Sir,
Pimozide is a high-potency conventional antipsychotic drug of the diphenylbutylpiperididine 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 tetrabenzine 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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REFERENCES

1. McCreadie R, Mackie M, Morrison D, Kidd J. Once weekly pimozide versus fluphenazine decanoate as maintenance therapy in chronic schizophrenia. Br J Psychiatry 1982;140:280-6.
2. Mothi M, Sampson S. Pimozide for schizophrenia or related psychoses. Cochrane Database Syst Rev 2013;3:CD001949.
3. Naguy A. Psychotrophic drugs and prolonged QTc interval: Does it really that matter? Indian J Psychol Med 2016;38:185-6.
4. Mendhekar DN, Gupta D, Lohia D, Jiloha RC. Pimozide augmentation of clozapine in hebephrenic schizophrenia: A case report. Indian J Psychiatry 2003;45:55.
5. Sallee FR, Nesbitt L, Jackson C, Sine L, Sethuraman G. Relative efficacy of haloperidol and pimozide in children and adolescents with Tourette’s disorder. Am J Psychiatry 1997;154:1057-62.
6. Silva H, Jerez S, Ramirez A, Renteria P, Aravena N, Salazar D, et al. Effects of pimozide on the psychopathology of delusional disorder. Prog Neuropsychopharmacol Biol Psychiatry 1996;20:331-40.
7. Puri BK, Singh I. The successful treatment of a gender dysphoric patient with pimozide. Aust N Z J Psychiatry 1996;30:422-5.
8. Martins AC, Mendes CP, Nico MM. Delusional infestation: A case series from a university dermatology center in São Paulo, Brazil. Int J Dermatol 2016;55:864-8.
9. Feinberg SS, Kay SR, Eliovich LR, Fiszbein A, Opler LA. Pimozide treatment of the negative schizophrenic syndrome: An open trial. J Clin Psychiatry 1988;49:235-8.
10. Gunchuz-Bruce H, Oliver S, Gueorguieva R, Forselius-Bielen K, D’Souza DC, Zimolo Z, et al. Efficacy of pimozide augmentation for clozapine partial responders with schizophrenia. Schizophr Res 2013;143:344-7.
11. McArthur AW, Pollock M, Smith NA. Combined therapy with tetrabenazine and pimozide in Huntington’s chorea: Pilot study. N Z Med J 1976;83:114-6.
12. Cookson JC, Silverstone T, Wells B. A double-blind controlled study of pimozide versus chlorpromazine in mania. Psychopharmacol Bull 1980;16:38-41.
13. Post RM, Jimerson DC, Bunney WE Jr., Goodwin FK. Dopamine and mania: Behavioral and biochemical effects of the dopamine receptor blocker pimozide. Psychopharmacology (Berl) 1980;67:297-305.
14. Ernst M, Magee HJ, Gonzalez NM, Locascio JJ, Rosenberg CR, Campbell M. Pimozide in autistic children. Psychopharmacol Bull 1992;28:187-91.
15. Naruse H, Nagahata M, Nakane Y, Shirahashi K, Takesada M, Yamazaki K. A multi-center double-blind trial of pimozide (Orap), haloperidol and placebo in children with behavioral disorders, using crossover design. Acta Paedopsychiatri 1982;48:173-84.
16. Satoh M, Obara T, Nishigori H, Ooba N, Morikawa Y, Ishikuro M, et al. Prescription trends in children with pervasive developmental disorders: A claims data-based study in Japan. World J Pediatr 2016;12:443-9.
17. Delgado PL, Goodman WK, Price LH, Heninger GR, Charney DS. Fluvoxamine/pimozide treatment of concurrent Tourette’s and obsessive-compulsive disorder. Br J Psychiatry 1990;157:762-5.
18. Szepietowski JC, Reszke R. Psychogenic itch management. Curr Probl Dermatol 2016;50:124-32.

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