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SWITCHING AMONG ANTIPSYCHOTICS - FOCUS ON SIDE EFFECTS

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SUMMARY

Depression is a disorder held responsible for high morbidity in the overall population. Causes of depression vary, but lifestyle and stress can greatly contribute to its morbidity. Consumption of antidepressants is showing a trend in the economically developed countries. Apart from antidepressants, the treatment of depression can consist of other psychopharmaca. Depending on the severity of a disorder, that is - of psychotic symptoms, antipsychotics can be introduced in the treatment. Among those atypical antipsychotics have an advantage.

This paper will illustrate a course of treatment of a female patient, diagnosed with psychotic depression and treated with antipsychotics (i.e. olanzapine, ziprasidone), to which she developed side effects. To each of the antypsychotics the patient developed side effechts, causing in prolonged treatment and affected its course.

Key words: *psychotic depression- atypical antipsychotics- side effects*

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INTRODUCTION

Depression has become a problem of the society on a global scale, which is evident through a rise in the number of depressed patients that we encounter in our daily practice.

Depression is a mental disorder causing significant difficulties and disability. Antidepressants are used for depression treatment, as well as combinations with other medications, depending on the leading symptoms. When symptomatology reaches the psychotic level, administration of antipsychotics is indicated.

The selection of antipsychotics in the treatment of psychotic depression is completely up to the psychiatrists' choice. New generation antipsychotics are a common choice in treatment of psychotic symptoms, as reasons for that can be found in better adverse effects profile.

Due to their specific receptor affinity, side effects and efficacy, second- or third-generation antipsychotics (i.e. atypical antipsychotics) have an advantage over typical antipsychotics in depression treatment.

Among atypical antipsychotics olanzapine and ziprasidone have found their place in depression treatment. Both olanzapine and ziprasidone are generally well-tolerated.

Olanzapine is a thienobenzodiazepine analogue that binds to a large number of neurotransmitter receptors, including the dopamine D_1, D_2, and D_4 receptors, serotonin 5-HT_{2A}, 5-HT_{2C}, 5-HT_6, and 5-HT_3 receptors, histamine H_1 receptor, muscarinic receptors, α- and β-adrenergic receptors, γ-amino butyrate $(GABA)_{a1}$ receptor, and the benzodiazepine binding sites (Bymaster et al. 1996).

Olanzapine is associated with weight gain, which can pose a problem to the patient. Increased body weight affects their appearance, as well as everyday functioning in terms of limited physical activity (Muench & Hamer 2010).

Ziprasidone is a potent serotonin (5-HT) and dopamine (D_2) receptor antagonist. Its affinity at the 5-HT_{2A} receptor is 11-fold higher than at the D_2 site. It has moderate affinity for alpha-1 adrenergic and histamine (H_1) receptors and very low affinity for alpha-2 adrenergic and cholinergic (M1) receptors. It moderately inhibits 5-HT and norepinephrine (NE) reuptake.

Ziprasidone has pharmacologically important activity at serotonergic, dopaminergic and adrenergic receptors (Rossi et al. 2011). This pharmacological activity led to early speculation that the agent might have antidepressant or anxiolytic qualities as well as antipsychotic potential.

In comparative trials the most frequent treatment-emergent adverse events other than EPS or EPS-related events with ziprasidone were insomnia (16-25%), somnolence (3-21%), headache (6-15%), agitation (16%), vomiting (11%), nausea (10%), and anxiety (11%).

In the following case report we will describe a clinical case of a female patient who was treated with olanzapine due to psychotic depression. Due to increased body weight, the treatment with olanzapine was terminated. Ziprasidone was introduced next, to which she very soon developed a skin reaction (rash), due to which ziprasidone was immediately stopped.

CASE REPORT

A 51-year-old patient, married, no children, unemployed. First mental disturbances appeared in 2007 (3 years ago), when she contacted a psychiatrist for the first time. The clinical picture at the time included disturbances such as insomnia, anxiety, fears, stomach disorders, "nervous stomach". Lower doses of anxiolytic (sulpiride 50 mg, alprazolam 1 mg) over a few months resulted in improvement of her mental condition.

In May 2010, the patient noticed non-specific gynaecological conditions ("allergy or yeast infection"). Gynaecological examination was recommended, which she refused to do, so the general practitioner intervened with a single dose of intramuscular allergy therapy, after which she developed severe headaches.

Furthermore, general practitioner prescribed allergy pills (she couldn't tell which ones), after she felt mentally worse and grew more and more concerned. She started experiencing fears, having constant thoughts that bad things would happen, and became worried that she changed mentally. The patient lost her appetite and insomnia became more intense.

