

Appendix 3: Antipsychotics, mood stabilizers, antidepressants and other medications in the treatment of borderline personality disorder (BPD)

Antipsychotics

The drug class with the most supporting data is that of antipsychotics, olanzapine in particular. An early study of olanzapine showed reductions in anxiety, anger, paranoia and interpersonal sensitivity, but less than one-third of the sample completed the study.¹ Subsequent studies found more support for olanzapine: one found improvement on clinician ratings of BPD symptoms with an effect size of 0.77 when compared with placebo,² with another showing reduced aggression and depression compared with fluoxetine,³ or reduced anxiety and depression ratings compared with placebo when added to dialectical behaviour therapy.⁴ More recently, several larger trials have used a variety of outcome measures, including some specific to BPD. In one, olanzapine in doses between 2.5 and 20 mg/d led to faster reduction in symptoms, but there was no difference at 12 weeks, with an effect size of 0.03 (95% confidence interval [CI] -0.20 to -0.25).⁵ A related 12-week study found that olanzapine 5 to 10 mg/d, but not lower doses, led to reductions in BPD symptoms compared with placebo, with an effect size of 0.29 (95% CI 0.06 to 0.52), but the effect was more robust at 6 weeks than at 12 weeks.⁶ All studies reported adverse effects, particularly weight gain and metabolic changes, with olanzapine.

As for other antipsychotics, one study comparing aripiprazole 15 mg/d with placebo found decreases in almost all psychiatric symptoms at 8 weeks,⁷ with results stable after 18 months of open-label follow-up.⁸ Studies of ziprasidone,⁹ thiothixene¹⁰ and trifluoperazine¹¹ found minimal or no differences compared with placebo. Older studies with haloperidol found mixed results, with one reporting greater improvement compared with amitriptyline and placebo,¹² but another found no benefit initially¹³ and worsening of depression at 16-week follow-up.¹⁴

Mood stabilizers

Mood stabilizers are frequently prescribed in patients with BPD, under the assumption that affective instability may be related to changes seen in bipolar disorders. One older study found physician-rated improvements in mood, anxiety, suicidality and impulsivity with carbamazepine,¹¹ but a second study found no significant effects with carbamazepine.¹⁵ Two studies of lamotrigine showed a 45% greater reduction in affective lability with lamotrigine and also significant reductions in impulsivity after 12 weeks¹⁶ and reduced anger at 8 weeks,¹⁷ but the sample sizes were small and the completion rates low.

Topiramate was studied by one research group and was found to reduce psychiatric symptoms, anger and interpersonal difficulties and to improve health-related quality of life at 8 and 10 weeks;¹⁸⁻²⁰ reduction in anger remained significant at open-label follow-up at 18 months.^{21,22} Three studies of divalproex were limited by small sample sizes and high dropout rates: one showed no effects on aggression or depression in the intent-to-treat analysis,²³ another showed some reduction in impulsivity and aggression only among patients with higher baseline levels,²⁴ and a third, a 6-month study, showed 30%–40% reductions in interpersonal sensitivity and anger but only included patients who also had bipolar-II disorder.²⁵

Antidepressants

Antidepressants have been studied less extensively in BPD. One study of fluvoxamine showed significantly greater reductions on a subscale measuring rapid mood shifts when compared with placebo, with a significant advantage for fluvoxamine observed in the first 6 weeks of treatment and then diminishing afterward.²⁶ Two studies of fluoxetine for anger and impulsivity in BPD patients without a diagnosis of major depressive disorder showed reductions compared with placebo at 3 months, but no significant effect of medication on depressive symptoms was noted in the primary analyses.^{27,28} One study of fluoxetine in combination with dialectical behaviour therapy found no added benefit of the medication.²⁹ Of the monoamine oxidase inhibitors, phenelzine showed few benefits compared with placebo,¹³ particularly at 16 weeks,¹⁴ whereas evidence for the efficacy of tranylcypromine was limited by a small sample and the absence of standardized rating scales.¹¹ As for tricyclic antidepressants, amitriptyline was not found to be effective.¹²

Other medications

A study that tested alprazolam in a placebo-controlled crossover design found worsening of suicidality after 6 weeks, with no noted benefits.¹¹ Clonidine was found to produce a significant 18% decrease in hyperarousal compared with placebo during a 2-week treatment period, but the benefits were only significant among patients with comorbid post-traumatic stress disorder.³⁰ Single-dose intravenous naloxone was studied in comparison with placebo for the treatment of dissociative symptoms, but there was no benefit over placebo.³¹ Finally, one small study comparing ethyl-eicosapentaenoic acid with placebo found significantly greater reductions in aggression and depressive symptoms in the treatment group.³²

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