CLINICAL CASE

AMISULPRIDE – INDUCED HYPERPROLACTINEMIA- CASE REPORT

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Abstract

BACKGROUND: One of the most discussed adverse effect of antipsychotics is hyperprolactinemia. Dopamine antagonists block the D2 receptors of the lactotroph cells and prevent inhibition of prolactin secretion which determines increased levels of prolactin. Typical antipsychotics can increase the prolactin level up to 10 times the normal values, haloperidol and chlorpromazine producing a higher increase than olanzapine, prolactin increasing during the first week of treatment and returning to normal after 2-3 weeks. Atypical antipsychotics determine lower increasing in prolactin compared to first generation, but amisulpride and risperidone have been associated with higher levels of prolactin.

MATERIAL AND METHODS: We present the case of a 29 years old woman who developed hyperprolactinemia under treatment with Amisulpride, although the clinical evolution was improved.

CASE PARTICULARITIES: One of the particularities of this case was the high level of prolactin induced by treatment with Amisulpride, another particularity being the fact that patient’s work and social functionality was not impaired, even if the auditory hallucinations persisted.

CONCLUSIONS: Antipsychotic-induced hyperprolactinaemia should become a focus of interest in psychiatric practice. Antipsychoticele tipice cresc nivelul de prolactină până la de 10 ori valorile normale, haloperidolul și clorpromazina producînd o creștere mai mare decât olanzapina, prolactina crescînd în prima săptămână de tratament și revenînd la normal după 2-3 săptămâni. Antipsihoticele atipice determină o creștere mai mică a prolactinei comparativ cu prima generație, dar amisulpridul și risperidonul au fost asociate cu valori mai mari de prolactină.

BACKGROUND: Unul dintre cele mai discutate efecte adverse ale antipsihoticele este hiperprolactinemia. Antagoniștii dopaminergici blochează receptorii D2 ai celulelor lactotrofe și previn inhibiția secreției de prolactină ceea ce determină creșterea nivelului de prolactină. Antipsihoticele tipice cresc nivelul de prolactină până la de 10 ori valorile normale, haloperidolul și clorpromazina producînd o creștere mai mare decât olanzapina, prolactina crescînd în prima săptămână de tratament și revenînd la normal după 2-3 săptămâni. Antipsihoticele atipice determină o creștere mai mică a prolactinei comparativ cu prima generație, dar amisulpridul și risperidonul au fost asociate cu valori mai mari de prolactină.

MATERIAL ȘI METODE: Prezentăm cazul unei femei de 29 ani care a dezvoltat hiperprolactinăie mînă sub tratament cu Amisulprid, deși evoluția clinică a fost bună.

PARTICULARITĂȚILE CAZULUI: Una dintre particularitățile acestui caz a fost nivelul crescut de prolactină indus de tratamentul cu Amisulprid, o altă particularitate fiind faptul că funcționarea socială și profesională nu au fost afectate, deși halucinațiile auditive au persistat.

CONCLUZII: Hiperprolactinemia indusă de antipsihotice ar trebui să devină un element central al interesului în cazul tratamentului pacienților psihiatриci. Simptomele endocriine survin la un procent crescut de femei tratați cu antipsihotice ce determină creșterea prolactinei. Aceste simptome pot cauza un distress semnificativ și pot afecta componența la tratament. Prezența cicliurilor menstruale neregulate, simptomelor mamare și disfuncțiilor sexuale ar trebui evaluate înainte și în timpul tratamentului cu medicamente ce determină creșterea prolactinei și opțiunile de tratament ar trebui discutate cu pacientul.

CUVINTE CHEIE: antipsihotice, prolactină, efect adverse

BACKGROUND

One of the most discussed adverse effect of antipsychotics is hyperprolactinemia. Dopamine antagonists block the D2 receptors of the lactotroph cells and prevent inhibition of prolactin secretion which determines increased levels of prolactin. (1) Typical antipsychotics can increase the prolactin level up to 10 times the normal values, haloperidol and chlorpromazine producing a higher increase than olanzapine, prolactin increasing during the first week of treatment and returning to normal after 2-3 weeks. (2) Atypical antipsychotics determine lower increasing in prolactin compared to first generation, but amisulpride and risperidone have been associated with higher levels of prolactin. (3,4) A double-blind study of risperidone in schizophrenic patients showed that the prolactin increasing is dose-dependent and also an increase in prolactin level was observed in patients who were switched from haloperidol to risperidone. (5)

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Revised November 1, 2015, Accepted: January 9, 2017

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Received: 3 December 2015
Accepted: 22 December 2015

Ref: Ro J Psychiatry Psychother.2017;19(1) DOI: 10.37897/RJPP.2017.1.6
Another study on amisulpride showed that schizophrenia patients treated with this substance for 12 months experienced significantly increased prolactine level after 1 month at high dosing (1000 mg per day), the prolactine level declining after lowering the dose (200- 600 mg per day). (4) A review of 11 studies which involved 1247 patients treated with amisulpride showed that the incidence of hyperprolactinemia was similar for amisulpride, risperidone and haloperidol, but the safety profile of amisulpride is comparable to that of risperidone and superior to first generation antipsychotics (6)

CASE PRESENTATION
A 29 years old woman developed hyperprolactinemia under treatment with Amisulpride, although the clinical evolution was improved.

