did not predict schizophrenia outcomes over and above the effect of cannabis use.

Comment

Using cannabis in adolescence increases the likelihood of experiencing symptoms of schizophrenia in adulthood. Our findings agree with those of the Swedish study¹ and add three new pieces of evidence. Firstly, cannabis use is associated with an increased risk of experiencing schizophrenia symptoms, even after psychotic symptoms preceding the onset of cannabis use are controlled for, indicating that cannabis use is not secondary to a pre-existing psychosis. Secondly, early cannabis use (by age 15) confers greater risk for schizophrenia outcomes than later cannabis use (by age 18). The youngest cannabis users may be most at risk because their cannabis use becomes longstanding.⁵ Thirdly, risk was specific to cannabis use, as opposed to use of other drugs, and early cannabis use did not predict later depression. Our findings now require replication in large population studies with detailed measures of cannabis use and schizophrenia.

Although most young people use cannabis in adolescence without harm, a vulnerable minority experience harmful outcomes. A tenth of the cannabis users by age 15 in our sample (3/29) developed schizophreniform disorder by age 26 compared with 3% of the remaining cohort (22/730). Our findings suggest that cannabis use among psychologically vulnerable adolescents should be strongly discouraged by parents, teachers, and health practitioners. Policy makers and

law makers should concentrate on delaying onset of cannabis use.

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Contributors: LA participated in the study design, analysed and interpreted the data, and wrote the first draft of the paper. MC and RP participated in the study design and assisted with the analysis and interpretation of the data and the writing of the paper. RM, AC, and TEM participated in the study design and assisted with the interpretation of the data and writing of the paper. RP, AC, and TEM coordinated the collection of the data. LA, RP, and TEM are guarantors of the study.

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Drug points

Antibody deficiency associated with carbamazepine

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A 45 year old woman was referred to our immunology department with antibody deficiency and an eight month history of recurrent upper respiratory tract infections that required antibiotic therapy. Four years previously she was diagnosed as having epilepsy and was treated with carbamazepine. Serum immunoglobulins were measured repeatedly and showed antibody deficiency (IgG 4.5 g/l (range 6-16 g/l), IgM 0.3 g/l (0.5-2 g/l), and IgA 0.67 g/l (0.8-2.8 g/l)). Lymphocyte immunophenotyping and specific antibody production to tetanus toxoid, Haemophilus influenzae type B, and Pneumovax II vaccines were normal. In view of her recurrent infections she was treated with prophylactic oral antibiotics and her condition was monitored over several months. She stopped taking carbamazepine and three months later her IgG had increased to within the reference range (IgG 6.1 g/l, IgM 0.22 g/l, and IgA 0.74 g/l). By seven months the serum immunoglobulins were virtually normal (IgG 7.5 g/l, IgM 0.33 g/l, and IgA 0.89 g/l). At this point she had improved clinically with no active infections, and prophylactic antibiotics were discontinued without incident.

Antibody deficiency is a recognised, but rare, adverse effect associated with the use of carbamazepine, although the prevalence of this complication is unknown. The Committee on Safety of Medicines ADROIT database lists nine cases of hypogammaglobulinaemia or γ globulin abnormality related to the use of carbamazepine (R. Granados,

personal communication) and a handful of case reports have been published on the subject.¹⁻³ The British National Formulary does not, however, mention antibody deficiency as an adverse effect of carbamazepine. Many of the other cases report associated skin rashes. It is not known how many patients using carbamazepine develop symptomatic or asymptomatic antibody deficiency, compared with the total number using the drug, or how long it takes for antibody deficiency to develop or resolve. Similar antibody deficiency has been reported in association with the use of phenytoin, although isolated IgA deficiency is far more common with this drug.⁴

Patients requiring carbamazepine should have serum immunoglobulins measured if they experience recurrent or persistent infections. At present, the apparent rarity of carbamazepine related antibody deficiency precludes routine serum immunoglobulin assessment.

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