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AMENORRHOEA – CONSEQUENCE OF COMBINED TREATMENT WITH SULPIRIDE AND RISPERIDONE IN A PATIENT SUFFERING FROM SCHIZOPHRENIA

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SUMMARY

It is well documented that sulpiride causes hormonal adverse events, like amenorrhoea and galactorrhea, due to its mechanism of action. Furthermore, risperidone can produce amenorrhoea and galactorrhea also, due to its mechanism of action, which differs from that of sulpiride.

This case report is of a patient that was treated with large doses of sulpiride, but did not develop an adverse event like amenorrhoea. However, when risperidone was introduced into therapy it leads to the onset of amenorrhoea. Gynecologist saw it as the beginning of menopause. General practitioner questioned the existence of an intra-cerebral process that could produce amenorrhoea as well. Therefore, the patient was sent to perform an MRI of the brain, under work diagnosis of pituitary adenoma, which was later ruled out as a cause of the illness. Well experienced psychiatrist linked the loss of menstruation with the adverse event profile of sulpiride and therefore gradually discontinued sulpiride from therapy, while risperidone was left and subsequently menstrual cycle was restored.

Good knowledge of adverse events profile of antipsychotic medication used, especially when used in a combination, allows us to correctly question appearance of adverse events, to adequately treat them and lowers the cost of unneeded medical procedures.

Key words: *amenorrhoea - antipsychotic medication – sulpiride – risperidone - schizophrenia*

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INTRODUCTION

When treating patients suffering from schizophrenia it is often necessary to combine medicaments, antipsychotics of different groups and mechanisms of action, in order to control all of the different symptoms of illness (Kuroki et al. 2008). It has been shown that combining second and third generation antipsychotics, like sulpiride and risperidone, has very good efficacy (Conley & Kelly 2002).

It is well known that sulpiride can cause hyperprolactinemia due to its mechanism of action. Hyperprolactinemia can then lead to other serious adverse events like: gynecomastia, amenorrhoea and galactorrhea (Pane et al. 1985). Risperidone, third generation atypical antipsychotic, can also cause hormonal adverse events like amenorrhoea and galactorrhea (Lee & Han 1999)**.** Combined therapy with these two antipsychotics raises the possibility of developing hyperprolactinemia. Sometimes it is necessary, due to adverse event development, to discontinue one or both of these medicaments and switch to other third generation antipsychotics (Mong-Liang et al. 2008).

CASE REPORT

J.K., female born in 1954 was 49 years old at the time of amenorrhoea onset. That age is usually associated with menopause, but that was not the case with this patient, as she maintained regular menstrual cycle for three full years afterwards.

She has been treated at ten occasions in different psychiatric institutions in Croatia and Slovenia. Six of those hospitalizations were at the Psychiatric Clinic of KBC Rijeka, mostly under the diagnosis of schizophrenia. First hospitalization was in 1984, when she was 30 years old, and last in 2002, when she was 48. At the time of that hospitalization she started therapy with 3 mg of risperidone in the evening and 400 mg of sulpiride divided into two doses, along with a hypnotic, anxiolytic and SSRI antidepressant.

At the time of her last hospitalization she was in a catatonic stupor, oneiroid state, along with flexibilitas cerea, lasting for four days and then turning into catatonic agitation, at which time her therapy was changed. On the seventeenth day of her hospitalization sulpiride was introduced at 400 mg per day, divided into two doses. After one month of hospitalization she started taking risperidone and it was titrated up to 3 mg per day, taken in the evening.

Afterwards she was regularly treated at the outpatient clinic and stated that she was compliantly taking prescribed medications. In May of 2003, after seven full months of combined treatment with both antipsychotics, she stated that during the last six months of treatment she did not

have a menstruation. Gynecologist concluded that it was the beginning of the menopause, which is quite common for that age, while her general practitioner deemed necessary to send her for a MRI of the brain. Prolactin in the serum was 3086 mL/l – higher than normal.

Psychiatrist gradually lowered and discontinued sulpiride, while risperidone was continued.

At the following control exam she showed MRI of the brain, which was normal for her age. She stated that she regained her menstrual cycle upon sulpiride discontinuation, while her psychical state was unchanged. During the following three years she maintained regular menstrual cycle and in 2006 menopause began.

DISCUSSION

Treatment of patients suffering from schizophrenia, being outpatient or hospital based, frequently requires combining different kinds of antipsychotic and other medications, in order to as quickly and efficiently as possible treat underlying psychopathology (Marcus & Olfson 2008). It is well known that antipsychotic medication, especially typical, but also atypical antipsychotics can cause hyperprolactinemia, which can lead to amenorrhoea (Bostwick et al. 2009). Quite a number of medical studies established that risperidone, due to its mechanism of action, can raise prolactin levels and lead to hyperprolactinemia and in turn to amenorrhoea and other sexual adverse events (Kim et al. 1999, Haefliger & Bonsack 2006). We can raise the question if amenorrhoea would appear in this patient if these two antipsychotics were not combined. Point of interest is that sulpiride and risperidone cause hyperprolactinemia and related adverse events quite more frequently than other antipsychotics (Mong-Liang et al. 2008). Also, we have to keep in mind that the patient was in a preclimacteric period, which is characterized with certain somatic changes (especially hormonal ones).

CONCLUSION

Good knowledge of adverse events profile of antipsychotic medication used, especially when used in a combination, allows us to correctly question appearance of adverse events, to adequately treat them and lowers the cost of unneeded medical procedures.

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