

Part I

37-year-old man, had an 8-year history of treatment for paranoid schizophrenia with Denzapine 200 mg p.o./day. Patient was several times hospitalized. Subsequently, he has been living in a therapeutic community. He was a smoker since early adolescence and began to smoke cannabis at the age of 23 years, which rapidly increased to smoking daily. His consumption was regularly measured objectively through urine drug screenings in the therapeutic community. The screenings were always negative for other drugs. Following the last hospitalization, the patient was treated with Denzapine 600 mg/day. Due to intensifying paranoid ideas, the dose was raised to 700 mg, which clearly improved the paranoid symptomatology.

Question 1:

What is the active substance of Denzapine?

Question 2:

What is the mechanism of effect of Denzapine and what is its recommended therapeutic range?

Part II

Xanax was occasionally given as a concomitant medication only. Clozapine plasma levels were regularly controlled, confirming good patient compliance therapy.

Question 3:

What is the active component of Xanax? What is its mechanism of action?

Part III

Three months after the Denzapine dose augmentation, the patient decided to stop smoking both tobacco and cannabis (day 0). Cannabis smoking cessation was subsequently measured objectively by urine drug screenings. Approximately 1 month after smoking cessation, the patient appeared increasingly agitated, complaining about acoustic hallucinations and manifesting clear paranoid ideas. The symptoms worsened over the following 2 months, with the patient increasingly being confused. Three and a half months after smoking cessation, his clozapine plasma level was 1328 ng/mL and norclozapine was 715 ng/mL.

Question 4:

What would you suggest to do?

Question 5:

What could be the causation for this adverse effect?

Part IV

The Denzapine dose was reduced to 500 mg/day and the psychotic symptomatology disappeared within 1 week with plasma concentrations returning to the pre-smoking cessation level.

Question 6:

Is this adverse effect expected and preventable?