Asian Journal of Psychiatry 30 (2017) 180–184

Contents lists available at ScienceDirect

Asian Journal of Psychiatry

journal homepage: www.elsevier.com/locate/ajp

Regional update

Cannabis induced psychosis and subsequent psychiatric disorders

Dharav Shah, Prabhat Chand*, Mrunal Bandawar, Vivek Benegal, Pratima Murthy

Dept. of Psychiatry, National Institute of Mental Health And Neuro Sciences (NIMHANS), Bangalore 560029, India

ARTICLE INFO

Keywords:
Cannabis induced psychosis
Substance induced psychosis
Cannabis
Follow up
Long term course

ABSTRACT

Introduction: Long term change in diagnosis of patients having Cannabis induced psychosis (CIP) at the index evaluation is well recognised. Some patients are known to achieve complete remission while others go on to develop independent schizophrenia or mood disorders.

Aims: To study the long-term course of CIP and factors influencing it.

Method: Patients diagnosed as CIP (ICD 10: F12.5), admitted at NIMHANS, a tertiary neuropsychiatry centre at Bangalore, over the past 10 years were identified from medical records. 200 case records were identified and screened in detail. 57 met inclusion criteria and 35 patients could be followed up. Mean follow up duration was 5.75 years.

Results: Patients who completely abstained from cannabis after the 1st episode had no relapse of psychiatric illness. They showed marked improvement in socio-occupational functioning as well. All those who relapsed to cannabis use had a recurrence of illness. Half the patients with predominantly non-affective psychosis progressed to an independent psychiatric disorder; while only 7.7% patients with predominantly affective psychosis developed an independent disorder ($p = 0.01$). Besides this, early onset of cannabis use (≤ 18 years), younger age at onset of 1 st episode, positive family history of psychiatric illness, being unmarried and lower socio-economic status were associated with poor prognosis. Abstinence later in the course of illness did not improve outcome significantly.

Conclusion: Abstaining from cannabis early in the course of illness is critical for good recovery. The course of CIP is variable and categorising CIP into affective vs. non-affective psychosis can be useful in clinical practice.

1. Introduction

Cannabis is the most common illicit substance of abuse and the estimated prevalence of cannabis use in India is 3% in general population (Ray, 2004) and 11% among patients seeking treatment in the major centres across India (Murthy et al., 2010). Cannabis has been widely used across the world despite a growing body of evidence to suggest an association between cannabis and chronic psychosis (Andreasson et al., 1987; Le Bec et al., 2009). Studies have also shown that when taken by healthy volunteers, cannabis produces not just positive symptoms (paranoia & euphoria) but negative and cognitive symptoms as well; thereby mimicking typical features of Schizophrenia (D'Souza et al., 2004). Research has also indicated that 13% of cases of schizophrenia could be averted if all cannabis use were prevented (Zammit et al., 2002). Considering this close association, it is important to study what proportion of cases of Cannabis induced psychosis (CIP)[1] progress to develop an independent psychiatric disorder.

Short term outcome studies on CIP have consistently shown that complete remission of psychotic symptoms occurs in most cases (Kulhalli et al., 2007; Tunving, 1985). However, the long term course of CIP is not so well studied. Niemi-Pynttari et al. (2013) followed up 125 patients of CIP and found their 8 year cumulative risk of developing a Schizophrenia spectrum disorder to be 46%. Arendt et al. (2005) followed up 535 patients of CIP for at least 3 years and found that 44.5% converted to Schizophrenia spectrum disorders. Two similar studies wherein the proportion of patients with CIP was high, have also reported a high rate of conversion to Schizophrenia spectrum disorders in the long run (Crebbin et al., 2009; Komuravelli et al., 2011). There is lack of similar long term studies from India, where cannabis is the second most commonly abused intoxicating substance, next only to alcohol.

The current study, a case record review, was conducted to look at the long term stability of diagnosis of cannabis induced psychosis among inpatients of a tertiary neuropsychiatry centre in India. This study also looked at the factors that can influence the long term diagnosis and prognosis.

