; 3- mild users, comprising khat users with an index of 25–50%; 4- moderate users, comprising khat users with an index of 50–75; and 5- heavy users, comprising khat users with an index > 75%.

Statistical analysis

Descriptive analyses were performed using SPSS for Mac version 23. For analysis of age differences in terms of the proportion of patients whose initial antipsychotic treatment was substituted, both khat users and nonusers were categorized into three age groups (18–24, 25–44 and 45–64 years). The proportion of patients whose initial antipsychotic treatment was substituted was measured in each age group. Categorical comparisons were carried out using the χ^2 test. The level of significance was set as $P < 0.05$.

Ethical approval

The study was approved by the Jazan Health Human Research Ethics Committee (HREC No. 1437-SCBRE-03). Patient confidentiality was maintained by coding patients' files without disclosure of any private information.

Results

Patient characteristics

We included 1007 patients with newly diagnosed schizophrenia on antipsychotic monotherapy [mean (standard deviation) age: 33.6 (9.7) years, range: 18–77 years] (Table 1). Of those patients, 817 (81.1%) were men and 492 (48.9%) were khat users. Approximately 56% of patients achieved below secondary educational level, while 57.5% were unemployed. Of the 1007 patients, 193 (19%) were lost to follow-up after their first presentation. There was no significant difference between the proportion of khat users and non-khat users lost to follow-up after their first presentation (104/483, 21.5% vs 89/524, 17%, respectively).

Antipsychotic drugs

Atypical antipsychotics were more preferred than the typical agents (Table 2). The most commonly used atypi-

Table 1 Demographic characteristics of newly diagnosed schizophrenia patients between 1 January 2013 and 31 December 2016

Demographic characteristics	Khat users	Non-khat users	Total
Patients, n (%)			
Low	118 (11.7)	524 (52.0)	1007
Mild	123 (12.2)	–	–
Moderate	120 (11.9)	–	–
Heavy	122 (12.1)	–	–
Total	483 (48.0)	–	–
Age, mean (SD) years	33.3 (8.6)	33.9 (10.6)	33.6 (9.7)
Sex, n (%)			
Male	489 (59.9)	328 (40.1)	817 (81.1)
Female	3 (1.6)	187 (98.4)	190 (18.9)
Education, n (%)^a			
Less than high school	232 (52.6)	209 (47.4)	441 (43.7)
High school	186 (52.8)	166 (47.2)	352 (35.0)
Bachelor degree	35 (47.3)	39 (52.7)	74 (7.3)
Graduate degree	2 (40.0)	3 (60.0)	5 (0.5)
Not educated	35 (28.2)	89 (71.8)	124 (12.3)
Employment, n (%)^b			
Employed	188 (57.5)	139 (42.5)	327 (32.5)
Unemployed	264 (45.7)	314 (54.3)	578 (57.5)
Retired	32 (62.7)	19 (37.3)	51 (5.1)
Student	6 (16.7)	30 (83.3)	36 (3.6)
Housewife	0 (0)	13 (100.0)	13 (1.3)

^a11 cases missed (1.1%); ^b2 cases missed (0.2%).

cal antipsychotic drugs were olanzapine (46.3%), followed by aripiprazole (10.0%), and risperidone (9.3%). Haloperidol was the only typical antipsychotic used (15.6%).

Effects of khat use on antipsychotic drugs

Table 3 shows the effect of khat use on the retention rate of the initial antipsychotic drug. The difference in the initial drug retention rate between khat users and nonusers was significant (53.8% and 78.4% respectively, $P < 0.001$). The proportion of moderate and heavy khat users who changed their initial drug was significantly higher than that of low and mild khat users (55% and 49.2% vs. 35.6% and 44.7% respectively, $P < 0.001$). There was no significant sex difference between khat users and nonusers in terms of the proportion of patients whose initial antipsychotic treatment was substituted.

