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CASE REPORT

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Switch to quetiapine in antipsychotic agent-related hyperprolactinemia

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Abstract Novel antipsychotics (clozapine, risperidone, olanzapine, quetiapine) are effective in treating psychotic symptoms, also in neurological disease. Hyperprolactinemia is a side effect related to antipsychotics that can cause galactorrhea, gynecomastia, amenorrhea, anovulation, impaired spermatogenesis, decreased libido and sexual arousal, impotence, and anorgasmia, consequent to removal of tonic dopaminergic inhibition of prolactin secretion via hypothalamic dopaminergic receptor blockade in the tuberoinfundibolar tract. Hyperprolactinemia occurs more frequently during treatment with risperidone and olanzapine compared with clozapine and quetiapine. The therapeutic algorithm to antipsychotic-related hyperprolactinemia is the following: reduction in antipsychotic dose, addition of cabergoline, bromocriptine, amantadine, and/or switch to another antipsychotic. We propose switching to quetiapine in symptomatic hyperprolactinemia related to antipsychotics and describe five cases.

Key words Antipsychotic agent • Hyperprolactinemia • Risperidone • Quetiapine • Olanzapine • Clozapine

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Introduction

Novel antipsychotic agents (clozapine, risperidone, olanzapine, quetiapine) are effective against psychotic symptoms occurring in schizophrenia, schizophreniform disorder, delusional disorder, mood disorder, personality disorder, cognitive disorder, and in neurological diseases such as Parkinson's disease and epilepsy [1].

Unlike neuroleptics, these new antipsychotic agents may decrease psychotic symptoms without producing significant extrapyramidal side effects. Nevertheless, these medications do produce other side effects that clinicians must be aware of, such as hyperprolactinemia. Antipsychotic-induced hyperprolactinemia is consequent to the removal of tonic dopaminergic inhibition of prolactin (PRL) secretion due to the blockade of the dopamine receptor in the tuberoinfundibolar tract. Hyperprolactinemia can cause galactorrhea, gynecomastia, amenorrhea, anovulation, impaired spermatogenesis, decreased libido and sexual arousal, impotence, anorgasmia, and loss of protective effects of estrogen (i.e., increased risk of cardiac morbidity and osteoporosis in women) [2, 3].

It has been reported [3] that, among the new agents, risperidone is more likely to produce hyperprolactinemia, while this risk is consistently reduced with clozapine and quetiapine. Five cases are here reported of patients treated with antipsycotic agents with hyperprolactinemia-related side effects.

Case reports

Case 1

A 47-year-old female suffering from schizoaffective disorder (DSM-IV criteria) [4] was being treated with haloperidol (6 mg/day) and lithium (900 mg/day). On admission to the psy-

chiatric unit as outpatient, she presented with extrapyramidal side effects, such as tremor and stiffness. Lithium was in the therapeutic range (0.6 mEq/l). Haloperidol was switched to risperidone (4 mg/day) and extrapyramidal side effects disappeared.

After 2 months, she presented with anorgasmia and amenorrhea. PRL level was 85 ng/ml (normal value 3–30 ng/ml in females). Risperidone was switched to 400 mg/day of quetiapine (cross-tapering). Within 2 months menses and sexual function nomalized. PRL level fell to 13.7 ng/ml. Lithium was in the therapeutic range. Eight months later there was no recurrence of psychopathological symptoms, extrapyramidal side effects, or hyperprolactinemia-related side effects.

Case 2

A 28-year-old female outpatient was treated with risperidone at a dose of 4 mg/day for 4 months after discharge from the psychiatric unit where she was hospitalized for a brief psychotic disorder (DSM-IV criteria) [4]. During the visit she reported having amenorrhea for 2 months. Pregnancy was excluded. PRL level was 75 ng/ml. Risperidone was switched to 400 mg/day of quetiapine (cross-tapering in 15 days). Two months after menses and PRL normalized. One year later no side effects and psychopathological symptoms had occurred.