* Corresponding author.
E-mail addresses: dharavshah@gmail.com (D. Shah), prabhatkumarchand@gmail.com, chand@nimhans.ac.in (P. Chand), Drmrunal.nimhans@gmail.com (M. Bandawar), vbenegal@gmail.com (V. Benegal), pratimamurthy@gmail.com (P. Murthy).

[1] CIP = Cannabis induced psychosis, CIPD = Cannabis induced psychotic disorder, CIMD = Cannabis induced mood disorder.

http://dx.doi.org/10.1016/j.ajp.2017.10.003
Received 13 June 2017; Received in revised form 3 October 2017; Accepted 13 October 2017

2. Material and methods

2.1. Data collection

The study was initiated after obtaining ethical clearance from the institute ethics committee. The medical records of patients with a diagnosis of Cannabis Induced Psychotic Disorder (coded: F12.5 as per ICD 10) (World Health Organization, 1992) from January 2002 to October 2011 were obtained. Records of patients coded as having Cannabis Dependence were also screened. The case records contained notes of a detailed evaluation, wherein a postgraduate trainee evaluates the case through clinical interview with the patient and caregivers and then discusses the case with the consultant psychiatrist; following which the final diagnosis and treatment formulation are made (Chand et al., 2010). Study from this centre has shown that information from family members regarding drug use is highly reliable and corroborates with objective measures of substance use, like urine toxicology (Chand et al., 2014). The following criteria were used to screen the patients.

2.1.1. Inclusion criteria

- Having Cannabis induced psychotic disorder at index presentation, be it 1st episode or recurrence.
- Between 16–70 yrs. of age at the time of index presentation.
- Gender: Both male and female.
- Those residing within the city where the centre is located (so that personal follow up would be feasible).

2.1.2. Exclusion criteria

1) Established past history of independent psychotic disorder.
2) Psychotic symptoms were only transient; limited to the phase of Cannabis Intoxication or Cannabis withdrawal.
3) Primary diagnosis of any other Axis 1 disorders except substance dependence or abuse.
4) Medical illness that may significantly influence CNS function or structure (including mental retardation, significant head injury, seizure disorder, etc.).

The previous study (Kulhalli et al., 2007) focussing on psychopathology of cannabis related psychosis from the same centre has shown a substantial proportion of patients presented with affective symptoms (manic) i.e. grandiosity, excitement etc. But ICD 10 has only one category for cannabis induced psychosis unlike DSM IV. Hence patients included in the study were sub-classified into Cannabis induced psychotic disorder (CIPD) and Cannabis induced mood disorder (CIMD) (as per DSM-IV criteria) (Codes 292.1 and 292.84 respectively) (American Psychiatric Association, 1994), as per the clinical data in medical records. This was done to observe if there was any difference between the two groups with regards to their clinical course.

Socio-demographic data, baseline clinical details and follow up details were noted from the records. Patients along with their family members (care givers) were interviewed after being contacted either during follow up at the hospital or by a home visit. After taking an informed written consent, the participating subjects and one key informant (i.e. a close contact who knows the subject since prior to the onset of illness and who continues to be in contact during the course of illness) were interviewed using Psychiatric Research Interview for Substance and Mental Disorders for DSM IV (PRISM) (Hasin et al., 2006), Psychiatric and Personal History follow-up Schedule (PPHS) (Jablensky et al., 1992), a semi structured proforma and a symptom check list. PRISM is a clinician administered diagnostic interview designed expressly for assessing comorbid psychiatric disorders in individuals with substance use disorders. It helps in systematically differentiating between substance induced disorders and independent disorders. PPHS, used in International Pilot Study on Schizophrenia (IPSS), covers various domains like pattern, number and duration of episodes, substance use course, changes in work performance and income, etc.

The presence of cannabis and its metabolite was tested in the urine by using gas chromatography and mass spectrometry method (Sharma et al., 2012) for confirming the recent use of cannabis. Appropriate treatment and advice was provided to all patients contacted.

