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SHORT REPORT

Is cannabis an anti-antipsychotic? The experience in psychiatric intensive care

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Background Cannabis use is a major problem in inner cities and has been causally implicated in psychosis. Very few of the available hospital-based studies of the implications of cannabis usage have involved psychiatric intensive care units (PICU); but PICU receive many of the most challenging and resource-hungry—and incompletely understood—patients in the mental health system.
Aims To study the clinical impact of cannabis abuse in a PICU, and to compare the use of atypical and typical antipsychotics in this setting.
Method 115 patients admitted to a PICU consented to take part in an open label naturalistic study. BPRS, TCI-240, weight, length of admission and routine bloods were evaluated in all participants.
Results There was a high rate of cannabis abuse (71.3%) in the PICU population. Patients who abused cannabis spent longer in PICU because their psychoses were more severe. They were younger at first hospital admission. Cannabis also had metabolic implications, with higher blood glucose levels at admission and greater weight increase. Atypical antipsychotics were effective in treating psychosis inpatients positive to cannabis at admission.
Conclusion Our findings suggest that cannabis abusers had a more severe psychotic illness, especially in schizophrenia. There are additional complications in terms of weight gain for cannabis users.

KEY WORDS — Cannabis use; atypical antipsychotics; schizophrenia; weight gain; metabolism

BACKGROUND

Cannabis has been shown only comparatively recently to increase the risk of psychosis in adolescents (Arseneault *et al*., 2002) and young adults (van Os *et al*., 2002; Fergusson *et al*., 2003). Cannabis may increase the risk of schizophrenia by 30% (Zammitt *et al*., 2002). The consumption of cannabis in Europe and USA is going up (MacCoun and Reuter, 2001; Murray *et al*., 2002). This means that co-morbidity of psychosis and cannabis misuse will be seen more often by psychiatric services and lead almost certainly to an increased need for psychiatric services. Arseneault *et al*. (2004) have reviewed the evidence for a causal association between cannabis and psychosis.

However, psychiatrists often elicit an incomplete history of drug misuse in inpatients (Barnaby *et al*., 2003), despite a recent UK survey of mental health nurses that reported a 68% awareness of substance and alcohol misuse in the (Sandford, 1995). Earlier studies have shown in the USA a lifetime prevalence of substance misuse and alcohol misuse of 47% among users of psychiatric services (Regier, 1990). In the UK the prevalence ranges from 9% to 36% (Bernardt and Murray, 1986; Duke *et al*., 1994; Menezes *et al*., 1996; Brown, 1998).

Little is known of the impact of cannabis in psychiatric intensive care units (PICU), where patients are referred who are too disturbed to be accommodated safely on acute psychiatric wards. Unlike in many other countries, mechanical restraint is not employed in the UK. When a patient is very psychotic and disturbed in behaviour he or she usually is referred to a PICU. All such patients are detained under UK Mental Health legislation.

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Phillips and Johnson (2003) studied drug and alcohol misuse among inpatients with psychotic illness in two PICU and an 'open' psychiatric ward. They found that 89% of the patients had used illicit drugs or alcohol (or both) on the ward during a *previous* inpatient admission, and 83% used substances during the current admission. The rate of current use for cannabis in inpatient wards was 52%. These higher rates differ from previous reports that did not include patients in PICU (Menezes *et al*., 1996; Wright *et al*., 2000; McCredie, 2002).

Almost three-quarters of the British mental health organizations report that they are seeing more patients every year (King's Fund, 2003). One reason for this increase may be the increased use of cannabis and crack cocaine. Moreover, about half the people with psychotic illness in London's acute wards are also substance misusers and four out of five may continue to use the drug while in hospital (King's Fund, 2003). The need for more research into treatment for patients with psychosis and cannabis abuse has been pointed out by Weaver *et al*. (1999).

There is a general lack of psychopharmacological and service-oriented research amongst PICU patients—arguably the most vulnerable in psychiatry—despite the fact that it is possible to obtain informed consent from patients in PICU to take part in research.

No antipsychotic drug in the market is licenced for the treatment of drug induced psychosis. The majority of atypical antipsychotics have not been formally tested in populations positive to cannabis. Little is known about their efficacy or safety in that clinical context. The physician is therefore frequently faced with the clinical dilemma of prescribing medications off licence. Moreover, there are no currently available guidelines about the treatment of patients with drug-induced psychosis or psychotic patients positive to cannabis.

It may be that patients use the drug in an attempt to medicate themselves. However, cultural factors are also important. For example, cannabis use is rare among psychotic patients in Japan and in places where use of cannabis is widely condoned, either tacitly or otherwise, by society and law enforcement agencies.

