

Relative effectiveness of N-acetylcysteine and baclofen as anticraving agents in cannabis dependence – A retrospective study with telephonic follow-up

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ABSTRACT

Background: Cannabis dependence is associated with psychiatric, social, and legal consequences. Currently, there is no approved pharmacological treatment for cannabis dependence. Recent studies have reported the utility of N-acetylcysteine (NAC) and baclofen (BAC) in the long-term treatment of cannabis dependence, primarily as anticraving agents.

Materials and Methods: We reviewed the records of all patients who received inpatient treatment during 2015–2017 for cannabis dependence syndrome. We included cases only if cannabis dependence was noted as the primary focus for seeking inpatient care. Data are collected up to 6 months following discharge and analyzed using Kaplan–Meier survival analysis. The time to the first use of cannabis (in days) following discharge is compared between three groups – psychosocial intervention (PSI) only, BAC in addition to PSI, and NAC in addition to PSI.

Results: During the study period, 238 inpatients were diagnosed with cannabis dependence syndrome. However, cannabis dependence was the primary focus of treatment in only 72 patients. Among these patients, 29 (40.2%) received PSI only while 25 (34.8%) received BAC (mean dose = 55 mg per day, standard deviation [SD] = 2.5 mg) and 18 (25%) received NAC (mean dose = 1800 mg per day, SD = 500 mg) in addition to PSI. While 47 (62.5%) of the patients had comorbid psychiatric disorders, it was comparably distributed in the three groups. A survival analysis shows that the probability of cannabis-free survival is significantly higher in the NAC group as compared to the BAC group which is in turn higher than the PSI group ($\chi^2 = 12.1$, $P = 0.002$).

Conclusion: The use of anticraving medications, namely BAC and NAC, may be a useful option along with PSIs in patients with cannabis dependence and requires further exploration.

Key words: Anticraving, baclofen, cannabis, N-acetylcysteine

INTRODUCTION

A recent national survey has reported that India has approximately 2.5 million cannabis-dependent patients.^[1]

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The current national and international guidelines do not recommend the use of pharmacotherapy for the treatment of cannabis dependence to control craving or promote abstinence.^[2,3] As a result, psychosocial interventions (PSIs) such as cognitive behavioral therapy, motivational

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interviewing, and contingency management are considered the default mode of evidence-based treatment for cannabis dependence.^[4]

A recent research has reported N-acetylcysteine (NAC) and baclofen (BAC) as potential anticraving agents that can augment PSIs aimed at promoting abstinence from cannabis. However, the evidence is equivocal^[5,6] in the case of NAC and preliminary in the case of BAC.^[7,8]

In this study, we report the use of NAC and BAC for the treatment of cannabis dependence in patients who received inpatient treatment at a tertiary care addiction medicine center. Our objective is to compare the effectiveness of using an anticraving agent (NAC or BAC) in addition to PSI in promoting abstinence in cannabis dependence syndrome.

MATERIALS AND METHODS

We reviewed clinical data from the charts of the patients admitted with a diagnosis of mental and behavioral disorders due to the use of cannabinoids, dependence syndrome (F12.2), between January 1, 2015, and December 31, 2016, at the Centre for Addiction Medicine, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru, Karnataka, India. As a standard procedure, each patient is seen by at least two qualified psychiatrists before a diagnosis is made. In case of discrepancy, the case is reviewed by another psychiatrist and diagnosis is finalized based on consensus. All diagnoses are made using the International Classification of Diseases (ICD-10).^[9] We use a structured clinical assessment focusing on cannabis consumption (age at onset, quantity–frequency measures, duration of use, and ICD-10 criteria for dependence), comorbidities (medical, psychiatric, and substance use related), and family history (substance-related and psychiatric disorders). A limited set of these variables are then entered in an electronic database. This dataset was used to generate a list of cases with a diagnosis of F12.2.^[9] We included patients with multiple substance use disorders or dual diagnosis, only if cannabis dependence was noted as the primary focus of treatment. Each file was reviewed by two authors (VLN and SRPS), and data regarding sociodemographic variables, substance use, diagnoses, and cannabis use in the next 6 months following discharge were extracted. If the patient had dropped out from follow-up, they were contacted

over phone, as part of our typical follow-up protocol. During the telephonic conversation, they were asked regarding the details of substance use and improvement. They were also advised to follow-up at the hospital.

