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Article of the Month

THC can improve symptoms of schizophrenia

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Abstract

Scientists at the Rockland Psychiatric Center in Orangeburg, New York, reported of an improvement of schizophrenia symptoms in 4 patients who received oral dronabinol (THC) (Schwarcz et al. J Clin Psychopharmacol 2009;29(3):255-8). Only patients with a previous history of self-reported benefits from cannabis use were selected. In addition, they presented with a severe, refractory condition that made the possible benefits outweigh the risks. Dronabinol administration was initiated at 2.5 mg twice a day and subsequently raised to 5 mg twice a day in the second week and 10 mg twice a day in the third week. One of the patients needed 8 weeks to reach significant improvement, while the others responded to the therapy within a shorter period of time. Researchers noted that "this improvement seems to have been a reduction of core psychotic symptoms in 3 of the 4 responders and not just non-specific calming."
Keywords: cannabis, THC, dronabinol, schizophrenia, psychosis, case report

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Summary of Original Article

At the Rockland Psychiatric Centre in New York six patients, who were suffering from severe, chronic schizophrenia, were treated with dronabinol (THC) in agreement and cooperation with the State of New York Office of Mental Health [10]. In all of them the disease had been refractory against standard medication. The idea to use dronabinol emerged from the good response to the therapy by one patient, who was severely psychotic, assaultive, disorganised, and highly refractory to multiple treatment trials. When reviewing his history, doctors noted that he had a time span of several years with calm behaviour, during which he used cannabis. They decided to try dronabinol and observed that he became calm, logical, and cooperative within days. He was able to leave the hospital within a few weeks.

The authors received approval by the responsible authorities to try THC in further 3 patients, which was extended later to an additional 2 patients. From about 200 patients with chronic psychosis these 5 patients fulfilled the inclusion criteria: a history of sustained improvement by a previous chronic use of cannabis, an absence of significant polysubstance use, good physical health, a diagnosis of schizophrenia, and severe, long-standing illness refractory to standard treatment. All participants had tried numerous anti-psychotic medications with minimal or no response. Their condition was stable during the past months or years and there were no relevant changes of treatment within the months before the administration of THC. With the exception of dronabinol no changes in medication were made during the trial period.

Treatment was started with 2.5 mg THC twice daily, which was increased to 5 mg twice daily in the second and 10 mg twice daily in the third week. Administration of this medication was allowed for up to eight weeks and was continued thereafter if the patient responded.

Altogether six patients (5 men, 1 woman) aged between 21 and 43 years were included in the trial. Four of the 6 patients showed an improvement of clinical relevance. Three of the 6 patients showed a robust response with moderate to marked reduction of psychotic core symptoms. Two of these patients presented with an improvement within weeks after onset of dronabinol treatment, while the third patient needed eight weeks to attain significant improvement. These three patients were sufficiently stabilised with the cannabinoid treatment that they could be discharged from

hospital. Authors noted that the improvements in these three patients could not be explained by a non-specific calming effect of dronabinol. Improvements in the fourth patient were more limited, but he became calmer, more cooperative and less aggressive. No significant side-effects were observed in the six patients.
Authors concluded that these results would suggest "that the role of cannabinoids in psychosis may be more complex than previously thought. They open a possible new role for cannabinoids in the treatment of schizophrenia."

Background information

A number of patients suffering from schizophrenia have reported that they profit from a self-medication with cannabis [4], but this claim has never been investigated in a clinical study. To date, epidemiological studies reported only of a deterioration or unchanged severity of symptoms in patients with schizophrenia by the use of cannabis [7]. In addition, longitudinal studies have shown, that the use of cannabis increased the risk for the development of schizophrenic psychosis [1]. However, the risk was only increased for adolescents and young adults and only a small proportion of users developed a psychosis. It was suggested that vulnerable or genetically predisposed people may experience these negative effects from cannabis use [3].
Previously, positive consequences of cannabis use in schizophrenic patients observed in studies were restricted to its effects on cognitive performance. In two studies, patients suffering from schizophrenia who used cannabis showed a better cognitive performance than patients with schizophrenia, who did not use the drug [2,5]. However, another study found a deterioration of neurocognitive function associated with cannabis use by schizophrenic patients [9].
Dronabinol is the INN (international non-proprietary name) of a natural cannabinoid, the (-)-trans-isomer of delta-9-tetrahydrocannabinol, which is present in the cannabis plant. It is often called THC or delta-9-THC, since the other three isomers do not exist naturally. Dronabinol may be extracted from the plant but also be manufactured synthetically or semi-synthetically by isomerization of cannabidiol [11].
It is supposed that schizophrenia could be caused by a hyperactivity of the endocannabinoid system in at least some patients, the so-called endocannabinoid hypothesis of schizophrenia [8]. According to this hypothesis stimulation of the endocannabinoid system would cause psychotic symptoms, while the blockade of this system could treat schizophrenia. The current study shows, that in single patients stimulation of CB1 receptors may result in an improvement of psychosis. It is remarkable that the improvements were observed in patients with severe disease, who did not respond to other medications. It can be supposed that the high response rate observed is based on the selection of patients. Authors noted that the non-response to standard medication with dopamine-blocking substances might indicate that the psychotic symptoms of these patients were caused by changes in other systems such as the endocannabinoid system.
Another natural cannabinoid has been shown to possess therapeutic potential in schizophrenia. For example, cannabidiol (CBD) was effective in the treatment of psychotic symptoms of six patients suffering from Parkinson's disease [12]. In another study with 42 patients with acute schizophrenia, of whom half received 800 mg CBD daily for four weeks, the cannabinoid was as effective as amisulpride, an established antipsychotic drug [6]. Since CBD has a different mode of action than THC, these two cannabinoids may be beneficial in different patients.

Comment

It is well-known that dronabinol and other CB1 receptor agonists may cause opposite physical effects in different people, that they usually reduce but sometimes increase pain, that they usually reduce but rarely cause nausea and vomiting. This may also be true for psychiatric diseases and symptoms such as depression, anxiety and also schizophrenia, depending on cannabinoid dose and individual factors such as "endocannabinoid tone" that are currently not well understood. We are reminded of the complexity of the human brain and the remaining challenge to understand its function.

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