The patient presented to a private psychiatric facility in 2010 during an acute psychotic episode with auditory hallucinations, persecutory delusion and bizarre behavior. The patient was working for a software company, before the psychotic symptoms developed. She graduated Computer Sciences, lived with her mother and had a twin sister.

In 2010 the patient felt for a work colleague who didn't respond to her feelings. After a few months she left her job in order to hire at a bigger company. While she was working at the new company the psychotic symptoms started to develop beginning with auditory hallucinations (she was hearing her former colleague's voice) and persecutory delusion (she had the impression she's being followed by her colleague). She presented with her mother to a private psychiatric facility where the treatment was with 10 mg of Olanzapine, increasing gradually up to 20 mg for 3-4 months. Under this treatment the symptoms persisted, so Olanzapine was withdrawn and treatment with Quetiapine XR was initiated for 6 months without any improvement regarding symptomatology. The treatment was changed into Aripiprazole 15 mg 2 tablets/day, Clozapine 100 mg 3 tablets/day and Venlafaxine 75 mg 1 tablet/day. Venlafaxine was added because the patient started to present depressive symptoms (was disturbed and saddened by the voice she was hearing).

In 2013 the patient presented to “Prof. Dr. Alexandru Obregia” Hospital Emergency Unit with an acute psychotic episode with persecutory and commandatory auditory hallucinations related to her former colleague "he is communicating with me telepathically, he's telling me what to do and he knows everything that I do. He wants to annoy me really bad". At the time of admission the psychic state examination revealed the following: the patient was aware, cooperative, autopyschic and allopsychic oriented with spontaneous hypoprosexity, reduced flow and rhythm of thoughts and anxiety. Sleeping and appetite were normal, the patient presented no insight. One of the particularities of this case was the fact that patient's activity, work and social life weren't affected by the disease. The patient denies consumption of alcohol, nicotine and caffeine and the toxicological test was negative. The somatic examination was normal.

Treatment with Amisulpride 200 mg 1 tablets/day, Venlafaxine 75 mg 2 tablets/day and Lorazepam 1 mg 1.5 tablets/day was initiated. The clinical evolution was slightly improved so Amisulpride was increased to 3 tablets/day. The patient was discharged on request with the following treatment recommendations: Amisulpride 200 mg 3 tablets/day, Venlafaxine 75mg 2 tablets/day, Lorazepam 1 mg 1.5 tablets/day and Trihexyphenidilium 2mg 4 tablets/day. At home, the evolution under Amisulpride was good, the auditory hallucinations diminished and the patient could easily ignore them. Several months after discharged she developed amenorrhea. The gynecological consult was normal so she was referred to an endocrinologist who ordered the following tests: IGF-1, Cortisol, ACTH, Anti-tiroluglobulin antibodies, Testosterone, SHBG, TSH, fT3, fT4, FSH, Estradiol, Progesterone, LH and Prolactin. The only modified value was reported for Prolactin which was 4964 (reference values 102-496).

A pituitary MRI was performed and a glandular micro nodule was discovered, with no clinical significance. Considering the increased prolactin values, Amisulpride was withdrawn and the following treatment was started: Aripiprazole 30 mg/day, Venlafaxine 75 mg 1 tablet/day and Pramiracetam 600 mg 1 tablet/day. After one month the menstrual cycle reoccurred and prolactine level returned to normal. The evolution was very good so the doctor decided to withdraw Venlafaxine. After withdrawal, the depressive symptoms became more intense and the auditory hallucinations more vivid. Venlafaxine was reinstituted and at the present time the patient is well functioning at work and in social life, even if the auditory hallucinations persist, but she learned to ignore them. During the treatment with Aripiprazole, prolactin values returned to normal.

DISCUSSIONS
The most frequent causes of hyperprolactinemia were excluded: pregnancy (normal gynecological examination), hypothyroidism (normal thyroid hormones and ultrasound), prolactinomas (not revealed by MRI, normal pituitary hormones), kidney and liver disease (normal blood tests). Giving the fact that all other causes were excluded, the only probable cause remained was amisulpride induced- hyperprolactinemia. This diagnosis was also sustained by the decrease of prolactin after Amisulpride withdrawal.

One of the particularities of this case was the high level of prolactin induced by treatment with Amisulpride, another particularity being the fact that patient's work and social functionality was not impaired, even if the auditory hallucinations persisted.

CONCLUSIONS
Antipsychotic-induced hyperprolactinaemia should become a focus of interest in the drug treatment of psychiatric patients. Endocrine symptoms occur in a large proportion of women treated with prolactin-elevating antipsychotic drugs. These symptoms can cause significant distress and may affect compliance with medication. The presence of menstrual irregularities, breast symptoms and sexual dysfunction should be assessed before and during treatment with prolactin-elevating drugs and management options should be discussed with the patient.

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Conflict of interest: none declared
Financial support: none declared