Table 4 shows the effect of khat use on substitution of the initial antipsychotic drug according to age group. Khat users aged 25–44 and 45–64 years had a significantly greater rate of drug substitution compared to those in the nonuser group (70.4% and 69.2% vs. 29.6% and 30.8% respectively, $P < 0.005$).

Reasons for initial antipsychotic drug substitution

Table 5 indicates that lack of drug efficacy was the most common reason for switching initial antipsychotic drug in 51.7% and 48.4% of moderate and heavy khat users, re-

spectively. Drug adverse effects and noncompliance, although common in those treated with antipsychotics, led to changes in initial drug treatment in a few cases only.

Discussion

This study assessed drug treatment outcomes in a clinically important, but understudied, group of patients with schizophrenia who were khat users and in an area where most people use khat as a tradition. Almost half of schizophrenia patients were khat users. Substitution of initial drug was greater in khat users than nonusers, and in the moderate and heavy khat users than low and mild users. Lack of drug efficacy was the main reason for switching the initial antipsychotic drug. These findings indicate that khat use hinders the response to initial antipsychotic drug treatment for schizophrenia.

The management of schizophrenia has become an enormous challenge and opportunity, particularly in patients with a lifetime history of use of substances like khat (*Catha edulis*). The evaluation and treatment decisions that are implemented in this situation can have an important impact on the subsequent course and outcome of schizophrenia. This study is believed to be the first to address the interaction between antipsychotic drug and khat use in patients with newly diagnosed schizophrenia. The findings shed light on the many questions around appropriate treatment strategies and

Table 2 Frequency of use and maintenance dose of initial antipsychotic drug prescribed to patients with newly diagnosed schizophrenia

Drugs	Patients, n (%)	Maintenance dose, median (range)
Amisulpride	10 (1.0)	400 (200–800)
Aripiprazole	102 (10.1)	15 (5–30)
Clozapine	2 (0.2)	325 (250–400)
Haloperidol	157 (15.6)	10 (2–15)
Haloperidol (+ long-acting haloperidol)	7 (0.7)	10 (5–10)
Olanzapine	466 (46.3)	10 (5–20)
Paliperidone	74 (7.3)	6 (2–9)
Quetiapine	80 (7.9)	300 (100–800)
Risperidone	94 (9.3)	4 (1–8)
Risperidone (+ long acting risperidone)	6 (0.6)	5 (4–8)
Trifluoperazine	9 (0.9)	1 (1–1)

clinical recommendations for this important group of patients.

It has been suggested that excessive limbic dopaminergic activity plays a role in schizophrenia (dopamine hypothesis), with much emphasis on this role through the fact that the antipsychotic effect of typical drugs, such as haloperidol, is due to their blockade of dopamine (D₂) receptors (18). However, the dopamine hypothesis does not fully explain all aspects of schizophrenia. Diminished cortical or hippocampal dopaminergic activity has been found to underlie the negative symptoms of schizophrenia (e.g., emotional blunting, social withdrawal and lack of motivation). The atypical antipsychotic agents, which are potent serotonin (5HT_{2A}) receptor antagonists with less effect on D₂ receptors, have also been developed and proved to be more effective than the typical antipsychotic agents in treating negative symptoms of schizophrenia. The adverse effects, mainly extrapyramidal dysfunction, of the aforementioned drugs are fewer compared with those caused by typical antipsychotics (19). This finding

Table 3 Frequency of substitution of initial (first-line) antipsychotic drug prescribed to patients with newly diagnosed schizophrenia in association with khat use

Khat chewing index	Initial drug not substituted, n (%)	Initial drug substituted, n (%)	Total
Nonusers	411 (78.4)	113 (21.6)	524
Low users	76 (64.4)	42 (35.6)	118
Mild users*	68 (55.3)	55 (44.7)	123
Moderate users*	54 (45.0)	66 (55.0)	120
Heavy users*	62 (50.8)	60 (49.2)	122
Total	671 (66.6)	336 (34.4)	1007

*P < 0.001.

was also observed among patients using medication for schizophrenia at Jazan Psychiatric Hospital. Despite the efficacy of the antipsychotics, only 50% of the population responded. Poor response is associated with relapse, exacerbation, and premature discontinuation of treatment. Patients who fail to respond to treatment have a higher risk of hospitalization, and this could result in an increase in treatment cost (16,20).