Case 3

A 32-year-old female outpatient was treated with risperidone (4 mg/day) for 3 months for schizoaffective disorder (DSM-IV criteria) [4]. She reported amenorrhea and galactorrhea, which started 2 months before. PRL level was 114 ng/ml. Risperidone was reduced to 2 mg/day in 2 months but no endocrinological improvement occurred. Then, risperidone was switched to 350 mg/day of quetiapine (cross-tapering). Two months after menses and PRL normalized. Galactorrhea disappeared. One year later, no endocrinological and psychopathological symptoms had occurred.

Case 4

A 31-year-old male outpatient suffering from schizoaffective disorder (DSM-IV criteria) [4] was treated with risperidone (3 mg/day) and lithium (900 mg/day). After 5 months he presented with galactorrhea (PRL level was 57 ng/l, normal value in men 1–20 ng/ml). For that reason the patient stopped taking risperidone and a new severe psychotic episode occurred, with depressed mood, catatonic features and paranoid delusion. Hence he was admitted as an inpatient to the psychiatric unit in our hospital. In the hospital he was treated with lithium 900 mg/day, citalopram 20 mg/day, and quetiapine 800 mg/day. One month later, he was discharged. Seven months later, no psychopathological and endocrinological symptoms had occurred; PRL level was in the normal range.

Case 5

An 18-year-old female patient was admitted to the psychiatric unit for brief psychotic disorder in borderline personality disorder (DSM-IV criteria) [4]. Before she was admitted she was treated for borderline personality disorder with olanzapine (10 mg/day). The patient stopped taking olanzapine when galactorrhea and amenorrea occurred and the new psychotic episode with paranoid and depressive features occurred. She was treated as an inpatient with citalopram (20 mg/day) and quetiapine (200 mg/day). One month later, menses and endocrinological features normalized. The patient could resume her school attendance and successfully sat an examination.

Discussion

Hyperprolactinemia related to antipsychotic treatment may produce clinical endocrinological problems and, consequently, poor compliance and worsening of psychopathological symptoms [3, 5].

When clinical features of hyperprolactinemia occur during antipsychotic treatment, other causes of hyperprolactinemia should first be excluded, in particular, a pituitary or hypothalamic tumor. To this purpose a neurological visit and a pituitary magnetic resonance imaging is mandatory.

In antipsychotic agent-related hyperprolactinemia an assessment of systematic endocrine side effects should be the cornerstone of therapeutic intervention. Patients may be reluctant to voluntarily report symptoms they find embarrassing, and clinicians must ask about them. When patients are prescribed antipsychotics known to raise PRL they should be informed about endocrine symptoms and their presence should be assessed before treatment, and monitored regularly thereafter.

Before switching to another drug we evaluate the PRL, renal, hepatic, and thyroid function. To limit health costs, we use pituitary magnetic resonance imaging only when PRL levels do not normalize after treatment modification or when neurological signs are present.

When hyperprolactinemia-related clinical manifestation occur our approach is as follows: reduce the dose of the medication and/or add dopamine agonists such as bromocriptine, cabergoline, or amantadine [6], or discontinue the offending medication and prescribe another (we prefer to switch the antipsychotic and we add a dopamine agonist as a third step).

Dose reduction of antipsychotics may worsen the psychopathological symptoms without necessarily improving hyperprolactinemia. The addition of dopamine agonists may worsen or cause psychotic symptoms such as delusion and hallucination, beside increasing the risk of other side effects and the total expense.

Asymptomatic hyperprolactinemia should not automatically lead to switching to another antipsychotic drug [3]. When dose reduction of antipsycotic does not resolve symptomatic hyperprolactinemia, or is prevented by the psychopathological state, we usually switch to other antipsychotics. Olanzapine is associated with a decreased risk for hyperprolactinemia compared with risperidone [3, 7]; however, we have observed several cases of olanzapine-related hyperprolactinemia. Monitoring the PRL level during olanzapine treatment could be useful, since the increase of PRL level with olanzapine could be transient [7, 8].

