Pimozide: An Old Wine in a New Bottle!

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 has been used for behavioral facets in autism spectrum disorder (ASD) as shown in an open pilot study by Ernst *et al*.[14] Naruse *et al*.[15] conducted a multi-center, double-blinded, placebo-controlled, cross-over study involving 87 patients (aged 6–13 years) with behavioral problems, 34 of whom had autism where pimozide was superior to placebo. Pimozide is the only drug approved for ASD in Japan.[16]

Pimozide has also been used to augment selective serotonin reuptake inhibitor response in refractory obsessive-compulsive disorder (OCD) and obsessive-compulsive-related disorders. Delgado *et al*.[17] have reported on pimozide/fluvoxamine combination in resistant OCD with concurrent Tourette syndrome. It is similarly used, among others, for functional itch disorder.[18]

All these would converge into a "resurrection" of pimozide use in clinical practice, given demonstrated high-potency, broad-spectrum indications, FDA-approval at age 12, and, above all benign side effects profile, notably metabolic syndrome.

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Conflicts of interest
There are no conflicts of interest.

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