The potential role of oestrogens in relapse of recurrent affective psychosis

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This case demonstrates the potential role of oestrogens in the occurrence and relapse of bipolar affective disorder, and pointers towards possible treatment options. The case also demonstrates the potential iatrogenic harm of hormonal manipulation in a woman with a history of puerperal psychosis.

Case report

This female patient is now 47 years old and works as a fitness instructor. She is married and has two children and has no family history of psychiatric disorder. She presented to Accident and Emergency with florid symptoms of mania necessitating admission to a locked psychiatric ward under the Mental Health Act. She was disinhibited, garrulous, with flight of ideas, sleep disturbance and grandiosity. During her stay she sustained an injury to her leg while jumping off a bed.

Two days prior to her presentation she had been administered intramuscularly the gonadotrophin-releasing hormone antagonist (GnRH) analogue leuproreline acetate. This was to reduce the vascularity of endometrial fibroids in preparation for surgery.

Deucher and Brockington1 proposed a ‘unitary etiological hypothesis’ linking cases of puerperal psychosis and rare menstrual psychoses, where psychotic episodes occur premenstrually and at a time in the menstrual cycle where there is a sharp fall in circulating oestrogens and progesterone. The administration of the GnRH analogue and the menopause as seen in this case could also fit into this unitary hypothesis.

Discussion

This case is interesting in demonstrating a number of aspects of the association between oestrogen and psychosis. Her manic episodes have been associated with three different mechanisms where reduction in oestrogens are seen; postnatally, following a GnRH analogue, and menopausally.

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Regarding the use of the GnRH analogue, the data presented at the Drug Analysis Point on the Medicones and healthcare products Regulatory Agency website (www.mhra.gov.uk) have...
recorded 23 incidents of psychiatric symptoms following administration of this drug. However, the symptoms presented are non-specific with one episode of ‘altered mood’ and two cases of ‘mood swings’. There is no further information regarding these episodes. However, in a review article, Durmaine et al.² quote four cases of psychosis occurring after administration of Clomiphene and one case after administration of a gonaderelin agonist, both drugs acting to reduce oestrogens. Given this patient’s history of puerperal psychosis, should there have been caution in administering a GnRH analogue? This is a difficult question as the psychosis was 14 years previously. However, alternatives may have been considered with the patient if this caution had been picked up.

Menopausal changes associated with psychosis have been less documented overall and indeed in this case a full-blown psychosis did not occur. There is a suggestion that the menopause is a more gradual process and acute symptoms are less inclined to occur. Preserving the patient’s ovaries was a way of avoiding a precipitous fall in oestrogens until slower reductions start to take place naturally. The issue of using HRT in an attempt to avoid this reduction was certainly helpful for this patient. However, a recent review for the Cochrane Collaboration³ revealed that adjunctive oestrogens fared little better than placebo. In addition, the health risks associated with use of these drugs has to be weighed against the unproven avoidance of severe mental health symptoms. Ultimately this was a decision the patient came to herself and will be for a limited time. Cessation of these drugs may then paradoxically increase the risks of a more severe episode occurring in the future.

As regards the reported mechanisms by which oestrogens affect mental health, there are a number of reports in the literature. Oestrogen blocks dopamine as shown by increases in prolactin after they have been administered.⁴ A reduction in oestrogens could lead to a hyperdopaminergic state leading to psychosis.⁵ However, oestrogens have many complex mechanisms of action in many brain regions ranging from second messenger systems to effects on neuronal excitability and ion channels and calcium homeostasis, which in turn affect catecholaminergic and serotonergic pathways.⁶ These pathways and others have been implicated in psychosis.

This case therefore demonstrates the vulnerability a woman may have throughout the reproductive lifespan when a psychosis has occurred which may be linked with falls in oestrogen. This should be borne in mind when any exogenous agent is proposed that may induce similar hormonal changes.

References

1. Deucher N, Brockington I. Puerperal and menstrual psychoses: the proposal of a unitary etiological hypothesis. J Psychsom Obstet Gynecol 1998;19:104–10
2. Mahe V, Dumaine A. Oestrogen withdrawal associated psychoses. Acta Psychiatr Scand 2001;104:323–31
3. Chua WL, de Izquierdo SA, Kulkami J, Mortimer A. Estrogen for schizophrenia. Cochrane Database Syst Rev 2005; (4):CD004719
4. Demarest KT, Riegle GD, Moore KE. Long-term treatment with oestradiol induces reversible alterations in tubero-infundibular dopaminergic neurones: a decreased responsiveness to prolactin. Neuroendocrinology 1984;39:193–200
5. Davis KL, Kahn RS, Ko G, et al. Dopamine in schizophrenia: A review and reconceptualisation. Am J Psychiatry 1991;148:1474–86
6. Mcewen B, Alves S. Estrogen actions in the central nervous system. Endocrine Reviews 1999;20:279–307

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