Another cause of failure of treating schizophrenia symptoms is comorbid substance abuse, which commonly leads to dual diagnosis. Substance abuse, particularly amphetamines, is responsible for 40% of cases of psychosis (21). The dual diagnosis of schizophrenia and substance abuse comprises 50% of all schizophrenia patients (13), which is consistent with the results of the present study. It is often challenging to determine whether a patient has primary schizophrenia or substance abuse. Nevertheless, careful clinical interview and substance abuse screening may result in a rapid and accurate diagnosis. In the present study, khat (which is pharmacologically equivalent to amphetamine, but with lower potency) exacerbated schizophrenia symptoms, resulting in treatment failure (5,6). The treatment failure was more prevalent in the moderate and heavy khat users when we applied the khat chewing index, which determined the potential of drug substitution in association with the degree of khat use.

Much of the available information regarding the chemical constituents in khat arose from studies funded by WHO (3). Phenylalkylamines, which bear structural resemblance to the neurotransmitters dopamine and noradrenaline, are believed to be responsible for the psychostimulant nature of khat (22). These phenylalkylamines comprise cathinone and 2 diastereoisomers of cathine (norpseudoephedrine and norephedrine). Users of khat traditionally chew the youngest shoots and leaves, which contain the highest concentrations of cathinone (3). Cathinone appears to increase dopaminergic neurotransmission in a similar manner to amphetamine, by triggering presynaptic dopamine release and by inhibiting the reuptake of dopamine (23–25). Cathinone releases serotonin into the CNS (23). Therefore, khat can produce dose-dependent psychotic symptoms and worsen pre-existing psychosis. The risk-increasing effects have not yet been fully explained.

It is well established that the psychotic exacerbation of khat is dose dependent (1). The khat chewing habit varies from mild to excessive use among the Jazan population. Therefore, the khat chewing index was developed to determine the degree of khat use among individuals with schizophrenia. A total of 1007 patients aged 18–77 years were included in the present study. Data were collected to evaluate the changes in initial antipsychotic medication in relation to the 5 categories of khat use. A significant difference was observed in medication change between the groups. The results indicated a significant difference in medication change among patients with low, mild and heavy khat use compared with non-khat users. This suggests that the physicians usually administer the

Table 4 Comparison between khat users and nonusers in terms of proportion of patients whose initial antipsychotic treatment was substituted, according to age group

Age group (yr)	Number (%) of patients whose initial antipsychotic treatment was substituted		Total
	Khat users	Nonusers	
18–24	29 (48.3)	31 (51.7)	60
25–44	176 (70.4)	74 (29.6)	250
45–64	18 (69.2)	8 (30.8)	26
Total	223	113	336

maximum dose of antipsychotic drugs during the initial treatment, as observed in the present study.

Lack of drug efficiency was the most common reason for switching initial antipsychotic drugs, particularly among mild, moderate and heavy khat users. It significantly exceeded the development of intolerable adverse effects and noncompliance, which are more common in individuals with schizophrenia on antipsychotic drugs. This is despite the fact that, in the present study, antipsychotics were given at their maximum therapeutic doses. Failure to control schizophrenia symptoms prompts physicians to change the initial antipsychotic drug. This can be explained by the dual diagnosis of schizophrenia and khat use since khat intensifies the state of psychosis. This situation may require either increasing the dose or shifting to more efficient antipsychotics. To date, no pharmacological studies have reported the treatment decisions in this important group of patients. Until then, khat abstinence would be the mainstay of treatment, in addition to antipsychotic agents, psychological therapy, social support, and rehabilitation (11,17,26).