METHOD

The authors are currently engaged in an open-label, prospective, naturalistic analysis of individual predictors of the response to antipsychotic medication in PICU. The Local Research Ethics Committee of the Institute of Psychiatry has approved this study.

Part of the assessment involves completion of the Brief Psychiatric Rating Scale (BPRS, Overall and Gorham, 1988) every 2 weeks during the admission to PICU. The patients undergo urinalysis for drugs (including cannabis). This is in the form of a radioimmunoassay—CEDIA (cloned enzyme donor immunoassay: Microgenics, Inc)—measured in the pathology laboratory of the Bethlem Royal Hospital on a Hitachi Analyser 912 able to register concentrations of cannabinoids in excess of 20 ng/ml.

Patients also have a full blood count and estimation of serum cortisol and prolactin, liver and kidney function. Patients' weight is recorded weekly, and patients are also invited to complete the 240-item version of the Temperament and Character Inventory (TCI-240, Cloninger, 1987). They receive information about medication and doses, and discussion about choices of medication follows guidelines published by the UK National Institute of Clinical Excellence (2002). Patients give informed consent to the use of their anonymized data when they have capacity to do so. The *SPSS for Windows (v. 11)* software package for statistical analysis was used. One-way ANOVA was used for the analysis unless otherwise mentioned.

RESULTS

The PICU has 11 beds for males only. There were 179 admissions to the PICU between January 2001 and November 2003, of whom 115 gave written consent to use their anonymized data when they had capacity to do so.

Geographically, patients are drawn from the London Borough of Croydon, a socially heterogeneous catchment area with a total population of 330 000 (2001 census). The MINI score index (based on the 1991 census) for Croydon is 100.1 (range for wards 81.7 to 111.1).

The main diagnoses among the 179 admissions to the PICU, according to the International Classification of Diseases (ICD-10, WHO, 1992), were schizophrenia (F20—98; 54.7%); bipolar affective disorder (F31—21; 11.7%); psychotic depression (F32—7; 3.9%); personality disorder (F60-F69—14; 7.8% with drug induced psychosis 11); schizo-affective disorder (F25—2; 1.1%); drug-induced psychosis (F10-F19—19; 10.6%); acute and transient psychotic episode (F23—15; 8.3%); 3 were Not Otherwise Specified or unclassified.

Among the 115 patients who gave consent, the chief ICD-10 diagnoses were schizophrenia (F20—72 individuals; representing 61.7% of the group); bipolar affective disorder (F31—16; 13.9%); psychotic

depression (F32—5; 4.3%); personality disorder (F60-F69—14; 12.1%; with drug-induced psychosis 11); schizo-affective disorder (F25—1; 0.8%) and drug-induced psychosis (F10-F19—7; 6%).

Fifty-one (59.8%) patients were of African or Afro-Caribbean origin; 42 (48.3%) were white, 13 (15%) were Asian, with 2 (2.3%) from the Middle East, and 7 (8.1%) described themselves as of mixed race.

Eighty-two (71.3%) patients reported past cannabis abuse. Sixty-four percent of the patients of Afro-Caribbean or African origin (33/51) reported previous cannabis abuse, compared with 78% of the white patients (33/42). Eight cannabis abusers were Asian, with one from the Middle East, and seven described themselves as of mixed race.

The patients with a history of cannabis abuse were younger when they were admitted to hospital for the first time (22.98 ± 7.5 years vs 28.0 ± 8.81 ($F = 6.078$; $p < 0.016$)). This age difference was more significant in patients with schizophrenia, where 50 of 71 reported a history of cannabis abuse (22.15 ± 5.76 vs 30 ± 9.45 ($F = 11.141$; $p < 0.002$)).

Sixty nine (60%) patients tested positive to cannabis on admission. They had more previous admissions to hospital than patients who tested negative to cannabis (4.08 vs 2.2; $p < 0.05$). If patients suffering from diabetes ($n = 7$) were excluded, patients positive to cannabis tended also to have more severe psychotic symptoms on admission than those who tested negative (BPRS $= 98.5 \pm 23.7$ vs 88.3 ± 24.8 ($F = 4.495$; $p < 0.036$), as well as higher glucose levels on admission (5.3 ± 1.08 mmol/l vs 4.8 ± 0.8 ($F = 4.641$; $p < 0.035$)).

