

Cannabis use and age of admission to a psychiatric unit for first episode of psychosis

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Abstract

Background: Research has implicated that cannabis has an aetiological role in psychosis, and thus one can hypothesize that the onset of psychosis in patients who use cannabis occurs earlier in life than those who do not use cannabis

Aim: The aim of this study is to assess the possible influence of cannabis on the age of onset of patients with first episode of psychotic illness admitted to a psychiatric unit in the Maltese Islands.

Methods and sample: This study is a one year prospective study that includes all ICD-10 first episode psychosis patients admitted to a psychiatric hospital in the Maltese Islands. Age of admission to hospital was used as proxy for age of onset of psychosis. Use of cannabis prior to admission was ascertained by urine testing.

Results: The mean age of admission to hospital for first onset psychosis for patients whose urine was positive to cannabis was 24.63 years old, and for patients whose urine was negative to cannabis was 44.63 years old. This difference was statistically significant, using the Mann Whitney-U test $p=0.001$.

Conclusion: The results indicate that cannabis use can precipitate an earlier onset of psychotic illness. Considering the widespread use of cannabis, and that earlier age of onset of psychosis is associated with worse prognosis, this issue is of public health concern.

Keywords

Cannabis, psychosis, Malta, age, onset

Introduction

Malta is an archipelago in the Mediterranean Sea, with a population of approximately half a million people. There are three National Health Service units that offer treatment for psychiatric patients. The largest is Mount Carmel Hospital, with around 600 beds. Smaller units exist within two general hospitals: Mater Dei Hospital (main island) and in Gozo General Hospital (sister island Gozo). There is also a private hospital that occasionally admits patients with mental illness as well.

Several case-control studies have shown that patients with schizophrenia are more likely to use cannabis than other psychiatric patients or normal controls.¹⁻⁴ In 1987 Andreason *et al.*⁵ published a seminal paper of a follow-up study on a cohort of 45,570 Swedish conscripts. In this cohort the relative risk for schizophrenia among high consumers of cannabis was six times more than in non-users of cannabis. Similar results were replicated in other follow-up studies.⁶⁻⁹ Thus one can conclude that it is very possible that cannabis can have an aetiological role in the development of schizophrenia.

Due to this aetiological role, one can thus hypothesize that cannabis use can hasten the onset of psychotic illness and schizophrenia. Four studies

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conducted on patients with first episode of psychosis concluded that patients with psychosis who abuse cannabis have an earlier age of onset of illness compared to those who do not.¹⁰⁻¹² Sungrayes *et al.*¹³ conducted a study on 116 patients with first episode psychosis and subsequent diagnosis of schizophrenia (after a 12-month follow-up). Their findings showed that cannabis use was significantly associated with a decrease in age of first antipsychotic treatment, and that this correlated with frequency of cannabis use.

Malta is a small country and thus it lends itself well to epidemiological studies that are based on the whole population. This research project is part of a larger study which involved calculating the incidence of psychosis of patients requiring admission to hospital on the Maltese Islands reported to be 26.0 per 100,000, (95% CI: 25.9-26.1).¹⁴ We chose the Maltese Archipelago to test if the findings from studies reported elsewhere (that show that cannabis is associated with an earlier age of onset of psychosis) could be replicated in a study based on the whole population of a country.

Methods

Sample

The study design used was a prospective cross-sectional study. The inclusion criteria for this study were all patients with a first episode of psychosis admitted to a psychiatric ward at any of the three government hospitals over one year. In Malta there is only one non-government hospital that admits patients with mental illness. Admissions for psychosis in this unit are very rare, and during the year of study there were no admissions of patients that fulfilled the inclusion criteria of the study. Participations included persons of all age, sex and ethnical background that were permanently resident in Malta. Tourists and irregular immigrants not living in the community were excluded from this study.

Clinical assessment of the patient sample

As part of the formal admission assessment the senior doctor established if this person suffered from a psychosis. After the patient was seen by the consultant psychiatrist and multidisciplinary team (MDT) the diagnosis was confirmed or dismissed. Only people with a diagnosis of psychosis by the MDT were included in the study.

Age of onset of psychosis

Age of admission to hospital was used as proxy for age of onset of psychosis.

Assessment of cannabis use

Use or otherwise of cannabis by the patients prior to the admission was ascertained by means of urine testing within the first few days of admission.

Data protection

All patients were invited to participate in the study, and were free to decline. Informed consent was given. They were informed that all data collected would be anonymous and confidential and that this study would not negatively or positively effect the treatment they received in hospital.

This study was approved by the relevant hospital authorities.