Records of inpatient admissions in past 10 years were screened. But some of them had been admitted for recurrence and had been following up at the centre since many years. Thus we could study the clinical course over significantly long follow up durations. A total of 200 case records were reviewed of which 57 satisfied the inclusion and exclusion criteria. They were contacted in the following year and their follow up data was collected. A minimum follow up duration of 1 year was ensured. Data was analysed by using the Statistical package for social sciences (SPSS), version 21.0. Fisher's exact test was used for qualitative data and *t*-test was used for quantitative data.

3. Results

Of the 57 patients eligible for the study, detailed interviews could be carried out in 35 patients. Nineteen could not be traced due to inadequate contact details or shifting of place of residence. Another 3 patients refused consent to participate in the study. Among the 35 interviewed patients, 20 patients with regular follow-ups were interviewed at the hospital. Those who were not in regular follow up were contacted via telephone or home visit. Seven patients agreed for a home visit. Due to concerns about stigma 8 patients consented only for a telephonic interview. Urine testing could not be done in those who were interviewed only telephonically (Table 1).

3.1. Baseline demographic & clinical variables

All 35 subjects were male and only 5 were married. Half (48.6%) were from lower economic strata (monthly family income < Rs. 10,000). A majority (65.7%) had not received more than secondary level of education. Baseline clincal information was as shown in Table 2.

Family History of Psychiatric illness (other than substance dependence) was present in 20% of the subjects. As per DSM IV criteria, 22 were having Cannabis induced psychotic disorder and 13 were having Cannabis induced mood disorder at index episode. An episode of CIMD took significantly more time to respond as compared to an episode of CIPD. Average time of response (> 50% reduction in symptoms) after starting treatment was 10.05 days for CIPD (SD = 6.44) and 15.75 days for CIMD (SD = 6.92); (p = 0.02).

3.2. Diagnosis on long term follow up

Of those initially diagnosed with CIPD, in 9 patients (41%) the diagnosis got revised at follow-up to independent psychotic disorder and in 2 patients (9%) to independent mood disorder, as per PRISM. While

Table 1
Follow up details.

Variables	Percentage (frequency)
Type of interview	
Interview in Hospital	57.1 (20)
Home Visit	20 (7)
Telephonic interview	22.9 (8)
Duration of follow up since 1st episode	
1 yr	11.4 (4)
1–5 years	45.8 (16)
≥5 years	25.7 (9)
≥10 years	17.1 (6)

Table 2
Baseline clinical variables.

Variables	Median (range)
Age at onset of cannabis use	18 (8–66)
Age at 1st episode of CIP	24 (18–68)
	Percentage (frequency)
Duration of 1st Episode	
< 1 month	20 (7)
1–3 months	31.4 (11)
3 months–1 year	34.3 (12)
> 1 year	14.3 (5)
Onset	
Acute	48.6 (17)
Insidious	51.4 (18)
ECTs needed to be given	28.6 (10)
No of joints of cannabis/day	
0–5	45.8 (16)
> 5	51.4 (18)
No clear info	2.9 (1)

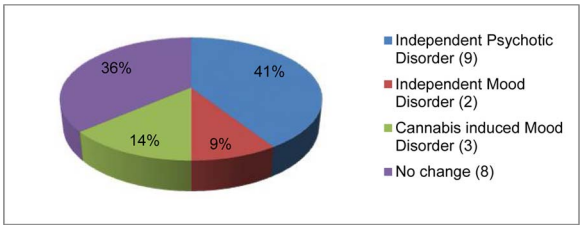

Fig. 1. Current diagnosis of those initially diagnosed as Cannabis induced psychotic disorder (22 patients).

