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Amantadine toxic effect and acute psychosis – a case report

Dariusz Gruca[1], Krzysztof Antoniak[1], Marcin Wais[1], Marlena Zając[1],

[1]Studenckie Koło Naukowe przy Klinice Toksykologii, Uniwersytet Medyczny w Lublinie

Dariusz Gruca; dariusz.gruca1@gmail.com; ORCID: 0000-0002-5583-1229;
Krzysztof Antoniak; krzyss.anton@gmail.com; ORCID: 0000-0001-8065-081X
Marcin Wais; marcin.wais0805@gmail.com; ORCID: 0000-0003-4757-8582
Marlena Zając; marlenzajac11@gmail.com; ORCID: 0000-0002-6251-0175;

Abstract:

Introduction and purpose: The pandemic of COVID-19 has induced patients to use different ways to struggle with SARS-CoV-2 infection. Amantadine has become more popular as a supportive drug in the treatment of COVID-19 symptoms. This report presents a case of a young, previously healthy woman hospitalized in the Toxicology and Cardiology Department because of acute psychosis induced by amantadine intoxication.

Brief description of the state of knowledge: Acute psychosis can be caused by several medications, including psychostimulants, antibiotics, antivirals, and antiparkinsonians. Amantadine has primarily dopaminergic with some anticholinergic properties and is used predominantly as an adjuvant agent in the management of Parkinson's disease treatment. Psychomotor agitation, insomnia, excessive verbosity, delusions, and behavioral disturbances which are typical toxic effects of amantadine primarily affecting the central nervous system which were presented by patient described in this case report.

Conclusions: Our case illustrates the negative effects of amantadine on the central nervous system when given at the recommended dose to young, healthy women. Despite being rare, this induced psychosis may become more common, especially while becoming more popular as a supportive drug in COVID-19 treatment. While prescribing amantadine clinicians should be aware of the rapid onset of its psychotic complications.

Key words: amantadine; intoxication; acute psychosis; COVID-19;

1. Introduction

The pandemic of COVID-19 has induced patients to use different ways to struggle with SARS-CoV-2 infection. Amantadine has become more popular as a supportive drug in the treatment of COVID-19 symptoms. This report presents a case of a young, previously healthy woman hospitalized in the Toxicology and Cardiology Department because of acute psychosis induced by amantadine intoxication. The patient had typical symptoms of COVID-19 and took the drug in doses not exceeding the maximum daily dose.

2. Case report

A 38 years old woman was admitted to the Toxicology and Cardiology Department due to Amantadine poisoning. The woman with no history of chronic diseases due to an episode of fever, runny nose, and sore throat was diagnosed with symptoms of SARS-CoV-2 infection in vaccinated patients. A test for COVID-19 was not performed. Amantadine was prescribed by a doctor and the patient took the drug for 3 days (600-800 mg – total amount of the drug). The symptoms of infection resolved while insomnia, followed by agitation, wordiness, delusions, and behavioral disturbances occurred.

On admission, the patient was conscious, with efficient cardiopulmonary function, without logical contact, with psychomotor agitation and excessive verbosity. Pupils were equal and reactive. The patient required immobilization with safety belts to the bed.

Laboratory tests:

Morphology	
RBC [4-5.20] [mln/µ]	3.98
HGB [12-16] [g/dl]	11.4
HCT [37-49] [%]	32.8
Leu [4.3-10] [10^3/µl]	9
MCH [27-34] [pg]	28.6
MCHC [32-36] [g/dl]	34.8
MCV [80-99] [fl]	82.4
PLT [150-400] [10^3/µl]	271
RDW-CV [11.50-14.50] [%]	14.6

Biochemistry	
Creatinine [0.50-0.90] [mg/dl]	0.49
eGFR [ml/min/1.73m^2]	124
Na^+ [135-145] [mmol/l]	141.2
K^+ [3.50-5.10] [mmol/l]	3.7
Glucose [70-99] [mg/dl]	105
AST [5-32] [U/l]	21
Urea [15-46] [mg/dl]	9.78
CRP [0-5] [mg/l]	1.84
CK [26-192] [U/l]	71

Toxicology	
Amphetamine in urine	none
Methamphetamine in urine	none
Opiates in urine	none
Cocaine in urine	none
Cannabinoids in urine	none
Ketynones in urine	none
Mephedrone in urine	none
AB-PINACA	none
Ecstasy in urine	none
Phencyclidine in urine	none
LSD [ng/ml]	<0.5 ng/ml
Ethyl alcohol [g/l]	0

Treatment included: Midazolam Kalceks, Neorelium, Kalium Chloratum 15%, Magnesium Sulfate Kalceks, Dexaven, Lignocainum, Haloperidol WZF.