While this study had a number of strengths, including the number of individuals studied, it was also limited by its retrospective nature, which we attempted to minimize. In particular, the psychiatric assessment of symptoms, the causative relationship between khat use and antipsychotic efficacy, and the reason for antipsychotic switching, which were revisited and confirmed by the treating psychiatrists. The mean age of patients

suggests that even if the diagnosis had been recent, the onset of signs and symptoms could have been earlier. This finding could be explained by the fact that mental health conditions in Saudi Arabia are still considered to be a stigma. The Saudi National Health and Stress Survey (unpublished technical report, 2019) showed that 34% of Saudis meet the criteria for a mental health condition in their life, and only 5% of Saudis seek treatment for their mental health condition in a given year.

The study was limited by the self-reported use of khat, which meant that there was greater potential for information bias arising from the patients. However, taking into account that khat use is a traditional practice in the region, investigating the degree of khat use among patients is part of the daily practice in clinics, and precise information is always obtained. Another potential limitation was the lack of data on the titration pattern of drug dose. This could be explained by the fact that treating physicians usually start with the maximum well-tolerated dose of the antipsychotic drug in khat users. Moreover, we cannot exclude the fact that other confounding factors (e.g., other substance abuse, comorbidities, and adherence to treatment) may have contributed to the necessary change in initial antipsychotic medication (treatment failure). Hence, a prospective study is warranted to determine other confounding factors.

Conclusion

Khat is popular among schizophrenia patients, which makes them vulnerable to drug treatment failure. As we anticipated, antipsychotics were initiated using the maximum therapeutic dose in areas (such as Jazan) where psychostimulant drugs are used. This study opens the door for prospective studies to try and understand the phenomenon of khat use in schizophrenia and encourage the authorities to adopt more aggressive measures to avoid khat use.

Table 5 Cause of initial (first-line) antipsychotic drug substitution in khat users and nonusers

Khat chewing index, n (%)	Adverse effects	Lack of efficacy	Treatment noncompliance	Other reasons	Not substituted	Total
Nonusers	18 (3.4)	42 (8.0)	2 (0.4)	51 (9.7)	411 (78.4)	524
Low users	0 (0.0)	35 (29.7)	2 (1.7)	5 (4.2)	76 (64.4)	118
Mild users*	3 (2.4)	50 (40.7)	0 (0.0)	2 (1.6)	68 (55.3)	123
Moderate users*	1 (0.8)	62 (51.7)	0 (0.0)	3 (2.5)	54 (45.0)	120
Heavy users*	0 (0.0)	59 (48.4)	0 (0.0)	1 (0.8)	62 (50.8)	122
Total	22 (2.2)	248 (24.6)	4 (0.4)	62 (6.2)	671 (66.6)	1007

* $P < 0.001$.

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Competing interests: None declared.

Effets de la consommation de khat sur la réponse aux médicaments antipsychotiques chez les patients atteints de schizophrénie récemment diagnostiquée : étude rétrospective

Résumé

Contexte : Le khat contient de la cathinone de type amphétamine, qui peut déclencher une schizophrénie et exacerber une psychose préexistante. Cependant, on ne sait toujours pas si l'utilisation du khat complique le résultat du traitement de la schizophrénie.

Objectifs : Notre objectif était de tester l'hypothèse selon laquelle les patients atteints de schizophrénie qui consomment du khat ne répondront pas au traitement antipsychotique standard.

Méthodes : Nous avons procédé à une étude rétrospective sur une série de patients qui se sont présentés dans une clinique psychiatrique pour adultes à l'hôpital psychiatrique Al-Amal de Jazan, en Arabie saoudite, entre le 1^{er} janvier 2013 et le 31 décembre 2016. Les patients souffrant de schizophrénie nouvellement diagnostiquée et suivant une monothérapie antipsychotique (n = 1007, 817 hommes) ont été inclus dans l'étude et classés en deux catégories : les consommateurs et les non consommateurs de khat. Un indice de consommation du khat a été mis au point pour mieux catégoriser les personnes ayant une consommation faible, légère, modérée et importante. Les médicaments antipsychotiques ont été examinés afin de déterminer leur potentiel et la cause de la substitution en association avec la consommation de khat.