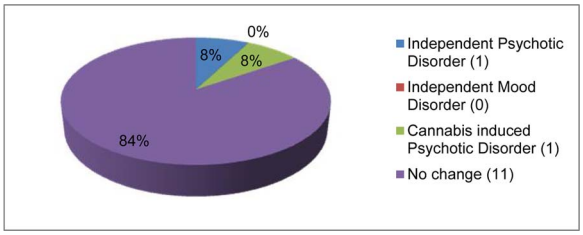

Fig. 2. Current diagnosis of those initially diagnosed as Cannabis induced Mood disorder (13 patients).

of those initially diagnosed with CIMD, only 1 patient (7.7%) progressed to independent psychotic disorder and none to independent mood disorder (Figs. 1 and 2).

3.3. Predictors of progression to independent psychiatric disorder

Besides diagnosis of CIPD at index episode (p = 0.01), early onset of cannabis use ≤18 years (p = 0.03), a younger age (< 22 years) at onset of 1st episode (p = 0.04) and a positive family history of psychiatric illness (p = 0.03) also predicted progression to an independent psychiatric disorder. Relapse of cannabis use after 1st episode was also associated with progression; but failed to reach statistical significance (p = 0.07). None of those who abstained after the 1st episode progressed to an independent psychiatric disorder; while 41.4% of those who relapsed to cannabis use developed it (Table 3).

'Duration of 1 st episode', 'duration of untreated illness during 1 st episode' and 'type of onset' (acute vs. chronic) were also analysed but did not show an association with change in diagnosis. Multifactorial analysis by logistic regression didn't show any significant associations; probably because of the small sample size.

Table 3
Predictors of progression to an independent psychiatric disorder.

Predictor variable	Independent Disorder on follow up	Cannabis induced disorder on follow up	Fisher exact test.
			P value
Index episode			
Cannabis induced psychosis	11	11	0.01
Cannabis induced mania	1	12	
Family history of Psychiatric illness			
Present	5	2	0.03
Absent	7	21	
Age at onset of Cannabis use			
≤18 years	10	10	0.03
> 18 years	2	13	
Age at onset of 1st episode			
≤22 years	9	8	0.04
> 22 years	3	15	
Subsequent cannabis use			
Complete abstinence	0	6	0.07
Relapse of cannabis use	12	17	

Table 4
Course of illness and cannabis use in the interval Period.

	Percentage (frequency)
Favourable course	60 (21)
Complete recovery	11.5 (4)
No relapse but residual personality change	5.7 (2)
One or more relapses with near full remission	42.9 (15)
Unfavourable course	40 (14)
One or more relapses against a background of marked personality change	31.4 (11)
Continuous psychotic illness	5.7 (2)
Initial good response but now continuous psychotic illness	2.9 (1)
Cannabis use pattern since index episode	
Did not use at all after index episode	17.1 (6)
Continued problematic use after discharge but now abstinent or occasional use	25.7 (9)
Abstinence after discharge but later relapsed to problematic use	48.6 (17)
Never abstained	5.7 (2)
No definite info	2.9 (1)
At least 1 period of abstinence from cannabis for more than 1 year	48.6 (17)
Had Problematic Extra-pyramidal symptoms	31.4 (11)
Attempted suicide at least once	14.3 (5)
Clear history of road traffic accident due to cannabis use	11.4 (4)

3.4. Course of illness

The most common pattern of course seen was of one or more relapses with complete recovery inter-episodically (in 43% patients). Though 60% patients had a favourable course of illness as shown in Table 4, complete functional recovery with regular paid employment could be achieved in only 22.9%. Also 54% of subjects were being perceived to be dangerous to self or others by the key informant. Thus a large proportion of subjects were not able to resume adequate socio-occupational functioning.

Hailing from higher socioeconomic status (p = 0.01), later age of starting cannabis use (p = 0.01), later age at onset of 1st episode (p = 0.04) and abstinence from cannabis after 1st episode (p = 0.06) predicted a favourable course. While onset of cannabis use after 18 years (p = 0.02), an older age at onset of 1 st episode (p = 0.02) and

being married at the time of 1 st episode (p = 0.05) predicted a higher probability of the person working regularly in paid employment.

