Antipsychotic medication, prolactin elevation, and ovarian function in women with schizophrenia and schizoaffective disorder

Carla M. Canuso, Jill M. Goldstein, Joanne Wojcik, Ree Dawson, Danielle Brandman, Anne Klibanski, Joseph J. Schildkraut, Alan I. Green

Commonwealth Research Center, Boston, MA 02115, USA
Harvard Department of Psychiatry at the Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115, USA
Harvard Medical School, Boston, MA 02115, USA
Massachusetts General Hospital, Boston, MA 02115, USA
Harvard Institute for Psychiatric Epidemiology and Genetics, Boston, MA 02115, USA
Frontier Science Technology, Boston, MA 02115, USA

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Abstract

Some, but not all, antipsychotics elevate serum prolactin. Antipsychotic-induced hyperprolactinemia is thought to account for high rates of menstrual dysfunction and diminished estrogen levels in women with schizophrenia. However, few studies have directly assessed the relationships between prolactin, menstrual function, and ovarian hormone levels in this population. Sixteen premenopausal women with schizophrenia and schizoaffective disorder, eight treated with an antipsychotic with prolactin-elevating potential (five with typical antipsychotics and three with risperidone) and eight treated with an antipsychotic with prolactin-sparing potential (seven with olanzapine and one with clozapine), were studied for eight weeks. Data were collected on menstrual functioning and on serum prolactin, estradiol, and progesterone levels, and were compared between subjects who received an antipsychotic with prolactin-elevating potential and an antipsychotic with prolactin-sparing potential, and between subjects with hyperprolactinemia (N=6) and normoprolactinemia (N=10). Additionally, peak ovarian hormone levels were compared to normal values. While mean prolactin levels of subjects who received an antipsychotic with prolactin-elevating potential were significantly greater than those of subjects who received an antipsychotic with prolactin-sparing potential, and between subjects with hyperprolactinemia (N=6) and normoprolactinemia (N=10). Additionally, peak ovarian hormone levels were compared to normal values. While mean prolactin levels of subjects who received an antipsychotic with prolactin-elevating potential were significantly greater than those of subjects who received an antipsychotic with prolactin-sparing potential, there were no differences in rates of menstrual dysfunction or in ovarian hormone values between the two groups. Additionally, similar rates of menstrual dysfunction and ovarian hormone values were observed between the hyperprolactinemic and normoprolactinemic subjects. Moreover, irrespective of medication type or prolactin status, most subjects had peak estradiol levels below normal reference values for the periovulatory phase of the menstrual cycle. While our
Typical antipsychotic medications, and the novel antipsychotic risperidone, frequently elevate serum prolactin levels through the antagonism of dopamine D2 receptors located on lactotrophes within the pituitary (Green and Brown, 1988; Ereshefsky and Lacombe, 1993; Foord et al., 1983). Such antipsychotic-induced hyperprolactinemia is a dose-related phenomenon (Green and Brown, 1988), appears to occur with greater magnitude in women compared to men (Kuruvilla et al., 1992), and has been found to be a factor in menstrual dysfunction known to occur in women treated with these medications (Meltzer, 1985). Within the past decade, novel antipsychotics (i.e. clozapine, olanzapine, quetiapine and ziprasidone) with less potential to elevate prolactin have become available (Kane et al., 1981; Beasley et al., 1996; Casey, 1996; Daniel and Copeland, 2000), and are beginning to be used specifically in female patients who experience antipsychotic-induced hyperprolactinemia (Bunker et al., 1997; Canuso et al., 1998). Despite the development of this clinical practice, there are no studies that have assessed the differential effects of antipsychotics with prolactin-elevating potential and antipsychotics with prolactin-sparing potential on menstrual and ovarian function in women with psychotic disorders.

While it is known that serum prolactin elevation due to medical causes (e.g. pituitary adenomas) is often associated with menstrual cycle dysfunction and estrogen deficiency (Yazigi et al., 1997), data regarding the relationship between antipsychotic-induced hyperprolactinemia and ovarian function in women with schizophrenia are limited. Most studies of women treated with typical antipsychotics have reported high rates of menstrual abnormalities (50–75%) (Polishuk and Kulcsar, 1956; Sandison et al., 1960; Beaumont et al., 1974; Ghadirian et al., 1982; Sullivan and Lukoff, 1990). Yet, several recent studies have shown an absence of difference in the prolactin levels of schizophrenic women with and without menstrual dysfunction (Prentice and Deakin, 1992; Riecher-Rossler et al., 1994; Magharious et al., 1998). However, very few studies have examined the relationship of prolactin and gonadal steroid levels in this population. Although a recent study of acutely psychotic female inpatients found no correlation between prolactin and estradiol levels, and no difference in the estradiol levels of patients on and off antipsychotic medications (Huber et al., 2001), another study of outpatients with schizophrenia found an inverse relationship between prolactin and estrogen levels (Smith et al., 2002). Interestingly while both these studies, as well as others (Riecher-Rossler et al., 1994, 1998; Oades and Schepker, 1994), have reported diminished levels of estrogen in women with schizophrenia, the etiology of such low estrogen levels in this population has not been carefully evaluated.

We report here data from a preliminary study of 16 premenopausal women with schizophrenia and schizoaffective disorder who were treated with either an antipsychotic possessing prolactin-elevating potential or an antipsychotic medication with prolactin-sparing potential. In this naturalistic pilot study, we explored the hypothesis that women with schizophrenia or schizoaffective disorder, who are treated with an antipsychotic with prolactin-elevating potential, would have higher prolactin levels, greater menstrual dysfunction, and lower ovarian hormone values than patients treated with an antipsychotic with prolactin-sparing potential. Furthermore, we sought to begin to clarify the relationship between levels of prolactin, menstrual cycle function, and levels of estrogen in these women.

2. Methods

2.1. Subjects

Female outpatients at the Massachusetts Mental Health Center (MMHC) were recruited for partic-
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