For analysis, patients were classified into three groups. Group 1 – Patients who only received PSI, i.e., individual and family psychoeducation and group therapy for relapse prevention (PSI); Group 2 – Patients who received NAC in addition to the interventions received by Group 1 (NAC); and Group 3 – Patients who received BAC in addition to interventions received by Group 1 (BAC). A Kaplan–Meier survival analysis was done with “cannabis use following discharge” as the event of interest in R software (R Foundation for Statistical Computing, Vienna, Austria).^[10] Incomplete information was incorporated into the model as right-censored data.

This study is approved by the Institutional Ethics Board.

RESULTS

A total of 238 patients with a diagnosis of cannabis dependence were admitted in the period under review. However, only 72 male patients fulfilled the inclusion criteria and thus constituted the sample for this study. Table 1 reports the distribution of cases across three treatment groups, treatment details, and outcome in this sample.

Around two-thirds (65.2%) of patients had a comorbid psychiatric illness. Schizophrenia, substance-induced psychotic disorder, and bipolar affective disorder were the most common diagnoses at the time of admission [Table 2]. The three groups did not differ with respect to associated comorbid psychiatric illness [Table 3].

Survival analysis revealed that those in the NAC group had the highest probability of survival, i.e., less chance of relapse compared to BAC and to PSI alone ($P < 0.05$) [Figure 1].

DISCUSSION

This study reports the self-reported outcome of a sample of patients who received inpatient treatment for the treatment of cannabis dependence; a majority of whom

Table 1: Proportion of cases in different groups, age of the first use of cannabis, and age of seeking current treatment among three groups

Group	n (%)	Mean (SD)			Number of patients abstinent after 6 months (percentage of n of the group), n (%)
		Age at the first use of cannabis in years	Age at the time of the first contact in years	Mean dose/day, mg	
PSI alone	29 (40.2)	17.62 (3.08)	22.37 (4.13)		5 (17)
BAC with psychosocial intervention	25 (34.8)	19.36 (4.88)	23.64 (5.59)	55 (2.5)	10 (40)
NAC with psychosocial intervention	18 (25)	18.64 (3.96)	27.5 (8.58)	1800 (500)	11 (61)
Total	72 (100)	18.47 (4.02)	24.09 (6.26)		26 (36)

PSI – Psychosocial intervention; BAC – Baclofen; NAC – N-acetylcysteine; SD – Standard deviation

also suffered from a comorbid psychiatric illness and provide preliminary evidence to support the use of anticraving agents. We found that patients are more likely to abstain if they receive pharmacotherapy in addition to the standard treatment. Furthermore, patients receiving NAC are more likely to abstain than patients receiving BAC.

NAC has been found promising in neuropsychiatric conditions involving glutamatergic pathways.^[11] It is thought to correct the glutamatergic dysfunction which is one of the critical processes in addiction.^[12,13] BAC also fared better compared to PSI alone, which could be because of its effect on gamma-aminobutyric acid-ergic dysfunction in patients with chronic cannabis use.^[14] We used BAC at

doses which were equivalent to the doses found efficacious in alcohol dependence.^[15] This study provides a basis for exploring the potential role of BAC as an anticraving agent for cannabis dependence. In the study, 5/29 (17%) patients maintained well on PSIs alone, significantly less than the other groups. As there are no approved agents for the management of cannabis dependence, psychotherapy forms the frontline management plan. Contingency management, motivational enhancement therapy, and cognitive behavioral therapy have some evidence for managing cannabis dependence.^[4]

Limitations

As a retrospective study, this study is prone to bias associated with the study design. We cannot rule out confounding by indication in this study. Urine cannabis testing was done for some patients but was not included in the study due to missing data for a substantial number of patients, and also, there was no specific timeline at which the urine testing was done. In patients who were lost to follow-up, a telephonic follow-up was done to find the status of the patients' condition, which could have made a difference in terms of reliability of the information obtained through the telephonic follow-up. Although there was no difference between the groups concerning comorbid psychiatric disorders, two-thirds of the patients had a comorbidity. Hence, we cannot generalize these findings to patients with only cannabis dependence. Considering the study included only inpatients, usually admitted with severe problems, generalizability of the findings to patients with mild cannabis use-related problems treated on an outpatient basis is difficult.

