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Case Reports

Cabergoline-induced psychotic exacerbation in schizophrenic patients

Shen-Chieh Chang, M.D.[a], Chun-Hsin Chen, M.D., M.S.[a,b], Mong-Liang Lu, M.D., M.S.[a,b,*]

[a]*Department of Psychiatry, Taipei Medical University-Wan Fang Medical Center, Taipei, Taiwan*
[b]*Department of Psychiatry, School of Medicine, Taipei Medical University, Taipei, Taiwan*

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Abstract

Introduction: Hyperprolactinemia is a well-recognized side effect of antipsychotic treatment. Cabergoline, a dopamine agonist, has been introduced on the market to treat hyperprolactinemia, even secondary to antipsychotic use.
Case Report: In this article, we described two schizophrenic patients who received cabergoline to treat their antipsychotic-induced hyperprolactinemia and developed a subsequent psychotic exacerbation. The first patient received amisulpride as antipsychotic medication, and the second one took risperidone and fluoxetine for her psychotic and depressive symptoms, respectively. Both patients improved significantly their psychotic symptoms in 1 week without changing their former antipsychotic regimens.
Discussion: To the best of our knowledge, we found no previous report of cabergoline-induced psychotic exacerbation in schizophrenic patients who received antipsychotics. We brought up questions whether schizophrenic patients on amisulpride or with the addition of fluoxetine may have higher risk to experience psychotic worsening. We also highlighted the possible role of dose-dependent nature in cabergoline-induced psychotic exacerbation, suggesting that the single starting dose of 0.5 mg or higher might be unsafe in schizophrenic patients.
Conclusion: These cases suggest that cabergoline, like other dopaminergic agents, should be used with caution in psychotic patients and the dose should be as low as possible.

Keywords: Cabergoline; Schizophrenia; Antipsychotics; Hyperprolactinemia

1. Introduction

Hyperprolactinemia, which is a well-recognized side effect due to antipsychotic treatment, can cause galactorrhea, menstrual irregularities, sexual dysfunction and even osteoporosis [1]. Dopamine serves as the major prolactin-inhibiting factor. It is secreted into portal blood by hypothalamic neurons, binds to receptors on lactotrophs in the anterior pituitary gland and inhibits both the synthesis and secretion of prolactin. The antipsychotic drugs can tonically block dopamine D_2 receptors in this tuberoinfundibular tract to disinhibit prolactin secretion [1].

To treat antipsychotic-related hyperprolactinemia, the algorithm suggests reducing the existing antipsychotic dose, switching the existing medication to another antipsychotic agent and adding a dopamine agonist. Both dose reduction of current antipsychotics and switching to prolactin-sparing antipsychotic drug have the risk of psychotic relapse. Thus, the relatively safe strategy is to add a dopamine agonist, such as bromocriptine, amantadine or cabergoline [2]. The results of previous studies suggested that adding bromocriptine or amantadine can reverse antipsychotic-induced hyperprolactinemia without worsening the psychotic symptoms of schizophrenic patients [2,3], although some case reports mentioned variable results [4,5].

Cabergoline, an ergot derivative with a high affinity for dopamine D_2 receptors, was introduced in the mid-1990s to treat hyperprolactinemia, even secondary to antipsychotic use [6]. Cabergoline was found to be superior to bromocriptine in treating hyperprolactinemia, due to its longer half-life, better efficacy and less adverse effects [6]. Its potential to induce psychotic symptoms has not yet been assessed, but no worsening of psychotic symptoms in patients receiving cabergoline has been reported [2,7,8]. Here, we present two schizophrenic patients with antipsychotic-induced hyperpro-

* Corresponding author. Department of Psychiatry, Taipei Medical University-Wan Fang Medical Center, Taipei, Taiwan. Tel.: +886 2 29307930x53951; fax: +886 2 29334920.
E-mail address: mongliang@hotmail.com (M.-L. Lu).

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lactinemia who suffered from psychotic exacerbation after having received cabergoline.

2. Case report

2.1. Case 1

Ms. A, a 32-year-old woman with a 10-year history of schizophrenia, was admitted to our inpatient ward due to her acute psychotic exacerbation. Having been treated unsuccessfully with adequate trials of trifluoperazine, haloperidol, risperidone and olanzapine, the patient was treated with amisulpride 600–1000 mg/day regularly in the past 2 years with significant improvement in both positive and negative symptoms.

