Case report

Very low dose risperidone induced galactorrhea in a young girl: a case report

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Summary

Risperidone, a benzisoxazole derivative atypical antipsychotic was more effective than haloperidol (typical antipsychotic) in stimulating prolactin levels. Studies showed that low-dose risperidone (0.75-2mg/day, mean (±SD) dose 1.26(±0.42) led to significant increase of serum prolactin levels of different age group after 4-12 weeks of treatment when no patient had other physical condition or adverse effects known to affect prolactin level. Low dose risperidone induced galactorrhea and other physical symptoms in a short period was not a very common one. A 17 years old girl suffering from obsessive compulsive disorder and major depressive disorder developed galactorrhea with breast tenderness and heaviness only 2 weeks after taking low dose risperidone (1 mg). This case report might concern for special attention for prescribing risperidone to young female patients.

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Introduction

Prolactin is a polypeptide hormone that is secreted and released by lactotroph cells in the anterior pituitary gland related to the circadian pattern. This hormone is secreted in response to diverse physiological stimuli, but principally via the inhibitory action of dopamine. Auto-regulation of prolactin release also contributes to further control.[1] Hyperprolactinemia is clinically defined as a plasma prolactin level of >20ng/mL for men and >25ng/mL for women.[2] Some symptoms associated with hyperprolactinemia in women include menstrual irregularities, sexual impairment, breast enlargement and galactorrhea.[3] The prevalence of prolactin elevation is more often than not underestimated. Hyperprolactinemia is most frequently occurred with neuroleptics and antidepressants. Neuroleptic-induced hyperprolactinemia is more common in women than in men.

Atypical antipsychotic agents such as olanzapine, quetiapine, clozapine and risperidone have shown to increase prolactin level. Among them risperidone, however, is a widely used atypical agent that has shown more pronounced and continuous elevations in prolactin levels due to a stronger, more prolonged dopamine receptor blockade.[4,5] Even low doses of risperidone used either as an augmentation of treatment with antidepressants, benzodiazepines, mood stabilizers or as a monotherapy could be associated with hyperprolactinemia.[6]

Case summary

A 17 years old girl, who was a student of class ten came to psychiatrist with the complaints of irritability, lack of enjoyment, sleep disturbance, suicidal thoughts for six months. There was also history of impulsive self-harm as wrist cutting and avoidance of sharp instruments for two years. She avoided sharp cutting instruments like knife as she feared of self-injury when she saw them. She had no significant family history of mental illness. Her birth history was uneventful with normal childhood development history. She had good relation with family and peer group, she was social and her hobby was painting. For above complaints she took different psychiatric consultation and took different psychotropic drugs but no significant improvement occurred. Mental state examination revealed her mood was depressed. She had obsessive impulse and suicidal thoughts. There was no hallucination or delusion and her insight remained intact. The she was diagnosed as a case of obsessive-compulsive disorder (OCD) and major depressive disorder Then, at that time she advised sertraline 100 mg (gradually increased) and risperidone (1 mg) as an augment therapy. After two weeks, she complained breast enlargement, breast tenderness with secretion. On examination, breast was tender. There was oozing of whitish fluid (milk) from both nipples. Investigation report of serum prolactin level was 92 ng/dl. Then risperidone was stopped and she was advised quetiapine 50 mg and starting of cabergoline. After 1 month of these medications her prolactin

level came back to normal. On the following months of follow-up, there was no re-emergence of galactorrhea. Then psychiatrist intended to continuing treatment with sertraline and quetiapine.

Discussion

This case demonstrated a clinically significant relationship between risperidone administration and resultant hyperprolactinemia with significant adverse effects. The patient's prolactin level was high when she was treated with risperidone and the prolactin level dropped with symptoms relieved by one month after stopping this medication. The likelihood of risperidone causing physical side effects like galactorrhea and breast tenderness and hyperprolactinemia. Furthermore, the patient's prolactin level remained normal while receiving quetiapine (50 mg/day).

Although pharmacotherapy of major depressive disorder and also obsessive-compulsive disorder was preferably recommended with selective serotonin reuptake inhibitors (SSRIs) which were currently considered the drug of choice in these patients.[7,8] Near half OCD patients did not respond desirably to monotherapy with these agents, yet even after switching to another drug in the family. Previous findings indicated that adding an antipsychotic to the regimen exerted improved response to SSRI therapy in patients. This observation was most significant with risperidone.[8] Several studies demonstrated that risperidone might be associated with increased serum prolactin level and related symptoms. However, this effect was mainly experienced when using higher doses of risperidone (i.e. more than 2 mg/day). Risperidone was shown to more frequent hyperprolactinemia compared to most other second-generation antipsychotics, but less than first generation ones. Notwithstanding, the serum prolactin levels induced by risperidone therapy was significantly higher than that associated with conventional antipsychotic medications.[9,10] Some studies showed that there was a significant correlation between risperidone daily doses and plasma prolactin levels and even low-dose risperidone led to the significant increase of serum prolactin levels after 12 weeks of treatment. However, no significant data had been so far published on the prolactin related adverse effects of low dose risperidone (d"2mg) in short duration of treatment used as an add-on therapy.[6,10-12]

It was unlikely the co-administration of sertraline in this patient was a factor in causing the increased prolactin level. Risperidone was metabolized to an active metabolite 9-hydroxyrisperidone in the liver via the cytochrome P450 2D6 pathway. While it was known that SSRIs could inhibit the 2D6 pathway, the degree to which this occurred varies within the class. Fluoxetine and paroxetine were potent inhibitors of 2D6 and would be most likely to increase plasma levels of risperidone in patients to a clinically measurable degree. Sertraline, citalopram, and escitalopram were weak enzyme inhibitors and would have minor effects on risperidone levels. Co-administration of risperidone with any of these three SSRIs would likely not contribute to clinical changes in a patient. Sertraline and other medications the patient were taking provide no clinically significant drug interactions with risperidone that could lead to increased plasma concentrations.[6,13] This case report was consistent with literature that had shown that risperidone can cause hyperprolactinemia.

Conclusion

In this case reported, we mentioned a young girl who experienced galactorrhea and breast tenderness with an increase in serum prolactin level following psychotropics administration. Regarding our patient, co medication with very low-dose risperidone established increased level of prolactin with bilateral breast discharge and pain. This neuroendocrine effect was reversed following risperidone withdrawal and cabergoline treatment. So, it was shown that, even low doses of risperidone used either as an augmentation of treatment with antidepressants, benzodiazepines, mood stabilizers or individual therapy could cause early side effects to young girl. The psychiatrists should keep in mind the subsequent clinically relevant endocrinological side effects of risperidone especially in young patients.

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