Methylphenidate-induced psychosis in a young antipsychotic-naïve female patient

Zaburzenia psychotyczne indukowane stosowaniem metylofenidatu u młodej kobiety dotychczas nieleczonej przeciwpsychotycznie

Patryk Walichniewicz[*1], Michał Lew-Starowicz*[2]

[1] *Psychiatric Ward, Bielanski Hospital, Warsaw, Poland*

[2] *Department of Psychiatry, Centre of Postgraduate Medical Education, Warsaw, Poland*

KEY WORDS:

- methylphenidate
- side effects
- psychosis
- diagnosis and treatment
- case report

ABSTRACT

Methylphenidate (MPD) is commonly prescribed for patients with Attention Deficit/Hyperactivity Disorder (ADHD). Although used off-label, MPD forms part of complex and multifactorial treatment regimen for narcolepsy and hypersomnia, together with including behavioural interventions. The drug is sometimes also prescribed off-label to subjects with other mental illness or somatic condition to improve intellectual outcome, ease fatigue or enhance the ability to concentrate. Common side effects include headache, insomnia, decreased appetite and hypertension. Concurrently, clinicians should be aware of relatively rare but potentially threatening adverse effects including agitation and psychotic symptoms. Several case reports regarding MPD-induced psychosis have been published, but most of them regard children or teenagers (1) and much less is known about drug-induced psychosis in adults (2). In this article, we present a case report of MPD-induced psychosis in a 31-year-old, antipsychotic-naïve patient. Careful evaluation including clinical examination, medical and family history and possible early signs of psychosis is recommended each time before MPD treatment will be initiated.

SŁOWA KLUCZOWE:

- metylofenidat
- efekty uboczne
- zaburzenia psychotyczne
- diagnoza i leczenie
- opis przypadku

STRESZCZENIE

Metylofenidat (MFD) jest powszechnie stosowany w leczeniu zespołu nadpobudliwości psychoruchowej z deficytem uwagi (ADHD). Pomimo bycia stosowanym poza wskazaniami rejestracyjnymi, lek wchodzi w skład złożonych i wieloczynnikowych schematów leczenia narkolepsji i nadmiernej senności, razem z interwencjami behawioralnymi. Jest także czasem przepisywany poza zarejestrowanymi wskazaniami celem poprawy funkcjonowania intelektualnego, zmniejszenia uczucia zmęczenia czy poprawy koncentracji. Do częstych działań niepożądanych zalicza się m.in. bóle głowy, bezsenność, wzrost apetytu i nadciśnienie. Jednocześnie, lekarze muszą być świadomi stosunkowo rzadkich, ale potencjalnie groźnych działań niepożądanych jakimi są pobudzenie oraz objawy psychotyczne. Dotychczas opublikowano kilka opisów przypadków psychoz wyindukowanych stosowaniem MFD, jednak większość z nich dotyczy dzieci i nastolatków (1), a znacznie mniej wiadomo na temat psychoz wyindukowanych lekiem wśród dorosłych pacjentów (2). W poniższym artykule został przedstawiony opis przypadku 31 letniej, dotychczas nieleczonej lekami przeciwpsychotycznymi pacjentki, u której w wyniku stosowania MFD wystąpiły zaburzenia psychotyczne. Każdorazowo, przed włączeniem do leczenia MFD, zalecana jest uważna ocena zawierająca badanie kliniczne, wywiad medyczny oraz dotyczący obciążeń chorobami psychicznymi w rodzinie, a także występowania u pacjenta możliwych wczesnych objawów psychotycznych.

Introduction

Methylphenidate (MPD) is a medication commonly prescribed for children and adult patients with Attention Deficit/Hyperactivity Disorder (ADHD) worldwide. Prevalence rates of ADHD in Poland are 0.3% in children and adolescents, and 0.8% in adults (1), while worldwide meta-analysis disclose the rates about 16% both in children (3) and adults (4).Such high difference in prevalence rates between Polish and world data may result from different methodology

*Address for correspondence: *Patryk Walichniewicz; Psychiatric Ward, Bielański Hospital, Cegłowska 80 Street, 01-809 Warsaw, Poland, e-mail: patryk.walichniewicz@outlook.com*