Statistics

All data was imputed into Microsoft Excel and analysed using SPSS. Statistical difference looking at age of onset of psychosis in the two groups (those testing positive for cannabis and those testing negative for cannabis), was first analysed using parametric tests for continuous data (2 sample t-test). To increase the robustness of the statistical analysis a non-parametric test (Mann-Whitney U test) was used. This backed the statistical analysis of the 2 sample t-tests and also ensured that our sample was normally distributed - hence reducing any bias that could arise from having extreme outliers of age in the data.

Results

During the year of study there were 100 patients (males=55, females=45) with first episode of psychosis who were permanently resident in Malta and were admitted in one of all the in-patient psychiatric units of the Government Hospitals.

All patients were asked to provide urine for analysis to ascertain the use or not of cannabis prior to the admission. 83 patients (males=39, females=36), accepted to have their urine analysed. Patients who refused urine testing were 10 males and 7 females. The mean age of the patients accepting urine testing was 42 years (CI=38.8 - 44.0), and the mean age of patients refusing urine testing was 29 years. This difference was statistically significant, Man Whitney $p=0.047$. The difference in sex between the patients who refused and did not refuse urine testing was not statistically different.

Eight patients (9.6%) tested positive for cannabis, by urine analysis, the mean age was 24.63 years (95% CI 20.1 – 29.3), and the mean age of admission of patients who resulted negative for cannabis in urine testing was 44.63 years. The difference was statistically significant, Mann Whitney $p=0.001$.

The difference in sex distribution within the group of patients who were positive to cannabis in urine testing was not statistically different from that of patients who where negative to cannabis in urine testing; Fisher's exact test, p 2 sided=0.279, p 1 sided=0.194.

Discussion

This study was able to reproduce the result from previous studies carried out in other countries, that reported an association between cannabis use and earlier age of onset of psychosis.

There can be various reasons for this association. The association could be coincidental or a result of confounding variables which were not accounted for in this study. Cannabis is used more in the younger generations. Therefore, there is a greater chance that patients who start suffering from psychosis at an earlier age, have also been using cannabis, than those who start suffering from psychosis at an older age. Another reason could be because of trends in substance misuse, where by males tend to misuse illicit substances more than females. Males also tend to have an earlier age of onset of psychotic illness than their counterparts in general. The fact that in this study the difference in sex distribution within the group of patients who tested positive for cannabis in urine was not statistically different from that of patients who were negative for cannabis in urine testing, indicates that the association found in this study between cannabis use and earlier age of onset of psychosis could not be due to this bias.

It is also possible that the association between cannabis use and earlier age of onset of psychosis is because cannabis use precipitates psychosis in vulnerable individuals or that it could be the sole predisposing factor for psychotic illness in certain individuals. The fact that cannabis use can precipitate psychotic illness in vulnerable individuals is supported by the knowledge that cannabis as a substance can precipitate psychotic like symptoms in individuals who misuse this substance.¹⁵⁻¹⁶ Furthermore, epidemiological studies have reported that had individuals not misused cannabis (prior to developing a psychotic illness) they would have never developed a psychotic illness in their lifetime.^{9, 17}

All the causes discussed above are not mutually exclusive, and it is possible that the reason for the association between cannabis and age of onset of psychosis is a combination of the above factors.

Validity and limitations

One of the main strengths of this study is that it included admissions for a whole population of a country (there were no admissions for psychosis in Malta's private hospital over the period of study). The authors are aware that there may have been some other patients who suffered from cannabis induced psychosis that were treated within the private sector, but instead of being admitted to hospital were managed using home treatment. Further discussion was carried out with consultants working in this area of speciality in Malta, and we were told that home treatment could have been used in a few cases if any, during the time period when the study was carried out. Due to this

limitation this authors suggest that the data is reported with care.

Since urine analysis was used to assess cannabis use by the subjects, the information about use of cannabis is very accurate and not subject to any bias. Future research could include the use of hair analysis, which would provide a better idea of the drug use patterns.

It is very difficult to ascertain the exact time of the onset of psychosis. Thus we decided to use a proxy measure for onset of psychosis, which is the age of hospitalization for age of onset of psychosis. This can create a bias towards patients with insidious onset having their illness reported as starting at a later age than those with acute onset. This is because patients with acute onset of psychosis generally are admitted closer to the onset of their psychosis than those with a more insidious onset.

Seventeen out of the 100 patients who fulfilled the inclusion criteria for the study refused to have their urine tested for use of cannabis. Those who had a statistically significant younger age than those who did not refuse. There can be many reasons why patients refused to have their urine tested. Clinical experience in Malta shows that since in Malta smoking cannabis is illegal, patients who use cannabis are extremely reluctant to divulge this information. In fact it is common clinical practice to suspect that those who refuse to provide urine samples have a higher probability of having used illicit drugs prior to their admission. So it is likely that a significant number of those who refused to have their urine tested in the study could have been tested positive for cannabis. Considering that those who refused urine testing were younger than those who agreed to have their urine tested, the bias that their refusal to participate in the study might have caused is against, not in favour of the hypothesis of the study that cannabis use results in an earlier age of onset of psychosis.

