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Dextroamphetamine and Pramipexole Combination for Treatment-Resistant Unipolar Depression

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Targeting dopamine is critical in the management of treatment-resistant depression (TRD). This case report highlights the potential role of the combination of dextroamphetamine and pramipexole in the management of treatment-resistant unipolar depression. Using dopaminergic medications in the management of TRD may lead to better outcomes.

CASE REPORT

The patient was a 40-year-old man with TRD stage III¹ who had good response to four sessions of electroconvulsive therapy in the past. The following medications had not worked for him: fluoxetine, sertraline, escitalopram 30 mg, citalopram, venlafaxine, mirtazapine 45 mg, bupropion 300 mg, buspirone 60 mg, and methylphenidate 10 mg (the patient noted that taking methylphenidate 10 mg felt like “being in a roller coaster”). The dose of several medications and the duration and details on whether the patient was on any combination of antidepressants was not available in his medical history. His Patient Health Questionnaire-9 score decreased from 25 to 10 in over a period of 35 weeks. His functioning improved in the following areas: he was able to go out socially with people, get out of the house more often, enjoyed riding his motorcycle, read books, listened to music, and drove on a long distance trip with his friend.

The patient was monitored on a regular basis via phone calls in between regularly scheduled follow-up appointments. Medication titrations were conducted during the phone calls. Interventions from each follow-up visit are shown on Table 1.

DISCUSSION

When clinicians manage treatment-resistant patients, it is important to do a detailed psychotropic history. Otherwise, they are likely to prescribe medications from the same class

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that are unlikely to work. Knowing the patient's medication history can allow clinicians to try novel medications, off-label combinations or off-label doses.

There is evidence that the combination of clomipramine, dextroamphetamine, pramipexole, and aripiprazole is safe and effective for TRD.^{2–4} Clinicians have a limited number of options with dopaminergic medications and therefore often neglect to target dopamine.^{5–10} A dopamine transporter photoaffinity ligand, (±)-2-(N-tert-Butylamino)-3'-[I-125]-iodo-4'-azidopropiophenone, had modest affinity with bupropion.¹¹ In the (I-123)IBZM single photon emission computed tomography study, atypical antipsychotic drugs, including 30 mg/day of aripiprazole, had no clinical benefit in patients with severe TRD despite their strong occupancy of dopamine 2 and 3 receptors.¹² An article describing how mesolimbic dopamine regulates motivated behavior was recently published.¹³ Commonly used medications to target dopamine in routine clinical practice, such as bupropion and aripiprazole, may have weak dopaminergic action. Hence, greater use of more potent medications such as dextroamphetamine and pramipexole may provide clinicians more options to target dopamine to treat patients with TRD.

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TABLE 1**Medication Titration During Each Visit**

		Patient	
Timeline	PHQ-9 Score	Medication	Intervention
Week 0	25	Nortriptyline 75 mg Liothyronine 50 mcg	Stopped current medications Clomipramine 75 mg HS
Week 5	22	Clomipramine 225 mg HS (total clomipramine concentration was 312 ng/mL [normal, 220–500 ng/mL]) Clomipramine (194 ng/mL) and desmethylclomipramine (118 ng/mL) concentration	Clomipramine 225 mg HS Started pramipexole 1 mg HS
Week 11	19	Clomipramine 225 mg HS Pramipexole 1 mg BID	Increased clomipramine to 150 mg AM and 150 mg HS (patient had gastroesophageal reflux when the entire dose was taken at bedtime) Increased pramipexole to 1 mg TID
Week 22	21	Increased clomipramine to 150 mg AM and 150 mg HS (total clomipramine concentration was 618 ng/mL) QTc 463 ms Pramipexole 1 mg TID	Decreased clomipramine to 225 mg HS Pramipexole 1 mg TID Started dextroamphetamine 10 mg
Week 25	17	Clomipramine 225 mg HS Pramipexole 1 mg and 2 mg HS Dextroamphetamine 20 mg AM, 10 mg noon, 10 mg early PM	Started aripiprazole 5 mg AM
Week 32	13	Clomipramine 225 mg HS Pramipexole 1 mg and 2 mg HS Dextroamphetamine 20 mg AM, 10 mg noon, 10 mg early PM Aripiprazole 15 mg AM	Increased dextroamphetamine to 40 mg AM, 10 mg noon, 10 mg early PM
Week 35	10	Clomipramine 225 mg HS Pramipexole 3 mg HS Dextroamphetamine 20 mg AM, 10 mg noon, 10 mg early PM Aripiprazole 15 mg AM	Tapered and stopped aripiprazole (patient did not see any response) ¹¹ Increased pramipexole to 4 mg HS

Abbreviations: AM, in the morning; BID, two times daily; HS, at bedtime; PHQ-9, Patient Health Questionnaire-9; PM, in the afternoon; QTc, corrected QT interval; TID, three times daily.