Published and financed by Centre of Postgraduate Medical Education; https://doi.org/10.36553/wm.74

used in the studies (5); apart from that, the prevalence rates in the countries which use DSM-5 diagnostic criteria are twice as high as those of the countries which use ICD-10 (6). MPD was approved by Food and Drug Administration (FDA) for patients 6 years of age or older and the usual doses range from 10 to 60 mg/day (7) (and 60 mg/day is a maximum dose suggested in the summary of product characteristics) but dosing regimens up to 100 mg/day were also recommended (8). It is also FDA-approved as a second-line treatment for narcolepsy and hypersomnia in adults (9). It happens to be used off-label (10) to enhance cognitive performance, to alleviate fatigue, especially in patients suffering from cancer [it may counteract opioid-induced somnolence and increase analgesic effects of opioids (11)], apathy in Alzheimer's disease (12) or refractory depression in geriatric population (13). The drug shows quite a high efficacy in treating negative symptoms of schizophrenia (14). It is worth mentioning that some research shows efficacy of MPD in reducing the frequency of incidents of self-harm or suicide attempts (15). In some places it is also used to cure treatment-resistant cases of bipolar disorder (16) or major depressive disorder, but this application is controversial (17). Most patients diagnosed with ADHD (regardless of their age) benefit from the therapeutic effects of MPD with minimum side effects (18, 19).

Pharmacological properties

MPD is a mild central nervous system (CNS) stimulant, structurally similar to amphetamine, but its exact mechanism of action is not fully described – MPD is believed to block the reuptake of NA and DA into the presynaptic neurone and increase the release of noradrenaline (NA) and dopamine (DA) into the extraneuronal space (20). This creates its stimulant effect localized mainly in the prefrontal cortex (21). This activation results in increased inhibition of impulsiveness. The substance is also a mild 5-HT1A receptor agonist and this additional mechanism contributes to the increased level of DA (22). In Poland the drug is available only for oral administration, but abroad transdermal patches are also in use.

MPD has a potential of abuse due to euphoric feeling when consuming high doses of the drug (23) [e.g., intranasally in doses up to 200 mg orintravenously from 40 to 1000 mg (24)]. Common side effects of methylphenidate include headaches, insomnia, hypertension, nausea and emesis, diarrhoea, dizziness, and anxiety. Less frequently, methylphenidate use may cause pancytopenia, seizures, agitation, sensitiveness or even psychotic symptoms such as hallucinations or delusions. As it was presented in the article by Moran et al., (25), in which they assessed almost 340 000 adolescents and adults diagnosed with ADHD, the risk of methylphenidate-induced psychosis amounts to 0.1%. The authors also concluded, that amphetamine was of greater risk to induce psychosis than MPD. In another study (26) the MPD-induced psychosis risk was assessed as 0.25%.

Concurrently, there are studies in which authors did not detect an increased risk of psychotic events after starting MPD treatment (27) (patients aged 12-30 years at the start of treatment were included; the risk of MPD-induced psychosis in a 12-week observation was similar for patients with and without a history of psychosis and did not differ from the risk of psychosis in general population).

The differences in the studies still need further investigation, as in currently available articles study groups differ in numbers, inclusion criteria as well as observation time are not alike.

Case report

(the patient's personal data was anonymised in order to prevent identification of a person)

A 31-year-old female, single, PhD student, was admitted straight from the outpatient clinic to the psychiatric ward because of her violent behaviour and attempted suicide. She had never been hospitalized nor had she suffered from any somatic diseases. Positive family history of mental illness (her mother's sister was suffering from schizophrenia while mother's brother committed a suicide).

On the day of admission she came to the psychiatric outpatient clinic, not having made any appointment, and demanded psychiatric consultation. She presented with disorganized behaviour, incoherent speech, catatonic behaviour (excited catatonia characterised by bizarre, non-goal-directed hyperactivity, impulsiveness), derailment, freezing, brakes in train of thoughts persecutory delusions and third person auditory hallucinations of imperative nature. She mentioned that she had not slept for a couple of days because of fear of waking up dead. She admitted having written a suicide note which she then burnt. When the psychiatrist informed the patient about the fact that she was going to be referred to the psychiatric ward, she abruptly took out a knife, cut her wrist and tried to run out and attacked the physician who was trying to stop her. Physical restrain had to be used.