The patient visited our gynecology clinic in early 2006 for her over-1-year-long amenorrhea. At that time her plasma prolactin level was 220.16 ng/ml (normal range: less than 25 ng/ml). The serum estradiol level was below 28 pg/ml. She had normal follicle-stimulating hormone (FSH, 5.82 mIU/ml) and luteinizing hormone concentrations (LH, 8.87 mIU/ml). The gynecologist prescribed cabergoline 0.5 mg twice a week to relieve her hyperprolactinemia. Within 6 h after the first dose of cabergoline, the patient became agitated and developed bizarre delusions such as that the sun would withdraw her thoughts and that people would remove her spiritual energy (*Qi* in Chinese). Thus, she needed an emergent hospitalization due to delusion-related violent behaviors.

During admission, the patient remained at the same amisulpride dose of 800 mg/day and discontinued the subsequent carbergoline use. Her psychotic symptoms improved 1 week later, and her prolactin level dropped to 85.3 ng/ml.

2.2. Case 2

Ms. B, a 44-year-old woman, has a 24-year history of schizophrenia. Having failed in adequate trials of various first-generation antipsychotic agents, the patient was successfully treated with risperidone 4.5 mg/day over the past 2 years. She also received fluoxetine 40 mg/day for her depressed mood.

The patient visited the gynecology clinic in early 2006, complaining about her 1-year-long amenorrhea. Her plasma prolactin level was elevated to 377.6 ng/ml. The plasma FSH and LH levels were both within normal ranges, 16.02 and 7.12 mIU/ml, respectively. The finding of her skull X-ray film showed a normal sella turcica. The result of abdominal sonography excluded the possibility of polycystic ovarian syndrome. Then, she was prescribed cabergoline 0.5 mg twice a week for the hyperprolactinemia. She experienced psychotic exacerbation following the first dose of cabergoline, presenting with auditory hallucinations, delusion of reference, excessive anxiety and dysphoric mood.

Under the impression of iatrogenic exacerbation of psychotic symptoms, we treated her with the same dose of risperidone and discontinued her cabergoline. She showed progressive improvement in the psychotic and mood symptoms over 1 week.

3. Discussion

To the best of our knowledge, this case report described cabergoline-induced psychotic exacerbation of schizophrenic patients for the first time. Previous studies suggested that cabergoline can safely and effectively treat risperidone-induced hyperprolactinemia in psychotic patients [2,7,8] and can successfully inhibit lactation in patients with postpartum psychosis during treatment with risperidone or haloperidol without worsening psychotic symptoms [9]. Amisulpride, a substituted benzamide derivative, has been reported to have high risk in causing hyperprolactinemia, possibly due to its poor blood–brain barrier penetration and higher dopamine D_2/D_3 receptor occupancy at the pituitary gland [10]. The safety of cabergoline treatment in amisulpride-induced hyperprolactinemia has not been discussed before. Whether patients receiving amisulpride were more liable to experience aggravation in psychotic symptoms compared to those receiving risperidone after being given cabergoline may need further exploration.

Some researchers also found that fluoxetine may induce hyperprolactinemia [11]. This could explain the extraordinarily high prolactin level in the second case, who received risperidone and fluoxetine at the same time. Since the previously reported risperidone-treated cases did not develop psychotic exacerbation after being given cabergoline, we wondered whether the simultaneous use of fluoxetine accounted for this complication.

Some studies have reported the development of hallucinations in nonpsychotic patients who received high-dose (2–5 mg/day) cabergoline [12,13]. For treating antipsychotic-induced hyperprolactinemia, the starting dose of cabergoline in antipsychotic-induced hyperprolactinemia has been suggested to be 0.125–0.25 mg/week [8]. One case report showed that gradual increment up to 3.5 mg/week did not induce psychotic worsening [7]. Our patients both received a relatively high first dose of 0.5 mg cabergoline and developed psychotic exacerbations. The higher starting dose of carbergoline might account for the increasing risk of psychotic worsening in schizophrenic patients.

4. Conclusion

The rapidity of psychotic exacerbation and improvement in our patients weighs in favor of a strong role for cabergoline. Based on these two reported cases, we suggest that cabergoline, like any other dopaminergic agents, should be used with caution in psychotic patients and the starting dose should be as low as possible.

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