The clinical symptoms most significantly associated with an unfavourable course of illness were 'poor self care' (p = 0.01) and 'motor retardation' (p = 0.06). Manic syndrome tended to have a better prognosis e.g. 'motor hyperactivity' was associated with the person working regularly in paid employment (p = 0.06). However, grandiose delusions were associated with the person not working well (p = 0.02)

3.5. Qualitative observations on impact of subsequent cannabis use on outcome

There were 6 patients who were abstinent from cannabis ever since the index episode; 3 of them had CIMD and 3 had CIPD. All 6 of them did not have any further relapses. Five of them showed marked improvement in their occupational functioning as well. 1 of them had become a rag-picker while using cannabis; but now he has been working consistently since past 4 years. 1 of them had changed 8 jobs before admission and had significant domestic violence. Now he has been working consistently in 1 company since the past 8 years and his wife finds him to be a completely changed person, pleasant to live with. 1 of them had a continuous psychotic illness for 1 year and was absconding from home most of the time during this period. However, he remitted completely on stopping cannabis use and is maintaining improvement since 3 and half years. Fourth one also had significant socio-occupational dysfunction in past; but now has stable employment since 4 years. These 4 had stopped medications either immediately or within a few months of discharge, and yet continue to maintain remission from their symptoms. Fifth patient chose to resign from his job after the index episode as he found that his cognitive functioning was no longer sharp enough to enable him to do his job efficiently. However, he perceived that his cognitive abilities improved gradually, though not fully. After 18 months he took up another job demanding high level of accountability and long working hours; and had been doing it well since 6 months.

The converse was true as well. All those who relapsed to cannabis use had a relapse of illness also. One patient who had initially shown good response relapsed on restarting cannabis use and now has been having a continuous illness which is not responding even to Clozapine now. Two others had been absconding from home for prolonged durations. Another 2 patients have developed chronic amotivation syndrome; although they are abstinent from cannabis for more than a year now. Another 6 are having severe socio-occupational impairment with frequent altercations with family members & neighbours. Even in patients diagnosed with independent psychiatric disorder, most of the symptom relapses were precipitated by relapse of cannabis use. Both the subjects who didn't stop cannabis use at all after the index presentation have not had any period of remission till current follow up. One of them ended up wandering on the streets for many years and has been currently placed in a beggar's home.

3.6. Co-existence of psychotic and manic symptoms

Majority of the patients of CIP had the simultaneous presence of both manic & psychotic symptoms. Of those with a diagnosis of a mood disorder, 50% had suspiciousness, 50% had fearfulness and 43.8% had auditory hallucinations at least once during the course of illness. Similarly many of those with a diagnosis of a psychotic disorder had manic symptoms i.e. euphoria (63.2%), grandiosity (63.2%), increased indulgence in pleasurable activities (57.9%) and motor hyperactivity (42.1%) during the symptomatic phase. Interestingly, few patients who had presented with a predominantly psychotic disorder initially developed a predominantly mood disorder on follow up; and vice-versa. In 4 patients with an initial presentation of psychotic nature, the psychotic symptoms subsided following treatment; but a predominantly manic syndrome emerged. In 2 patients with CIMD who did not stop cannabis use, the manic syndrome lasted for more than a year.

4. Discussion

In our study, 34% of patients diagnosed with CIP at the time of first evaluation progressed to develop an independent psychiatric disorder at the end of 5.7 years (mean). This is slightly lower than the conversion rate of around 45% seen in the previous 2 studies on long term course of CIP done by Niemi-Pynttari et al. (2013). and Arendt et al. (2005). Rate of conversion was higher (50%) in the subset of patients with CIPD. Abstinence from cannabis use after the 1st episode itself was strongly associated with a favourable course and outcome; while persistence with cannabis use resulted in a drastically worse prognosis in many. This is consistent with existing literature (Gonzalez-Pinto et al., 2009; Zammit et al., 2008)

Younger age at onset predicted a poor outcome. This is in agreement with findings of previous studies which have also found age to be a predictor of illness course (Arendt et al., 2005). Similar to the vulnerability of the developing brain of adolescents to the toxic effects of alcohol (Hiller-Sturmhofel and Swartzwelder, 2004); it has been observed that adolescent cannabis exposure significantly impacts the *endo*-cannabinoid system of brain (Hurda et al., 2014).