When examined for the first time at the ward, the patient remained agitated; asyndetic thinking, tachyphrenia, delusions of reference and mood decline were observed. She confirmed experiencing auditory hallucinations and suicidal thoughts and her affect remained blunt. The train of thoughts was so disturbed that it was impossible to get a full history. EEG and brain CT were normal. No traces of illicit substance were found in urine samples.

As it was later established, the patient turned to a psychiatrist for the first time 2 years earlier, when she was suffering from declined mood after facing some problems in her personal life. She was then diagnosed with depressive disorder, and Asperger's syndrome was suspected. Sertraline and then Duloxetine were prescribed with no significant effect. As the patient started complaining of impaired concentration and lack of energy, she was also advised to start MPD and Agomelatine and later MPD and Bupropion treatment. She had been taking MPD for 15 months and stopped 2 months before hospitalization because of mental hyperactivity, racing thoughts and persistent delusions of self-accusation. She also became suspicious, experienced periods of derealization and the symptoms reached the level of persecutory delusions. The patient felt so anxious that she decided to carry a knife around. The above-mentioned symptoms started after 3-month therapy of MPD, lasted for a year and resulted in hospitalization need.

At the ward, the patient was treated with Olanzapine and the dose was gradually augmented to 15 mg per day. The patient's mental condition improved, the train of thoughts became logical and linear, the facial expression lively and affect was of normal range, appropriate to context. The patient was no longer delusional, she denied experiencing any hallucinations, her mood remained stable and concentration improved. Psychological care was also provided (consisting of work with shame and guilt but also psychoeducation about psychosis risk factors).

After 18 days she was discharged with the diagnosis of acute schizophrenia-like psychotic disorder (F23.2) and further medical care in an outpatient clinic was recommended.

The patient decided to continue working on her PhD dissertation and come back to work.

The patient has continued her treatment in the outpatient clinic – she complained about feeling drowsy and difficulty in memorizing and recalling but she did not suffer from delusions or other positive symptoms. It was decided to shift from Olanzapine to Aripiprazole – the patient became more active, it became easier for her to concentrate and she did not have any troubles in remembering. Nevertheless, she presented some problems with waking up early but the symptoms disappeared when the rules of sleep hygiene were implemented.

Discussion

Psychosis may be induced by a variety of psychoactive substances but it is worth bearing in mind that it may later prove to be the first symptom of schizophrenia, bipolar disorder as well as a brain tumor. Therefore, rigorous analysis of a patient's health condition, substance abuse and family history in pair with thorough examination are essential to treat the patient properly and effectively. Following consultations in an outpatient clinic are of great importance to control patient's health, adjust the dose of the antipsychotic drug and evaluate the diagnosis.

In the above-mentioned case the diagnosis of acute schizophrenia-like psychotic disorder was made since the patient did not fulfil diagnostic criteria of depressive disorder (F32), schizoaffective disorder (F25) or recurrent depressive disorder (F33), nor the time criteria of schizophrenia (F20). The time gap between first psychotic symptoms and full psychopathological syndrome was shorter than 2 weeks, and no indications of substance abuse or organic-related condition were established. All the drugs prescribed prior to the hospitalization have stimulating potential; although they are likely to improve mental outcome and the capability of concentration, considering patient's positive family history of mental illnesses they should not have been prescribed. The patient ought to have been more thoroughly examined as the first complaints on lack of concentration or insomnia highly probably were the initial symptoms of psychotic disorder. The patient required antipsychotic medication, and treatment with Olanzapine resulted in symptom remission. As less than one third (28) of patients maintain this initial diagnosis (F23.2) (29) (a half changes to schizophrenia; one sixth to schizoaffective disorder) (30), the patient requires regular psychiatric follow-up appointments in order to further adjust the medication, verify diagnosis and prevent relapse.

Conclusions

- Clinicians should be aware of medical and evidence-based indications to use methylphenidate.
- Both registered and off-label prescription requires appropriate risk-benefit assessment both due to safety reasons and the fact that MPD tends to be misused and overused due to its euphoric properties.
- Psychosis represents relatively rare but potentially threatening side effect of methylphenidate use.
- Careful evaluation including clinical examination, medical and family history and possible early signs of psychosis is recommended each time before MPD treatment will be initiated.

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