Urinalysis indicated that 29 (25%) patients took cannabis *during* admission. They spent longer in hospital (97.6 days vs 49.5 ($F = 14.366$; $p < 0.001$)); they were younger (mean age 27.5 ± 6.5 years vs 32.6 ± 9.2 ($F = 7.525$; $p < 0.007$)); had been hospitalized earlier in life (mean age 20.4 ± 4.2 years vs 25.9 ± 8.7 ($F = 7.481$; $p < 0.008$)) and more often (5.1 ± 5.7 times vs 3.1 ± 2.0 ($F = 4.969$; $p < 0.029$)). They also put on more weight over 6 weeks (10.2 kg vs 2.2; ($F = 5.738$; $p < 0.05$)) on the same hospital diet. At 6 weeks, only 7 (24%) of this group had been discharged from PICU compared with 60 (74%) of patients who did not use cannabis during admission (chi-square $= 18.6$; $p < 0.001$).

One hundred and ten patients were treated with antipsychotic medication. The main ICD-10 diagnoses were schizophrenia (F20—72 individuals; representing 66% of the group); bipolar affective disorder (F31—15; 13%); psychotic depression (F32—5; 4%); personality disorder (F60-F69) with drug-induced psychosis (F10-F19—11; 10%); schizoaffective disorder (F25—2; 0.8%) and drug-induced psychosis (F10-F19—5; 5%).

Of the 67 patients positive to cannabis at admission 54 were treated with an atypical antipsychotic drug and 13 with typical. There were statistical differences in favour of atypical antipsychotics at day 14 (74.5 ± 23.6 versus 91.2 ± 15.0; $F = 4.995$; $p < 0.029$) and 28 (69.5 ± 20.6 versus 83.9 ± 20; $F = 3.901$; $p < 0.054$) in BPRS scores.

DISCUSSION

Our findings are in keeping with studies that have raised concerns about the use of cannabis and the risk of subsequent psychosis.

One leading authority (Murray, 2004) was recently quoted as describing this link between cannabis and psychosis as the 'number one problem facing the mental health services in inner cities'. In addition to clinical and service use issues the metabolic consequences of cannabis usage are the subject of continuing research.

Menezes *et al*. (1996) studied the same area of South London as our unit serves. They found that the 1-year prevalence for any substance problem was 36.3%, (alcohol, 31.6%; drug problems 15.8%). The prevalence of harmful cannabis use in patients of community mental health teams was 25.2% in 2003 (Weaver *et al*., 2003). This is far less than the observed current prevalence among our patients.

Here, cannabis use during admission was a major predictor of length of admission on PICU among patients suffering from major psychosis and personality disorders. In the Menezes study (Menezes *et al*., 1996), the patients with substance problems had spent twice as many days in hospital in the previous 2 years compared with patients that did not have substance problems.

The higher rate of cannabis consumption at the time of admission in the present study differ from consumption at the time of admission in similar settings in the UK, 52%, (Phillips and Johnson, 2003), and 46% for first episode schizophrenics in Spain (San *et al*., 2003). There were also differences in the rate of use during admission, which was lower in our study (25% vs 52% Phillips and Johnson, 2003).

One explanation for longer admission is that the patients are detained against their will under mental health laws and their illness is consequently more severe. All the patients are reviewed by an independent tribunal, which considers the patient to be ill enough to warrant continued detention.

Urinalysis is currently employed to estimate cannabis use. This method is sensitive to amounts of cannabinoids of 20 ng/ml. Urinalysis is often less acceptable to patients than buccal swabs. However, there may be an increased role for the quantitative estimation of cannabis usage based on hair analysis. This potentially allows more precise and reliable estimation of recent historical use of cannabis, and had been developed for various substances, most recently alcohol (Wurst *et al*., 2004).

Our study confirms findings that the use of drugs is one of the main reasons for the increased use of psychiatric services in London (King's Fund, 2003). It appears that patients who are unable to desist from using cannabis despite being on a locked psychiatric ward are more severely affected by their underlying psychosis.

Swofford and his colleagues in USA reported that patients with substance abuse had higher BPRS scores at study onset and that patients receiving depot medication relapsed if they continued to misuse drugs (Swofford *et al*., 1996).

Atypical antipsychotics were effective in treating symptoms of psychosis in patients testing positive to cannabis. However, patients remained psychotic for longer periods when they continued to use the drug while on the ward.

Cannabis may be a perpetuating factor in psychotic illness. If patients use cannabis during admission their psychosis becomes worse and the length of admission prolonged, causing a block in beds and services and serious resource repercussions.

While we recognize that cannabis dependence is an important, narrowly researched and under-treated area, we recommend complete abstinence from cannabis by psychotic patients for their antipsychotic drug is to be effective.

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