Relationship between **substance abuse** and **first-episode psychosis** — a South African perspective

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Background. Co-morbidity between substance abuse and psychotic disorders is high. Few studies have examined the relationship between first-episode psychosis and substance abuse. Several questions emerge from this common relationship and many of them remain unanswered.

Objectives. To determine the effect of substance abuse on psychosis in terms of onset, duration, severity of symptoms, use of medication and outcome.

Method. Thirty-three subjects with first-episode psychosis, as well as primary caregivers, were interviewed regarding substance abuse and its relation to illness. Thirty-six control subjects were also interviewed.

Results. Twenty-seven per cent of subjects abused substances in the 3 months before onset of illness, and 77.8% of the abusers were male. Subjects in the first-episode psychosis group were more likely to choose cannabis as their substance of abuse than controls. They also started abusing substances at a younger age than controls. Subjects with first-episode psychosis who abused substances presented at an earlier age than non-abusers. Substances affected symptoms at baseline presentation.

Conclusions. Substance abuse has a significant impact on first-onset psychosis as far as age of onset and symptom severity are concerned. Subjects with an underlying vulnerability to psychosis seem to start abusing substances at an earlier age than the general population. Males are more likely to abuse substances than females.

The subject of substance abuse and psychosis has been studied extensively and many authors have discussed the relationship between drug consumption by psychiatric patients and illness outcome.[1-3] Previous attempts to determine'cause and effect' retrospectively have largely been unreliable, given the general lack of knowledge of early prodromal symptoms in most psychiatric disorders. Findings on the temporal relationship between substance abuse in general and illness onset are inconsistent, but some data suggest that cannabis abuse may precipitate schizophrenia.[4]

Most studies suggest a high prevalence of substance abuse in patients with psychotic disorders.[3] In fact, substance abuse by patients with schizophrenia seems to be the rule rather than the exception! Prevalence rates among young patients with schizophrenia range from 25% to 60%.[2,5] In a large Epidemiological Catchment Area study,[2] young schizophrenic patients abused alcohol or drugs three times as often as the same age groups in the general population.

This association raises further questions on the relationship between the two disorders, viz. whether substance abuse precipitates or is a consequence of schizophrenia, whether substance abuse affects the outcome of psychotic disorders and vice versa, whether there is a subgroup of patients with schizophrenia who are prone to abuse substances, whether there is a shared risk for the two disorders, and if there is any difference in treatment requirements and outcome over time between patients who abuse substances and those who do not.

Despite the aforementioned research into the relationship between the disorders, few studies have examined co-morbidity with first-episode psychosis. A recent study in the UK by Cantwell *et al*.[6] confirmed high rates (37%) of substance abuse at onset of first psychosis. It also showed young males to be the group most at risk. In another study of first-episode psychosis and substance abuse by Strakowski *et al*.[7] it was found that 56% of first-episode psychosis patients met the criteria for substance abuse, making it

the most common co-morbid diagnosis. Linszen *et al.*[8] found that cannabis abuse preceded the onset of psychotic symptoms in first-episode psychosis by 1 year, and Hambrecht and Hafner[4] reported that cannabis abuse was likely to precipitate schizophrenia.

In South Africa, and particularly the Western Cape, drug and alcohol abuse is an ever-increasing problem. In a South African Demographic and Health Survey,[9] 27.9% of all males aged over 15 years in the Western Cape reported alcohol dependence. In the Bridges high school survey[9] of five schools in the Cape Metropole (January - June 2000), 43% of all students indicated that they engaged in binge drinking and 23% of the students reported having tried cannabis at least once. Unfortunately, little is known about the prevalence of drug abuse in the general population, as most studies are conducted on specialised sample groups, e.g. trauma patients or school students.

Studies in the USA have reported high rates of substance abuse among young patients with schizophrenia.[2,10] Psychoactive substance abuse and schizophrenia both have their onset in adolescence and young adulthood. It could therefore be argued that by examining a group of patients with first-onset psychosis more unambiguous answers will be obtained and the course of the illness with or without substances may be compared more successfully.

In this study we specifically examined patients presenting with a first episode of psychosis in order to avoid a confounding factor present in previous studies, i.e. the uncertain effect of long-term illness and treatment on the diagnosis of co-morbidity.[7] By studying patients with first-episode psychosis many confounding factors are avoided and the illness can largely be observed in its 'natural' state.

Subjects and methods

Sixty-nine subjects were included in this study, 33 in the first-episode psychosis group and 36 in the control group. Permission for the study was obtained from the Ethics Committee of the University of Stellenbosch. All participants in the study gave written, informed consent. Subjects in the index group were drawn from a first-episode psychosis research group at Stikland Hospital who had already been subjected to several screening and symptom-evaluating tests, e.g. SCID (Structured Clinical Interview for the *Diagnostic and Statistical Manual-IV* (*DSM-IV*) and PANSS (Positive and Negative Syndrome Scale).