During her stay in the Toxicology and Cardiology Department, the patient was under the influence of psychotic experiences for 4 days, in the first days of hospitalization she was unable to be critical of her behavior, and significantly disinhibited in conversation and behavior. In the following days, the patient's somatic and psychological condition improved. The patient was consulted neurologically, several times psychiatrically, and psychologically. On the day of discharge, the patient was conscious, in logical contact, in increased psychomotor propulsion, and less inhibited in conversation and behavior. The patient was discharged from the department on day 6, referred, and transferred to the psychiatric ward for psychiatric reassessment and further treatment.

3. Discussion

Acute psychosis can be caused by several medications, including psychostimulants [1,2], antibiotics[3], antivirals[4], and antiparkinsonians [5]. Amantadine has primarily dopaminergic with some anticholinergic properties and is used predominantly as an adjuvant agent in the management of Parkinson's disease treatment [6]. The drug also has anti-viral activity against influenza A; however, high rates of anti-viral resistance limit its utility [6]. Due to some studies suggesting that amantadine has a significant influence on the inflammatory process, including the so-called "cytokine storm" and reduction of apoptosis and oxidative stress it was employed as a supportive agent in patients with COVID-19 which

refers to our case [7]. Our patient demonstrated symptoms such as psychomotor agitation, insomnia, excessive verbosity, delusions, and behavioral disturbances which are typical toxic effects of amantadine primarily affecting the central nervous system [8]. Anticholinergic agents may potentiate these effects. Neuropsychiatric adverse effects in the elderly, mainly with long-term use. Reports of psychosis associated with amantadine in young healthy patients have primarily been in the setting of overdose or combination with psychotropic medications [9]. A psychotic side effect of amantadine is theorized to relate to enhancing dopamine release via the antagonism of the N-methyl-D-aspartate receptor, ketamine which is an N-methyl-d-aspartate antagonist can induce the positive, negative, and cognitive symptoms of schizophrenia. [10,11].

There have been only five previous reports of rapid psychiatric complications among otherwise young and healthy individuals. The first report described an acute psychosis induced by an amantadine overdose[12], the second noted the emergence of psychosis after 100 mg of amantadine twice daily in combination with venlafaxine and quetiapine[9], the third study reported two cases of psychosis among 295 subjects in an amantadine antiviral trial [13].

The study from 2016 disclosed a case of a 28-year-old man suffering from a cold who presented with hallucination–delusion syndrome immediately after the use of medicine containing amantadine hydrochloride and acetaminophen [14]. The latest paper covers the case of a healthy 22-yeard-old Chinese man presenting with severe drug-induced psychosis after the intake of an over-the-counter (OTC) Chinese 'Cold and Flu' medication containing amantadine.
The patient presented symptoms such as disorientation, sleep disturbance, increasing agitation, visual hallucinations, persecutory auditory hallucinations, and disordered thought [15].

Our case illustrates the negative effects of amantadine on the central nervous system when given at the recommended dose to young, healthy women. Despite being rare, this induced psychosis may become more common, especially while becoming more popular as a supportive drug in COVID-19 treatment. While prescribing amantadine clinicians should be aware of the rapid onset of its psychotic complications.

4. Conclusions

Acute psychosis can be induced even in young patients with no history of chronic diseases who have taken the recommended dose of amantadine. Symptoms such as psychomotor agitation, insomnia, excessive verbosity, delusions, and behavioral disturbances are typical rapid toxic effects of amantadine on the central nervous system. Cases of psychosis associated with amantadine in young healthy patients have primarily been in the setting of overdose or combination with psychotropic medications. In elderly patients, the neuropsychiatric side effects of amantadine are related to long-term use. Prolonged symptoms of psychosis may be an indication of continued treatment in a psychiatric ward. More common use of amantadine as a supportive drug in SARS-CoV-2 infection may increase the frequency of this induced psychosis.

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