Data was solely collected from medical files without actually interviewing the respective MDT or patient's themselves. Gathering more information or using a standardised instrument may have helped further to answer the research question. It could have also helped to shed more light on possible confounding variables which may also affect age of onset.

Clinical implications

Studies report that the prevalence of cannabis use amongst young people is on the increase. This study concludes that there is an association between cannabis use and an earlier age of onset of psychosis. Early age of onset of psychosis is associated with worse prognosis. Thus: from a research perspective it

is very important that the nature of the association between cannabis use and earlier age of onset of psychosis is studied more in depth. From a service provision point of view, this is a public health concern, which encourages clinicians working with this age group to be more tuned to this association as well as to provide evidence for commissioners to support further development of early intervention services in the Maltese islands.

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References

1. Grech, A., Takei, N., Murray, R., Comparison of cannabis use in psychotic patients and controls in London and Malta 1998; *Schizophr Res*, 29: 22.
2. Schneier, F., R., & Siris, S.G., A review of psychoactive substance use and abuse in schizophrenia: patterns of drug choice. 1987; *Journal of Nervous and Mental Disease*, 175: 641-652.
3. Smith, J. & Huckler, S. Schizophrenia and substance abuse. 1994; *Br J Psychiatry*, 165: 13-21.
4. Warner, R., Taylor, D., Wright, J., Sloat, A., Springett, G., Arnold, S., Weinberg, H. Substance use among the mentally ill: prevalence, reasons for use, and effects on illness. 1994; *Am J Orthopsychiatry*, 64: 30-39.
5. Andreason, N., Allebeck, P., Engstrom, A., Rydberg, U. Cannabis and schizophrenia. A longitudinal study of Swedish Conscripts. 1987; *Lancet*, 2: 1483-1486.
6. Arseanult, L., Cannon, M., Poulton, R., Murray, R., Caspi, A., Moffit, T.E., Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. 2002; *BMJ*, 325: 1212-1213.
7. Fergusson, D.M., Horwood, L.J., Swain-Campbell, N.R., Cannabis dependence and psychotic symptoms in young people. *Psychol Med*, 2003; 33: 15-21.
8. Henquet, C., Krabbendam, L., Spauwen, J., Kaplan, C., Lieb, R., Mitichen, H.U., Van Os, J., Prospective cohort study of cannabis use, predisposition for psychosis, and psychotic symptoms in young people. *BMJ*, 2005; 330: 11-14.
9. Van Os, J., Bak, M., Hanssen, M., Bijl, R.V., de graaf, R., Verdoux, H., Cannabis use and psychosis: a longitudinal population based study. *Am J of Epidem*, 2002; 156: 319-327.
10. Compton, M.T., Kelley, M.E., Ramsay, E.C., Makenya, P., Goulding, S.M., Esterberg, M.L., Stewart, T., Walker, E.F., Association of Pre-Onset Cannabis, Alcohol, and Tobacco Use with Age at Onset of Prodrome and Age at Onset of Psychosis in First-Episode Patients. *Am J Psychiatry*, 2009; 166: 1251-1257.
11. Gonzalez-Pinto, A., Vega, P., Ibanez, B., Mosquera, F., Barbeito, S., Gutierrez, M., Ruiz de Azua, S., Vieta, E., Impact of cannabis and other drugs on age of onset of psychosis. *J Clin Psychiatry*, 2008; 69(8): 1210-6.
12. Veen N.D., Selten J., van der Tweel, I., Feller, W.G., Hoek, H.W., Kahn, R.S., Cannabis Use and Age at Onset of Schizophrenia. *Am J Psychiatry*, 2004; 161: 501-506.
13. Sugraney, G., Flamarique, I., Parellada, E., Baeza, I., Goti, J., Fernandez-Egea E., Bernardo M., Cannabis use and age of diagnosis of schizophrenia. *European Psychiatry*, 2009; 24(5): 282-286.
14. Camilleri N, Grech A, Taylor-East R. Socio-economic status and population density risk factors for psychosis: prospective incidence study in the Maltese Islands. *International Psychiatry, supplement of British Journal of Psychiatry*. July 2010; 7(3): 70-2.
15. Hall, W., Solowij, N., Adverse effects of cannabis. *Lancet*, 1998; 352: 1611-1616
16. Murray, R.M., Morrison, P.D., Henquet, C., Di Forti, M., Cannabis, the mind and society, the harsh realities. *Neuroscience*, 2007; 8: 885-895.
17. Zammit, S., Allebeck, P., Andreassen, S., Lundberg, I., Lewis, G., Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: historical cohort study. *BMJ*, 2002; 325: 1183-4