Since hyperprolactinemia appears to occur less frequently with clozapine and quetiapine, we switch to these drugs when necessary. Clozapine is indicated in resistant schizophrenia; regular hematological monitoring is required, given the risk of leukopenia. Quetiapine has a broad range of indications in psychosis. Since we did not observe hyperprolactinemia after quetiapine in our inpatients and outpatients, we prefere to switch to this drug when antipsychotic-related symptomatic hyperprolactinemia occurs, by cross-tapering (i.e., slowly decreasing the other antipsychotic and slowly increasing quetiapine, over few days in inpatients and over 15 days in outpatients). Thereafter, we check the endocrinological status after 1 and 2 months, also measuring the PRL level in the clinically normal patient. If endocrinological symptoms or PRL level are not normalized, we refer the patient for an endocrinological visit and for pituitary magnetic resonance imaging.

The limit of this study is the open-label nature, the female/male ratio, and the wide range of quetiapine daily dose (but this reflects the real clinical use of this drug). At follow-up, we observed a small change in body weight of quetiapine-treated patients (2–3 kg), but this side effect did not influence the patients' compliance with treatment.

Sommario *I nuovi antipsicotici (clozapina, risperidone, olanzapina, quetiapina) rappresentano degli strumenti utili nel trattamento delle psicosi anche in corso di malattie neurologiche. Tra gli effetti collaterali degli antipsicotici sono da ricordare le alterazioni endocrinologiche (amenorrea, galattorrea, impotenza, anorgasmia) indotte da iperprolattinemia, correlate al blocco tuberoinfundibolare dopaminergico. Questo effetto collaterale è maggiormente presente in corso di trattamento con risperidone e olanzapina, rispetto a clozapina e quetiapina. Sono possibili diverse strategie per contrastare l'iperprolattinemia, che vanno dalla riduzione del dosaggio dell'antipsicotico, all'associazione con cabergolina, bromocriptina, amantadina, e/o alla sostituzione dell'antipsicotico con un altro farmaco della medesima classe. Noi proponiamo la sostituzione dell'antipsicotico con quetiapina in presenza di collateralità endocrinologica da iperprolattinemia clinicamente evidente, descrivendo cinque casi clinici.*

References

1. Torta R, Keller R (1999) Behavioral, psychotic and anxiety disorder in epilepsy: etiology, clinical features and therapeutic indications. Epilepsia 40[Suppl 10]:S2–S20
2. Dickson RA, Glazer WM (1999) Neuroleptic-induced hyperprolactinemia. Schizophr Res 35[Suppl]:S75–S86
3. Wirshing DA, Erhart SM, Pierre JM, Boyd JA (2000) Nonextrapyramidal side effects of novel antipsychotics. Curr Opin Psychiatry 13:45–50
4. American Psychiatric Association (1996) Manuale diagnostico statistico dei disturbi mentali, IV edizione DSM-IV. Masson, Milan
5. Gracious B (2000) Atypical antipsychotics and hyperprolactinemia. International Drug Therapy Newslett 35:1–8
6. Tollin SR (2000) Use of dopamine agonist bromocriptine and cabergoline in the management of risperidone induced hyperprolactinemia in patients with psychotic disorders. J Endrocrinol Invest 23:765–770
7. Kim KS, Pae CU, Chae JH, Bahk WM, Jun TY, Kim DJ, Dickson RA (2002) Effects of olanzapine on prolactin levels of female patients with schizophrenia treated with olanzapine. J Clin Psychiatry 63:408–413
8. Maguire GA (2002) Prolactin elevation with antipsychotic medications: mechanism of action and clinical consequences. J Clin Psychiatry 63[Suppl 4]:56–62