Female Sex Hormone Augmentation Is Effective for Menopausal Psychosis

Nan-Wen Yu, M.D.1,2, Mei-Chun Hsiao, M.D.1,2,3, Chia-Yih Liu, M.D.1,2,3,4

Introduction

During menopausal transition, many women experience problems such as vasomotor instability, coronary heart disease, osteoporosis, memory loss, coldness feeling of peripheral limbs, emotional lability, sleep disturbances and urogenital atrophy. Psychosis is a known perimenopausal symptom [1], and patients with late-onset schizophrenia (onset after 45 years of age) are also more likely to be female patients [2]. Perimenopausal and menopausal psychoses are related to estrogen withdrawal [3].

Background: Perimenopausal women may have an increased vulnerability to psychosis. Antipsychotic drugs are considered effective for acute and maintenance treatment of menopausal psychosis. In those patients who respond poorly to antipsychotic agents, estrogen augmentation may be also beneficial. Case report: We present a 50-year-old woman experiencing psychotic symptoms with onset one year after the menopause. The patient with positive psychotic symptoms did not respond well to three different antipsychotic drugs at adequate dosage and duration. But she responded with a combination of antipsychotic drug and Premelle 2.5 (conjugated estrogen 0.625 + medroxyprogesterone 2.5mg) daily, and achieved a satisfactory treatment response. The patient’s psychotic symptoms were re-emerged after discontinuation of Premelle and were resolved after resuming Premelle treatment. Conclusion: Estrogen modulates the dopamine system in a mechanism similar to neuroleptic drugs and is an effective augmentation treatment for menopausal psychosis.

Key words: menopausal psychosis, Premelle, estrogen
(Taiwanese Journal of Psychiatry [Taipei] 2010;24:146-9)

In general, antipsychotic agents are effective in treating menopausal psychosis. Some authors have suggested that estrogen can be supplemented in patients who are unresponsive to antipsychotic treatment [4].

This paper reports the case of a 50-year-old woman who was suffering from a first episode of psychosis one year after the menopause. She failed to respond to treatment with antipsychotic agents but exhibited a better response to a combination of estrogen and antipsychotic drugs.
Case Report

A 50-year-old woman, previously in good health without systemic disease or mental illness history, developed insomnia, auditory hallucinations, disorganized thinking, incoherent speech, religious and persecutory delusions, and delusions of misidentification three months before her first visit to the psychiatric clinic. At that time, she had been through the menopause in the previous year. After being excluded for general medical condition-related and substance-induced psychosis, she was diagnosed as late-onset schizophrenia. She received trifluoperazine with the dose increase from 5 mg/d to 20 mg/d over a two-month period. The patient’s psychotic symptoms were persisted, and she received flupenthixol decanoate 20 mg with intramuscular injection once every two weeks. The patient had extrapyramidal symptoms following high doses of antipsychotic agents, and thus she received an anticholinergic agent. After a three-month treatment, she did not show any improvement. The oral antipsychotic drug, trifluoperazine, was changed to sulpiride, the dosage of which was increased up to 800 mg/d (in combination with a flupenthixol decanoate 20 mg IM once every two weeks). She still showed little improvement for another two months.

The patient did not have any contraindication for hormonal therapy. So, she was transferred to our women’s mental health clinic. Her flupenthixol decanoate was discontinued and Premelle 2.5 (conjugated estrogen 0.625 + medroxyprogesterone 2.5 mg) 1 tablet daily was administered. The patient’s psychotic symptoms then gradually subsided, from 7 to 3 on the visual analogue scale (VAS). Improved symptom after Premelle combination treatment included the subsiding of auditory hallucinations, lesser paranoid delusions, better cognitive function, more coherent speech, more social interaction and better quality of sleep. The patient’s extrapyramidal symptoms were markedly improved, seemingly being due to the discontinuation of flupenthixol decanoate. Premelle 2.5 table/d was tapered off to one tablet every other day six months later. She had been maintained with sulpiride 800 mg/d and Premelle table/d for two years. During that time, she did not have any psychotic symptom and medication side effect.

Premelle 2.5 was then tapered off. But the patient started to experience a relapse in psychotic symptoms three months later, with auditory hallucinations re-emerging and delusions becoming more prominent. The antipsychotic drug was changed to loxapine 50 mg/d, without any satisfactory response. The patient’s family was troubled by her irritable mood and agitated behavior, and asked the psychiatrist to resume estrogen treatment. Therefore, Premelle 2.5 was added at a dosage of one tablet every other day, and her positive psychotic symptoms disappeared again. Premelle treatment was continued for another year and then discontinued, and the patient has since remained stable with loxapine 50 mg/d for one and a half years.

Discussion

Estrogen withdrawal-associated psychoses have been reported in different situations, including puerperal and premenstrual psychoses, post-abortion psychosis, cessation of exogenous administration of estrogen-associated psychoses (such as cessation of the contraceptive pill), administration of an antagonist of estrogen receptors-related psychoses (such as the use of tamoxifen), and perimenopausal period-onset psychosis [3,5].
Psychopathologically, estrogen may act in a protective role in women. In a study measuring the levels of estrogen in patients with schizophrenia, Riecher-Rossler et al. found that estrogen level was correlated with the psychopathologic severity [6]. Postmenopausal women may also have an increased risk of suffering from psychosis compared to premenopausal women [1, 3].

A possible mechanism of estrogen-associated psychosis is mediated through modulation of the dopamine system on D2 receptors [7]. In animal studies, administering estrogen improves dopamine-related behavior and reduces the D2-receptor sensitivity in the CNS. The result of a pilot study also showed that estrogen administration in postmenopausal women is associated with a modest increase in dopamine transporter availability in the putamen [8].

In this case, we found that after receiving adjunctive augmentation of estrogen, patient’s symptoms of acute psychotic disorders were significantly relieved, and that the symptoms were relapsed after discontinuing estrogen augmentation. This clinical finding indicates that augmentation of estrogen plays an important role in pharmacodynamic and neurohormonal effects, resulting in helping antipsychotic drugs to act more efficiently and to influence dopamine receptors. Thus, those actions may consequently improve depressive or psychotic symptoms in menopausal women.

Moreover, estrogen has a restorative effect on the tyrosine hydroxylase enzyme system in the prefrontal cortex, and such revival effect is stronger when estrogen is combined with progesterone [9]. The hormone that we gave in this case, Premelle, is a combination of estrogen and progesterone, a composition that may strengthen the antipsychotic effectiveness.

Antipsychotic agents are used to treat different forms of psychosis. In treatment non-responders, augmentation with another antipsychotic drug or other medications such as mood stabilizers is considered. But high doses of antipsychotic drugs or augmentation with lithium or valproate acid can increases side effects such as neuroleptic-induced movement disorder [10]. If a woman has no contraindications for hormonal therapy, the short-term administration of estrogen might be a good treatment option in improving her menopausal psychosis.

This case report has two limitations. First, we did not check patient’s level of gonadohormone. Her menopause was determined by clinical manifestations only. Although the value of hormonal level is not needed in diagnosing menopause, hormone level might be associated with the treatment outcome which deserves further study. Second, the antipsychotic efficacy is related to estrogen theoretically. Premelle contains estrogen and progesterone. In the future case, augmentation with only estrogen might be a better way to clarify the pharmacologic mechanism.

This case report indicates that a combination of estrogen and antipsychotic agents is safe and effective in treating menopausal psychotic woman, and may be a good option for those with treatment-refractory menopausal psychosis.

References