Inclusion criteria for this study were: (*i*) age 14 - 55 years, male or female, in- or outpatient; (*ii*) *DSM-IV* diagnosis of schizophreniform disorder, schizophrenia and schizoaffective disorder; (*iii*) current psychotic symptoms requiring antipsychotic treatment in the opinion of the investigator; (*iv*) lifetime history of prior neuroleptic exposure of 4 weeks or less; and (*v*) informed consent form signed by subject and / or legal guardian or representative according to the regulations of the Ethics Committee.

Exclusion criteria for the study were: (*i*) serious physical illness; (*ii*) pregnant or breast-feeding women; (*iii*) subjects who had been treated with a long-acting depot neuroleptic; and (*iv*) mental retardation.

Substance abuse was not an exclusion criterion, but subjects were excluded if their conditions met criteria for intoxication or withdrawal states.

The control group was made up of individuals and their families / friends who presented to the day hospitals in the Stikland catchment area with non-psychiatric conditions. They were matched for age, gender and race.

Subjects and their primary caregivers were interviewed after resolution of the initial episode of psychosis. This included an interview with the patient (including the alcohol and substance questions of the Structured Clinical Interview for *DSM-IV*, Patient Edition (SCID-P)), as well as a separate questionnaire designed specifically for this study, dealing with use of substances and their relation to onset of symptoms. Furthermore, the researchers conducted an interview with the primary caregiver regarding the subject's substance use and its relationship to his / her illness, as perceived by the caregiver.

Subjects in the first-episode group were evaluated using the following rating scales on a regular basis: Positive and Negative Syndrome Scale (PANSS), Abnormal Involuntary Movement Scale (AIMS), Barnes Akathisia Scale, Simpson and Angus Rating Scale, Clinical Global Impression (CGI) and Calgary Depression Rating Scale.

Separate questionnaires concerning alcohol and drug habits and a repeat of the SCID drug and alcohol section were done on follow-up (telephonically or face-to-face) 3 - 6 months later.

Statistical methods

Data were analysed with the help of a specialised software package, Statistica (StatSoft, Inc.) under the supervision of a sta-

tistician. The chi-square test was used for categorical data and the Mann-Whitney U-test to compare groups. A significance level of 0.05 was used throughout.

Results

Characteristics of the sample

Thirty-three subjects were included in the first-episode psychosis group. Eighteen (55%) of these subjects were male and 15 (45%) female. The mean age was 29.25 years (± 9.07 years). Twenty-six (79%) of subjects were of mixed racial origin, and 7 (21%) were Caucasian.

Thirty-six subjects were included in the control group. They were matched for age, gender and race. Twenty (56%) of these subjects were male and 16 (44%) female. The mean age was 29.6 years. Twenty-eight individuals (78%) were of mixed racial origin, 5 (14%) Caucasian and 3 (8%) black. Individual interviews conducted with all these subjects elicited birth history and demographic data, while a separate questionnaire and the SCID-P drug and alcohol section established alcohol and drug habits. There were no statistically significant differences between the two groups in terms of age, gender or race.

Substance and alcohol use and abuse

Nine of the 33 first-episode psychosis subjects (27%) had used substances more than once a week in the 3 months before the onset of their first episode of psychosis. Seven of these 9 abusers (77.8%) were male. These findings are similar to those of previous studies which show substance abuse to be common in psychiatric populations (up to 30%).[3] Only 2 subjects were diagnosed as ongoing drug abusers at follow-up. In the control group, 4 of the 36 subjects (11%) had used substances more than once a week in the 3 months before the interview. Although there is a seemingly large numerical difference between the two groups, it did not reach statistical significance ($p = 0.124$, Fisher's exact test, two-tailed). The reason for this finding is most probably the small sample size, but it might also reflect high substance abuse rates in the general population of the Western Cape.

There was no significant difference between the two groups in terms of lifetime risk of substance use. Twenty-eight of 33 subjects in the study group admitted to having ever used a substance or alcohol, compared with 26 of 36 subjects in the control group ($p = 0.2$).

A most intriguing finding was a significant difference in the choice of substance between the study and control groups (Figs 1 and 2). Subjects from the first-episode psychosis group were more likely to choose cannabis than controls ($p = 0.03$).