CIPD at index admission had a much higher rate of progression to independent psychotic disorder (50%) compared to CIMD. On the other hand, an episode of CIMD took longer time to respond to treatment compared to an episode of CIPD. Thus differentiating between these two sub-groups at the time of diagnosis can be valuable in predicting the course of illness and deciding management plan.

Association of positive family history of psychiatric illness (other than that of substance use disorders) with the change to Independent psychotic disorder has been seen in a previous study also by Caton et al. (2007).

High prevalence of affective symptoms in cannabis induced psychosis seen in this study has been consistently documented in many previous studies also (Aggarwal et al., 2012; Nunez and Gurpegui, 2002; Kulhalli et al., 2007). Thus, co-existence of manic and psychotic symptoms appears to be a distinct characteristic of Cannabis induced psychotic and mood disorders.

The major limitation of our study remains that it is a retrospective chart review and has a smaller sample size. However, ours is a naturalistic sample and structured instruments were used to distinguish substance induced psychotic disorders compared to the independent psychotic disorder. Another advantage of the study was that, 43% of the patients included in the study had dropped out of routine follow up. Inclusion of such patients gave useful clinical data which generally doesn't come to the attention of practicing psychiatrists and adds to the validity of the results. The novel findings of this study need to be confirmed by prospective studies with a large sample size.

The results indicate that those who abstain from cannabis after an episode of CIP have a good prognosis; while relapse to cannabis use is associated with progression to independent psychiatric disorder, especially in those with non-affective psychosis at index episode.

Funding

None.

Conflict of interest

None.

Acknowledgements

Toxicology Laboratory of Centre for Addiction Medicine for providing cannabis urine drug testing facility.

References

Aggarwal, M., Banerjee, A., Singh, S.M., Mattoo, S.K., Basu, D., 2012. Substance-induced psychotic disorders: 13-year data from a de-addiction centre and their clinical implications. Asian J. Psychiatry 5 (3), 220–224.

American Psychiatric Association, 1994. Diagnostic and Statistical Manual of Mental Disorders, 4th edition. American Psychological Association, Washington.

Andreasson, S., Engstrom, A., Allebeck, P., Rydberg, U., 1987. Cannabis and schizophrenia A longitudinal study of Swedish conscripts. Lancet 330 (8574), 1483–1486.

Arendt, M., Rosenberg, R., Foldager, L., Perto, G., Munk-Jørgensen, P., 2005. Cannabis-induced psychosis and subsequent schizophrenia-spectrum disorders: follow-up study of 535 incident cases. Br. J. Psychiatry 187 (6), 510–515.

Caton, C.L., Hasin, D.S., Shrout, P.E., Drake, R.E., Dominguez, B., First, M.B., Samet, S., Schanzer, B., 2007. Stability of early-phase primary psychotic disorders with concurrent substance use and substance-induced psychosis. Br. J. Psychiatry 190 (2), 105–111.

Chand, P., Murthy, P., Arunachalam, V., Kumar, C.N., Isaac, M., 2010. Service utilization in a tertiary psychiatric care setting in South India. Asian J. Psychiatry 3 (4), 222–226.

Chand, P., Thirthalli, J., Murthy, P., 2014. Substance use disorders among treatment naïve first-episode psychosis patients. Compr. Psychiatry 55 (1), 165–169.

Crebbin, K., Mitford, E., Paxton, R., Turkington, D., 2009. First-episode drug-induced psychosis: a medium term follow up study reveals a high-risk group. Soc. Psychiatry Psychiatr. Epidemiol. 44 (9), 710.

