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CASE REPORT

Beneficial effects of add-on raloxifene in schizophrenia

A case report

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Abstract The role of estrogens in schizophrenia has been proposed from the observation of schizophrenia occurring later and with symptom severity being lesser in women. Utility of estrogens in treatment of psychoses, though seen to be useful, comes with inherent risks of neoplasias, given its agonistic action on breast and endometrium. This risk can be overcome with use of selective estrogen receptor modulators, like raloxifene. Raloxifene has been used in schizophrenia, with improvement in symptoms and cognitive functions. We report the use of raloxifene as an adjunctive treatment, with risperidone, in treatment-resistant form of schizophrenia. The patient, a 29-year-old woman, over a 7-month follow-up period, showed significant improvement in socio-occupational functioning, with reduction in symptom severity.

Keywords Schizophrenia · Selective estrogen receptor modulators · Raloxifene

Introduction

The role of estrogen in brain functioning is vital, with estrogen receptors being found in various areas of the brain. Their presence in the limbic system confers a neuromodulatory influence on emotions (Riecher-Rossler 2002). Its role in regulating blood flow and glucose metabolism in brain also makes it a neuroprotectant (Garcia-Segura et al. 2001). In the context of psychosis, it possibly acts as a psychoprotectant by modulating the monoaminergic neurotransmission and its effects on dopamine, serotonin and GABA (Garcia-Segura et al. 2001). The relation between estrogen and schizophrenia is robustly supported by the more frequent occurrence of late-onset schizophrenia, after age 40, in women—a finding attributed to the loss of ovarian function (Riecher-Rossler 2002). Though the prevalence of schizophrenia is equal among men and women, women have a lesser symptom severity. Further supporting this link, estrogens used as adjunctive treatment have been seen to ameliorate both psychotic symptoms and cognitive deficits (Shivakumar and Venkatasubramanian 2011; Wong et al. 2003). However, estrogens pose a high risk/benefit ratio due to agonistic action on breast and uterine endometrium, resulting in neoplasias. Selective Estrogen Receptor Modulators (SERMs), like raloxifene and tamoxifene, with agonistic action on brain and anti-estrogenic action on breast and uterus, overcome the non-specific effects of estrogens. Few studies have reported the successful use of SERMs, especially raloxifene, as an adjunctive therapy in schizophrenia and other psychoses, with improvement in symptoms and cognitive status (Kulkarni et al. 2008; Usall et al. 2011; Wong et al. 2003). Here, we report a case of early-onset schizophrenia which responded well to add-on Raloxifene.

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Case report

Ms. M, a 29-year-old single woman, was diagnosed with paranoid schizophrenia and presented with a four years duration, acute onset, continuous illness characterized by

auditory hallucinations, second and third person, delusions of persecution and love and thought broadcast, with significant acting out behavior and absent insight. She had comorbid hypothyroidism, diagnosed 2 years earlier, and was on thyroxine supplementation. She scored 70 on Scale for Assessment of Positive Symptoms (SAPS) and 89 on Scale for Assessment of Negative Symptoms (SANS). She had failed adequate trials of olanzapine, quetiapine and aripiperazole. With clozapine up to 400 mg/day, she showed about 50% response, as reported by her family; however, she did not tolerate further increases in dosage. We tapered and stopped using clozapine, and started the patient on risperidone, going up to 8 mg/day. After 3 weeks, patient showed partial improvement, with a SAPS score 50 and SANS score 72.

In follow-up after 3 months, patient had further improved. She scored 19 on SAPS and 13 on SANS. However, she had persistent auditory hallucinations, second and third person, with acting out behavior and significant socio-occupational dysfunction. She had poor social interaction, remained withdrawn and did not engage in any household activities, other than self-care. Her Clinical Global Impression—Severity (CGI-S) score was 5 (i.e., markedly ill). On treatment, she had developed amenorrhea, due to hyperprolactinemia, and weight gain.

On further interviews with the family, it was noted that patient had a history of symptom worsening around the time of her menstrual period, i.e., when estrogen and progesterone levels are expected to drop. Her serum estradiol level (during follicular phase) was within normal range (16.36 pg/ml). The patient was started on raloxifene 60 at mg/day (in view of the peri-menstrual worsening of symptoms); 1 week later, this was increased to 120 mg/day. Risperidone at 8 mg/day was continued.

In follow-up after 7 months, the patient and family reported an improvement of 70% from baseline, more than had been ever seen for this patient. Although she still scored 12 on SAPS and 10 on SANS, her CGI-S score was 3 (i.e., mildly ill) and Clinical Global Impression–Improvement (CGI-I) 1 (very much improved). The patient had improved remarkably in socio-occupational functioning. No new side effects were reported; however, weight gain and amenorrhea persisted.

Discussion

In the presented case report, significant improvement was noted in symptoms and socio-occupational functioning in a treatment resistant schizophrenia patient, with addition of raloxifene to risperidone therapy. No significant side effects were reported. Even though the symptom score showed only slight reduction, functioning, in terms of socialization, cognition and attention, was significantly benefitted. Use of SERMs as an adjunctive treatment in schizophrenia with positive results has been reported by few authors (Kulkarni et al. 2010). In the context of our earlier observation (Shivakumar and Venkatasubramanian 2011), the current case report further strengthens the role of raloxifene in treatment-resistant schizophrenia. The role of estrogen influence in schizophrenia has been established, and this case illustrates the successful application of selective estrogen modulation using raloxifene as an add-on therapy in schizophrenia.

Conflict of interest The authors declare no conflict of interest.

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