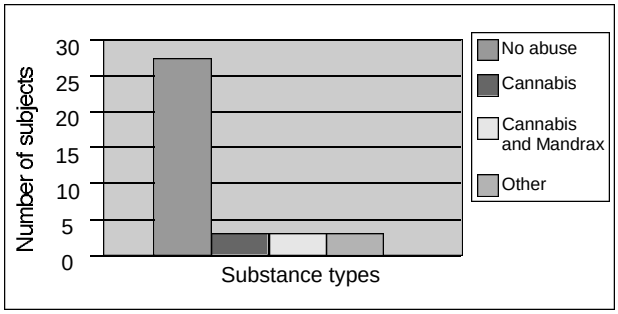

Fig. 1. Substances preferred by control group.

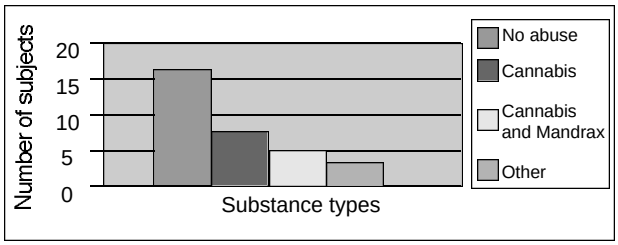

Fig. 2. Substances preferred by patient group.

There were no differences between subjects who abused substances and those who did not in terms of duration of untreated psychosis ($p = 0.15$), gender ($p = 0.10$), or family history of psychotic disorder ($p = 0.69$).

However, we found a significant difference between subjects in the first-episode group and controls in terms of age that they first used substances, with the first-episode group starting at a significantly younger age (10 - 15 years) than controls (15 - 20 years) ($\chi^2 = 10.02$, df = 4, $p = 0.04$).

Also, in the first-episode psychosis group, those subjects who abused substances had onset of psychosis at a significantly younger age than those who did not ($p = 0.01$).

Furthermore, we found significant differences between substance abusers and non-abusers in terms of symptom severity at baseline presentation. Abusers were more likely to have a higher PANSS positive score ($p = 0.01$), PANSS general psychopathology score ($p = 0.04$) and PANSS total score ($p = 0.01$). Although the difference in PANSS negative score did not reach the 0.05 level, there was a definite trend ($p = 0.053$). These differences

were only evident at baseline and were not found at 6-, 12- or 24-week follow-up interviews.

Further analysis of specific items on the PANSS showed that two items of the PANSS positive scale differed significantly between the two groups. These were the ratings P2 (conceptual disorganisation) and P3 (hallucinatory behaviour) ($p = 0.002$ and $p = 0.019$).

Discussion

Our results confirm that substance abuse is a significant problem among first-episode psychosis patients in the Western Cape. When interpreting the results it must be borne in mind that 'substance' in this study refers mainly to cannabis, as this was the drug most often abused by study subjects. Results cannot, therefore, be extrapolated to other substances of abuse, such as hallucinogens and stimulants.

Our results suggest that, in our study population, substance abuse did not affect the duration of the untreated psychosis. However, in those patients who abused substances, psychotic illness presented at a younger age than in those patients who did not. This finding can be interpreted in two ways. Firstly, it may indicate that patients with an inherently poorer prognosis (as seen with earlier onset) are at increased risk for abusing substances, either as a form of self-medication or because of a shared risk between the two disorders.[4] Alternatively, our finding may support the theory that substance abuse precipitates psychotic illness in the predisposed individual, thereby lending support to the so-called vulnerability hypothesis.[10]

The finding that patients started abusing substances at an earlier age than subjects from the control group is also of great interest and importance. It seems that patients who are predisposed to a psychotic illness are more prone to abusing substances than normal subjects of the same age. It is therefore possible that the two disorders (psychosis and substance abuse) share common risk factors.

Although 77.8% of patients who abused substances in the 3 months before their first psychotic episode were male, there were no significant gender differences between substance users and non-users on follow-up. This was probably due to the small number in the follow-up group.

The use of substances had a significant effect on PANSS ratings at baseline evaluation. Substance abusers scored higher on PANSS subscales for positive, negative, and general psychopathology, but also on PANSS total scores. Specific factors that correlated strongly were P2 (conceptual disorganisation) and P3 (hallucinatory behaviour). It seems, therefore, that substance-abusing subjects presented differently from the non-abusers, but that these differences were not observed at follow-up, probably as a result of the fact that these patients did not continue with the substance abuse after admission to hospital. This correlates with the fact that the number of substance abusers also decreased at follow-up. It suggests that substances in general and cannabis in particular cause increased severity of perceptual disturbances and thought process disorders in the acute phase of psychosis. This clinical effect may be mediated via the effect of delta-9-tetra hydrocannabinol on the dopamine receptors in the medial forebrain bundles,[8] but other, as yet unknown mechanisms may also be involved.