D'Souza, D.C., Perry, E., MacDougall, L., Ammerman, Y., Cooper, T., Yu-te, W., Braley, G., Gueorguieva, R., Krystal, J.H., 2004. The psychotomimetic effects of intravenous delta-9-tetrahydrocannabinol in healthy individuals: implications for psychosis. Neuropsychopharmacology 29 (8), 1558.

Gonzalez-Pinto, A., Alberich, S., Barbeito, S., Gutierrez, M., Vega, P., Ibáñez, B., Haidar, M.K., Vieta, E., Arango, C., 2009. Cannabis and first-episode psychosis: different long-term outcomes depending on continued or discontinued use. Schizophr. Bull. sbp126.

Hasin, D., Samet, S., Nunes, E., Meydan, J., Matseoane, K., Waxman, R., 2006. Diagnosis of comorbid psychiatric disorders in substance users assessed with the Psychiatric Research Interview for Substance and Mental Disorders for DSM-IV. Am. J. Psychiatry 163 (4), 689–696.

Hiller-Sturmhofel, S., Swartzwelder, H.S., 2004. Alcohol's effects on the adolescent brain: what can be learned from animal models. Alcohol Res. Health 28 (4), 213.

Hurda, Y.L., Michaelides, M., Miller, M.L., Jutras-Aswad, D., 2014. Trajectory of adolescent cannabis use on addiction vulnerability. Neuropharmacology 76, 416–424.

Jablensky, A., Sartorius, N., Ernberg, G., Anker, M., Korten, A., Cooper, J.E., et al., 1992. Schizophrenia: manifestations, incidence and course in different cultures. A World Health Organization ten-country study. Psychol. Med. Monogr. Suppl. 20, 1–97.

Komuravelli, A., Poole, R., Higgo, R., 2011. Stability of the diagnosis of first-episode drug-induced psychosis. Psychiatrist 35 (6), 224–227.

Kulhalli, V., Isaac, M., Murthy, P., 2007. Cannabis-related psychosis: presentation and effect of abstinence. Indian J. Psychiatry 49 (4), 256.

Le Bec, P.Y., Fatseas, M., Denis, C., Lavie, E., Auriacombe, M., 2009. Cannabis and psychosis: search of a causal link through a critical and systematic review. L'Encephale 35 (4), 377–385.

Murthy, P., Manjunatha, N., Subodh, B.N., Chand, P.K., Benegal, V., 2010. Substance use and addiction research in India. Indian J. Psychiatry 52 (7), 189.

Niemi-Pynttari, J.A., Sund, R., Putkonen, H., Vorma, H., Wahlbeck, K., Pirkola, S.P., 2013. Substance-induced psychoses converting into schizophrenia: a register-based study of 18,478 Finnish inpatient cases. J. Clin. Psychiatry 74 (1), 94–99.

Nunez, L.A., Gurpegui, M., 2002. Cannabis-induced psychosis: a cross-sectional comparison with acute schizophrenia. Acta Psychiatr. Scand. 105, 173–178.

Ray, R., 2004. The Extent, Pattern and Trends of Drug Abuse in India: National Survey. Ministry of Social Justice and Empowerment, Government of India & United Nations Office on Drugs and Crime, Regional Office for South Asia.

Sharma, P., Murthy, P., Bharath, M.S., 2012. Chemistry, metabolism, and toxicology of cannabis: clinical implications. Iranian J. Psychiatry 7 (4), 149–156.

Tunving, K., 1985. Psychiatric effects of cannabis use. Acta Psychiatr. Scand. 72 (3), 209–217.

World Health Organization, 1992. International Statistical Classification of Diseases and Related Health Problems: Tabular List Vol. 1 World Health Organization.

Zammit, S., Allebeck, P., Andreasson, S., Lundberg, I., Lewis, G., 2002. Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: historical cohort study. BMJ 325 (7374), 1199.

Zammit, S., Moore, T.H., Lingford-Hughes, A., Barnes, T.R., Jones, P.B., Burke, M., Lewis, G., 2008. Effects of cannabis use on outcomes of psychotic disorders: systematic review. Br. J. Psychiatry 193 (5), 357–363.