Two months later (July 2010), the patient reported to the psychiatric emergency, at which point a severe depressive episode with psychotic symptoms was diagnosed (F 32.3). A week after the therapy was introduced (i.e. sulpiride 100 mg/day, fluvoxamine 100 mg/day, alprazolam 1.5 mg/day, zolpidem 10 mg), her sleeping cycle and anxiety were regulated. Depressive symptoms were still noted (i.e. apathy, lack of motivation and interest, ideas of hopelessness).

Six weeks later, due to the incomplete remission of the illness, olanzapine of 5 mg was introduced in the evening dose, and sulpiride was stopped. The mental condition improved shortly. The patient attended regular ambulatory treatment, took the suggested psychopharmaca, and her mental condition reached full remission.

However, during the 3-month treatment, the patient had a big appetite, and she gained weight (14 kg). During the medical follow up a month later, further increase in body weight was noted (+ 4kg, 18 kg in total from the start of olanzapine treatment), along with the shin oedema. Despite the stable remission, olanzapine was stopped with the patient's consent due to the significant increase in body weight, but therapy with fluvoxamine, alprazolam and zolpidem in stable doses continued.

With the aforementioned therapy (without antipsychotics) the mental condition worsened (i.e. restlessness, fears followed with stomach disorders, "nervous stomach"). Within 15 days without antipsychotics the patient reduced her body weight by 4 kg. However, due to worsening of her mental condition another antipsychotic was introduced (ziprasidone 40 mg/day). After three days of therapy with antipsychotic, the patient developed itching all over her body (stomach, back, legs and arms), without skin manifestations, other than visible fresh skin damage, result of intensive nail scratching. After seven days ziprasidone was stopped.

The patient is now in the washout phase. She still complains about restlessness, especially nervous stomach, which she describes as a 'moving type', along with intense tension. Depressive symptomatology is not noticed in the actual clinical picture.

DISCUSSION

Treatment of the psychotic depression requires, apart from antidepressants, use of antipsychotics as well. Even though we are familiar with the side effects of the antipsychotics, those cannot be safely predicted. Atypical antipsychotics have an advantage over typical antipsychotics due to their equal efficacy and side effects profile of side effects. Antipsychotics may induce metabolic adverse effects. Excessive weight gain is more common in treatment of second- and third-generation antipsychotics, in comparison to the first generation antipsychotics (Ujike et al. 2008, Kroeze et al. 2003). This is explained by the affinity of second- and third-generation antipsychotics towards histamine H_1 receptors (Uzun et al. 2005).

Excessive weight gain has several deleterious effects in psychiatric patients, including stigmatization and further social withdrawn, and non-compliance with medication. Furthermore, excessive corpulence may evolve to a metabolic syndrome with a high-risk state for future cardiovascular morbidity and mortality in adult age (Goeb et al. 2010, Newcomer 2007).

Excessive weight gain is a common olanzapine side effect. Even though it is not considered to be a potentially lethal side effect, it can lead to a change in therapy (Uzun et al. 2005).

Ziprasidone can prove to be a good choice of antipsychotics among persons with excessive body weight or among persons that have been gaining body weight due to the effects of another antipsychotic, such as olanzapine for example. Ziprasidone was shown to have a very low liability for inducing movement disorders and weight gain (Green 2001).

Although some antipsychotics can cause allergic dermatitis and photosensitivity (chlorpromazine, levomepromazine, perazine), this is not typical of ziprasidone. However, some isolated cases are possible.

Even though dermatological changes related to ziprasidone are linked to longer exposure time in the higher dose patients, our experience proved just the opposite. Our patient used low therapeutic doses of ziprasidone, to which she developed a skin side effect in very short time.

In situations when two antipsychotics cause different side effects which require termination of therapy, the choice of antipsychotics in further treatment is very limited.

CONCLUSION

Side effects of antipsychotics are a potential risk in treatment of psychiatric patients. They limit the choice of the antipsychotics. The period of change can prolong the course of treatment, which risks the remission. Depending on the patient, they can become less cooperative.

Our patient developed side effects to two atypical antipsychotics. Olanzapine caused significant weight gain, which was an absolute indication to change the antipsychotic. Ziprasidone was introduced due to the low risk and impact on body weight. The patient developed a rash, which is a rare side effect, thus causing this medication to be stopped too.

Due to two different side effects to two atypical antipsychotics, the course of treatment has been significantly prolonged, which does not exclude the risk of worsening the mental condition and illness relapse. Consequently, it can lead to reduced level of patient cooperation and loss of confidence in the doctor.

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