There were no differences in outcome over a 6-month period between substance-abusing subjects and non-abusers. This may again be due to the fact that substance abuse was not an ongoing problem with most patients, but mainly seen before and at onset of the psychosis. This finding supports the suggestion that psychotic patients use substances (specifically cannabis) to self-medicate their symptoms.[11] It may also imply that initiation of adequate treatment (i.e. optimal symptom relief and minimal side-effects) removed the need for ongoing substance abuse.

It should be remembered, however, that substance and / or alcohol dependence were exclusion criteria in this study. This fact may have influenced our findings to some extent, and should be considered in the interpretation of the results. We also found no difference in the dosages of medication needed for remission between those who used substances and those who did not. Substance-abusing psychotic patients therefore did not constitute a more treatment-refractory group, as we initially thought.

In our study population, substance use is common in both the general and the psychiatric population. Substance use, even in fairly moderate quantities, may have an effect on the onset and presentation of psychotic illness, but does not seem to have a major effect on treatment response and outcome in a first-episode population. Once again, this statement should be read with the understanding that patients who were clearly substance-dependent were excluded from the study altogether.

There are certain obvious limitations to this study. One major point of criticism may be the fact that we did not use routine urine analysis to screen for substances. One of the problems with

questioning subjects about substance abuse is the unreliability of the information. This might be out of fear of prosecution or legal action and other confidentiality issues. We did attempt to overcome this problem by using collateral information from primary caregivers, but even this method is fallible. Primary caregivers often admitted that they were not sure about the patients' substance habits.

Although the age criteria included children from the age of 14 years, only adults were seen in this study, mainly due to the fact that Stikland Hospital only accepts adults.

As already mentioned, the sample size was fairly small, which might have compromised some of the results. The study population should be expanded to enhance the statistical power of the study.

Conclusion

The following conclusions may be drawn from this study: *(i)* there is a high co-morbidity between first-episode psychosis and substance abuse in South Africa (27%), although this needs to be seen against the background of a generally high level of substance abuse in this country; *(ii)* subjects who abuse substances present with the first episode of psychosis at a younger age than those who do not; (*iii*) first-episode psychosis subjects start abusing substances at a younger age than control subjects; (*iv*) substance abuse affects presenting symptoms of subjects with a first episode of psychosis; (*v*) first-episode psychosis subjects are more likely to choose cannabis as their substance of abuse; and (*vi*) males are more likely to abuse substances than females.

References

1. Andreasson S, Allebeck P, Rydemberg V. Schizophrenia in users and nonusers of cannabis. *Acta Psyciatr Scand* 1989; **79:** 505-510.
2. Regier DA, Farmer ME, Rae DS. Co-morbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiological Catchment Area (ECA) study. *JAMA* 1990; **264:** 2511-2518.
3. Menezes PR, Johnson S, Thornicroft G, *et al.* Drug and alcohol problems among individuals with severe mental illnesses in South London. *Br J Psychiatry* 1996; **168:** 612-619.
4. Hambrecht M, Hafner H. Substance abuse and the onset of schizophrenia. *Society of Biological Psychiatry* 1996; 1155-1163.
5. Test MA, Wallish L, Allness DJ. Substance use in young adults with schizophrenic disorders. *Schizophr Bull* 1989; **15:** 465-476.
6. Cantwell R, Brewin J, Glazebrook C, *et al.* Prevalence of substance misuse in first-episode psychosis. *Br J Psychiatry* 1999; **174:** 150-153.
7. Strakowski SM, Tohen M, Stoll AL, *et al*. Comorbidity in psychosis at first hospitalisation; *Am J Psychiatry* 1993; **150:** 752-757.
8. Linszen DH, Dingemans PM, Lenior ME. Cannabis abuse and the course of recent-onset schizophrenic disorders. *Archives of Psychiatry* 1994; **51:** 273-279.
9. Parry CDH, Pluddeman A, Bhana A, *et al*. *Monitoring Alcohol and Drug Abuse Trends in South Africa (July 1996 - December 1999)*. SACENDU, Research Brief, vol. 3. Cape Town: MRC, 2000: 1-16.
10. Linszen DH, Lenior ME. The recognition and management of early psychosis. In: McGorry PD, Jackson HJ, eds. *Early Psychosis and Substance Abuse*. Cambridge: Cambridge University Press, 1999: 363-375.
11. Dixon L, Haas G, Weiden PJ, Sweeney J, Frances AJ. Drug abuse in schizophrenic patients: clinical correlates and reasons for use: *Am J Psychiatry* 1991; **148:** 224-230.