Table 2: Details of the comorbid psychiatric illness in different groups

Group	Nil	SIPD	Schizophrenia	BPAD	Depression	Others	Total
PSI	8	8	6	5	1	1	29
BAC	12	2	3	4	1	3	25
NAC	5	3	2	5	0	3	18
Total	25	13	11	14	2	7	72

BAC – Baclofen; BPAD – Bipolar affective disorder; NAC – N-acetylcysteine; PSI – Psychosocial intervention; SIPD – Substance-induced psychotic disorder

Table 3: Comparison of the distribution of comorbid psychiatric illness between the groups

Comorbid psychiatric illness	Absent	Present	χ^2 (P)
PSI	8	21	2.97 (0.22)
BAC + PSI	12	13	
NAC + PSI	5	13	

BAC – Baclofen; NAC – N-acetylcysteine; PSI – Psychosocial intervention

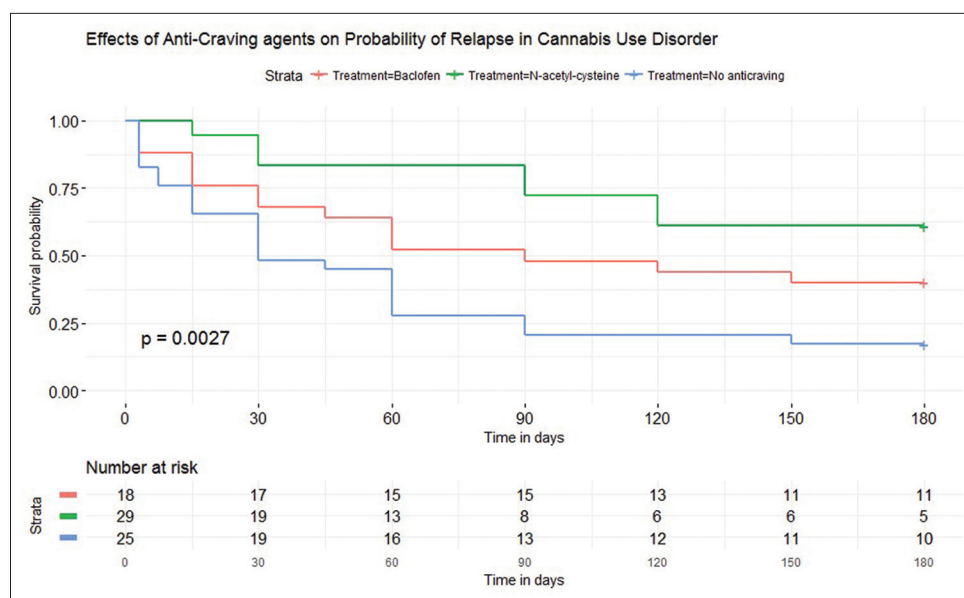


Figure 1: Survival curves of the three groups (psychosocial intervention vs. baclofen vs. N-acetylcysteine) illustrating N-acetylcysteine group had a better chance of survival and less chance of relapse compared to baclofen and to psychosocial intervention ($P < 0.05$)

Despite these limitations, there are positive indications that adding an anticraving may give better outcomes compared to PSI only. This study also provides a positive signal toward the use of BAC as an anticraving agent in persons with cannabis dependence.

CONCLUSION

The use of anticraving medications, namely BAC and NAC, may be a useful option along with PSIs in patients with cannabis dependence and requires further exploration.

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Conflicts of interest

There are no conflicts of interest.

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