Résultats : Il y avait 483 consommateurs de khat (48 %). L'olanzapine, l'halopéridol et l'aripiprazole étaient les médicaments les plus fréquemment utilisés (46,3 %, 15,6 % et 10 %, respectivement). Le taux de rétention du médicament initial différait entre les consommateurs et les non consommateurs de khat (53,8 % et 78,4 %, respectivement). La proportion de personnes ayant une consommation modérée et importante (55 % et 49 %, respectivement) qui ont changé leur médicament initial était supérieure à celle des personnes ayant une consommation faible et légère (35,6 % et 44,7 %, respectivement). Le manque d'efficacité du médicament a été la raison la plus populaire pour changer le médicament initial chez les personnes ayant une consommation modérée (51,7 %) et importante (48,4 %).

Conclusions : La consommation de khat entrave la réponse d'un individu au traitement antipsychotique initial de la schizophrénie. Des études supplémentaires sont nécessaires pour examiner les décisions thérapeutiques pour ce groupe de patients.

آثار استخدام القات على استجابة مرضى الفصام المشخصين حديثاً للأدوية المضادة للذهان: دراسة استرجاعية

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الخلاصة

الخلفية: القات يحتوي على «كاثينون» مشابه للأمفيتامين، ويمكن أن يؤدي إلى ظهور الفصام وتفاقم الذهان الموجود مسبقاً. ومع ذلك، لا يزال من غير المعروف ما إذا كان تعاطي القات يعقد ويفاقم نتائج علاج الفصام.

الأهداف: هدفت هذه الدراسة إلى اختبار فرضية أن مرضى الفصام الذين يستخدمون القات سيفشلون في الاستجابة للعلاج المعياري المضاد للذهان.

طرق البحث: درسنا بأثر رجعي سلسلة متتالية من المرضى الذين قدموا إلى عيادة نفسية للبالغين في مستشفى الأمل والطب النفسي في جازان، المملكة العربية السعودية، في الفترة ما بين 1 يناير / كانون الثاني 2013 و 31 ديسمبر / كانون الأول 2016. مرضى الفصام الذين تم تشخيصهم حديثاً على العلاج الأحادي بمضادات الذهان (العدد = 1007؛ 817 رجلاً) تم إدراجهم وتصنيفهم إلى متعاطي القات وغير القات. تم تطوير مؤشر مضع القات لتصنيف متعاطي القات المنخفض، والمعتدل، والمتوسط، والثقيل. تمت مراجعة الأدوية المضادة للذهان لتحديد إمكاناتها وسبب الاستبدال بالاشتراك مع استخدام القات.

النتائج: كان هناك 483 شخصاً (48٪) من مستخدمي القات. وكانت الأدوية الأكثر استخداماً هي أولانزابين وهالوبيريدول وأريبيرازول (46.3٪ و15.6٪ و10٪ على التوالي). واختلف معدل استبقاء العقار الأولي بين متعاطي القات وغير المتعاطين (53.8٪ و78.4٪ على التوالي). وكانت نسبة معتدلي التعاطي للقات وكثيفي التعاطي (55٪ و49٪ على التوالي) الذين غيّرُوا تعاطيهم الأولي أكبر من نسبة منخفضي التعاطي ومتوسطي التعاطي (35.6٪ و44.7٪ على التوالي). وكان عدم فعالية الأدوية هو السبب الأكثر لتغيير الدواء الأولي بين متعاطي القات المعتدلين (51.7٪) ومتعاطي القات بكثافة (48.4٪).

الاستنتاجات: يعوق تعاطي القات استجابة المصاب بالفصام للعلاج بالدواء الأولي المضاد للذهان. وهناك ما يبرر إجراء مزيد من الدراسات لاستقصاء قرارات العلاج لهذه الفئة من المرضى.

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