Bipolar in Women: Any Gender-based Difference?

Sir,

Literature abounds on gender-based differences in bipolar mood disorder. Here, I would try to summarize these salient features.

The prevalence of bipolar I is estimated to be circa 1.3% and is the same for both genders. Bipolar II, on the other hand, is more common in women. Bipolar disorder in women tends to be of later onset than male counterparts. Women appear overrepresented in later onset illness (45–49 years). Of greater concern, women face major delays in treatment up to 11 years from onset, because of failure to diagnose, compared with a 7-year delay among men.

Depression is the polarity of onset in bipolar women. Depression dominant polarity continues throughout life course in women. And hence, dysphoric or mixed manic presentations are commonplace. Women tend to have higher severity scores on Young Mania Rating Scale. Mood-incongruent psychotic features as well as more hallucinations are typically more reported in women. Women endorse more suicidal ideations and attempts albeit less violent than men.

Bipolar course in women is noted for rapid cyclicity, which by definition involves 4 episodes/years. This might be related to comorbid hypothyroidism, gonadal steroids effect, and antidepressant use. Moreover, seasonal pattern is readily recognized in women. Mood fluctuations go in tandem with hormonal fluctuations in reproductive life. Pregnancy and puerperium are critical periods for affective relapse, especially depressive. It is unwise to abruptly halt psychopharmacotherapy in pregnancy. Monotherapy, minimal effective dosing, using older therapeutics with established data and experience, avoiding the first trimester, close monitoring of serum levels when applicable, and psychotherapy are helpful strategies to pursue in pregnant bipolar women. As per American Psychiatric Association, electroconvulsive therapy remains a viable, effective, and safe option in pregnancy to the surprise of layman beliefs.

Bipolar women are plagued with a myriad of comorbidities both psychiatric and physical. Psychiatric comorbidities include anxiety (panic/obsessive-compulsive disorder/phobias), personality disorders, eating disorders, but less substance use disorders. Physical comorbidities entail endocrinopathies (thyroid dysfunction), obesity, and migraine. Clinicians should be vigilant to dig for these comorbidities that have both prognostic and therapeutic implications.

Misdiagnosis is common in women. Atypical depression is notoriously mistaken for unipolar, and hence, delaying bipolar diagnosis and accounts for higher antidepressants prescription pattern in women with subsequent mood destabilization. Women are superior to men regarding better treatment adherence. Gender has been shown to take its toll on the differential response to pharmacotherapy, for instance lithium-induced hypothyroidism and Atypical Antipsychotics-related metabolic syndrome are more noticeable in women. More treatment-emergent affective switch is described in bipolar women.

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REFERENCES
1. Hendrick V, Altshuler LL, Gitlin MJ, Delrahim S,
Sir,

Pimozide is a high-potency conventional antipsychotic drug of the diphenylbutylpiperidine group (2 mg ≈ 2–3 mg haloperidol). It selectively blocks D1–D2 receptors and additionally calcium channels. It has a long half-life (55–66 h) allowing dosing q >24 h and metabolized mainly by CYP3A4. It is metabolic friendly. It caused 5 kg weight loss in a study by McCreadie et al. [1] in chronic schizophrenia. This would be advantageous given the current rampant use of atypical antipsychotics at the expense of metabolic syndrome and without demonstrable superior efficacy (e.g., in CATIE, CUTLASS studies). This holds true as shown in a recent Cochrane database systematic review of pimozide for schizophrenia or related psychoses. [2] Concerns over torsadogenicity might be tempered by close monitoring of serum, potassium, and magnesium, and surface electrocardiogram. QTc prolongation is dose dependent with heightened risk beyond 16 mg/day. Hence, keeping the maximum daily dose at 10 mg/day and avoiding polypharmacy (notably CYP3A4 inhibitors) would be more prudent. Risk is cumulative and multifactorial and this should never deter clinicians from prescribing pimozide out of this “QTc phobia.” [3]

Of interest, Mendhekar et al. [4] have reported safe and effective pimozide augmentation to clozapine in resistant schizophrenia. Pimozide, an orphan drug, is FDA-approved for treating Tourette syndrome. Sallee et al. [5] have found it superior to haloperidol with less neurologic side effects. Pimozide is the European Medicines Agency-approved drug for treating schizophrenia and has long been the drug of choice in delusional disorders, notably somatic subtype as shown by Silva et al. [6] Puri and Singh. [7] have reported a successful pimozide treatment of a case of gender dysphoria superimposed on intellectual disability. Similarly, Martins et al. [8] described a case series of delusional parasitosis (Ekbom's syndrome) successfully treated with pimozide. Interestingly, pimozide helped in treating deficit-state schizophrenia as reported by Feinberg et al. [9] However, in a recent randomized controlled trial by Gunduz-Bruce et al., [10] the efficacy of pimozide augmentation for clozapine partial responders in schizophrenia was questioned.

Pimozide might also be used for treating Sydenham's chorea for its dopamine blockade actions. Similarly, McArthur et al. [11] reported its use in combination with tetrabenazine for treating Huntington's disease. Owing to calcium channel blockade, it confers antimanic properties as demonstrated by Cookson et al. [12] and Post et al. [13]

Pimozide: An Old Wine in a New Bottle!