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GALACTORRHEA - SIDE EFFECT OF RISPERIDONE IN COMBINATION WITH DEPAKINE CHRONO IN A PATIENT WITH BIPOLAR DISORDER

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SUMMARY

Risperidone, as all atypical antipsychotics, can cause hyperprolactinemia which can in turn lead to galactorrhea. Mood stabilizers, one of which is valproic acid and its derivate „Depakine Chrono", are rarely linked with symptomatic hyperprolactinemia and do not alter prolactin concentrations.

This case is based around a patient suffering from a bipolar disorder that has been psychiatrically treated in an outpatient clinic during four years. Bipolar disorder treatment was started with carbamazepine, but later it was discontinued due to adverse events and extreme increase of liver transaminases. Treatment was continued with introduction of lithium, but the patient stated that she could not tolerate it. Subsequently, her endocrinologist advised for lithium discontinuation due to very severe osteoporosis. At the beginning of 2009, lithium was discontinued and Depakine Chrono was introduced. Due to patient's psychotic decompensation it was necessary to introduce risperidone into treatment and soon afterwards her psychotic symptoms settled. After several months of treatment her mood lowered, she began to feel sedated, psychomotorically retarded and that lead to dose lowering of Depakine Chrono and risperidone, at which point galactorrhea as a serious adverse event occurred.

Occurrence of galactorrhea at lower risperidone doses in this case might be partially explained by recent studies that showed that lower doses of risperidone can also improve psychic state, but could also cause adverse events.

Although galactorrhea, as a direct consequence of hyperprolactinemia caused by risperidone has mainly been researched with higher doses of this atypical antipsychotic, we have to keep in mind that lower doses could also cause serious adverse events.

Key words: *galactorrhea – risperidone - Depakine chrono - bipolar disorder*

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INTRODUCTION

Probably the best treatment for patients with bipolar disorder is a combination therapy of mood stabilizers with antipsychotics, especially third generation ones or atypical antipsychotics (Riecher-Rössler et al. 2009). Risperidone, as all atypical antipsychotics, can cause hyperprolactinemia. Hyperprolactinemia is an endocrine disorder which can be caused by physiological, psychical and pathologic causes. Some medicaments are also causes of hyperprolactinemia. Risperidone is one of them and frequently causes hyperprolactinemia, especially in women (Torre & Falorni 2007). Symptoms of hyperprolactinemia can be in the form of: gynecomastia, galactorrhea, sexual dysfunctions, oligomenorrhea or amenorrhea (Haddad & Wieck 2004). As already mentioned, galactorrhea can result from hyperprolactinemia, and can also be caused by antipsychotic medication and occurs in 1-2 % of women (Chung & Eun 1998, Molitch 2008). Mood stabilizers, one of which is valproic acid and its derivate „Depakine Chrono", are rarely linked with symptomatic hyperprolactinemia and do not alter prolactin concentrations (Marken et al. 1992). Interactions between psychotropic drugs and prolactin occur at the Hypothalamic-pituitary-thyroid axis and Hypothalamic-pituitary- gondal axis levels. Scientific research showed that valproate can also cause endocrine disturbances and disorders, one of which is syndrome of polycystic ovaries (Elenitza 2005).

CASE REPORT

This case report is of a patient who developed galactorrhea after dose lowering of risperidone and Depakine Chrono. This case is especially interesting because she did not develop that adverse event when treated with higher doses of those medications.

Female patient, fifty years old, married and mother of two children works as a pastry cook and has been treated for bipolar disorder for four years.

In 2006, during the first exam at the Psychiatric Clinic in Rijeka, psychiatrist noticed depressive symptoms within the spectrum of bipolar disorder. During the previous year she started the treatment with lithium, which she took regularly, but stated that she could not tolerate it. Before lithium she was treated with carbamazepine (Tegretol) for a short period of time, but it was discontinued due to adverse events and extreme

increase of liver transaminases. While she was treated with lithium she was often nauseous, gained weight (around 15 kilograms per year) along with constant swelling of shins. Psychical condition was partly better due to treatment with a mood stabilizer, but mood oscillations persisted, along with verbalization of depressive ideas and work problems, which was the reason why she requested help of a psychiatrist. Her menstrual cycle was regular until the onset of menopause in 2007.

Previously she did not suffer from any severe somatic illness. Family anamnesis is negative. Negates drug allergies. Does not smoke nor drinks alcohol. Until 2009 treated for bipolar disorder with lithium and a small period of time with quetiapine, but due to severe sedation it was discontinued. SSRI antidepressant was also occasionally needed to control severe depression symptoms, but it was discontinued upon mood stabilization and occurrence of hypomanic symptoms. On one occasion she was treated in the day hospital setting due to a long period of sick leave from work.

At the beginning of 2009, endocrinologist established that she suffers from very severe osteoporosis, which could have been caused or aggravated by antidepressants or lithium. As the patient stated that she has troubles tolerating lithium and with severe osteoporosis taken into consideration, lithium was discontinued and Depakine Chrono introduced with its dose titrated to 1000 milligrams in the evening, which the patient tolerated very well, without adverse events. Afterwards risperidone (Rispolux) was introduced to treat psychotic decompensation and it was gradually titrated to 4 milligrams in the evening. After about a month of treatment, psychotic symptoms settled and the patient got more tired, slower, with restricted movements and of lowered mood and that lead to dose decrease of risperidone to 2 milligrams and Depakine Chrono to 500 milligrams in the evening. Three weeks afterwards, the patient stated that „milk leaks from her breasts“ and that it began a week after dose lowering of both medications (galactorrhea was clearly seen at the examination). That led to gradual discontinuation of risperidone while Depakine Chrono at 500 milligrams remained in therapy. A month afterwards, at the control examination there was no galactorrhea present. Patient stated that galactorrhea ceased about a week upon risperidone discontinuation. Subjectively she felt better, in a good mood, without psychotic symptoms.

DISCUSSION

Combining antipsychotic medication with mood stabilizers is the most frequent and arguably most efficient option for treatment of bipolar disorder **(**1**).** Valproate combined with risperidone is a very efficient combination, especially when treating acute mania in the bipolar disorder spectrum (Yatham et al. 2003). It´s a well know fact that antipsychotics, especially atypical, but typical as well, can cause hyperprolactinemia which can in turn lead to galactorrhea (Bostwick et al. 2009).

There is a number of research studies that showed that risperidone, due to its mechanisms of action, can increase prolactin levels and induce hyperprolactinemia and galactorrhea (Conley 2000).

The question is why galactorrhea occurred in our patient after risperidone and valproate dose decrease? Although there are reports in the literature that dose increase of atypical antipsychotics increases their efficiency, it also leads to increased incidence of adverse events (Kinon et al. 2008).

Occurrence of galactorrhea at lower doses of risperidone in our patient might be partly explained by recent studies which state that lower doses of an antipsychotic can improve psychical state of the treated patient, but at the same time can cause adverse events (Meltzer & Huang 2008).

CONCLUSION

Although galactorrhea, as a direct consequence of hyperprolactinemia caused by risperidone has mainly been researched with higher doses of this atypical antipsychotic, we have to keep in mind that lower doses could also cause serious adverse events.

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