Successful Management of Difficult-to-Treat Aggression With Low-Dose Propranolol in a Patient With Intellectual Disability: A Case Report

To the Editor: People with intellectual disability often exhibit various behavioral problems, which are referred to as "challenging behaviors." Aggression is among the commonest of these, affecting about 7% of this population.[1] The management of aggression in these patients involves both behavior therapy[2] and medications.[3] Various medications, such as lithium, anticonvulsants, and antipsychotics, have been used, but their evidence base is limited[3–5] and recent research suggests that antipsychotics, in particular, should not be routinely used.[6]

Propranolol is a centrally acting β-adrenergic antagonist used in a variety of medical conditions. It has also been used to manage aggression in various neuropsychiatric conditions, including organic brain syndromes,[7,8] schizophrenia,[9] dementia,[10] and intellectual disability.[11,12] Doses used in these studies have been as high as 520 mg/d,[13] but some authors have reported benefits at much lower doses.[10,14] The following is the case of a young man with intellectual disability, epilepsy, and severe aggression who responded remarkably to low-dose propranolol.

Case report. Mr A, a 20-year-old man diagnosed as having moderate intellectual disability and generalized epilepsy, presented to our clinic with severe aggression, both verbal and physical, occurring with little or no provocation over the past 3 years. These episodes would last up to several hours and often led to food refusal. Before this, he could attend to his personal needs, helped his mother in household tasks, and could communicate in short sentences despite an articulation defect. However, after the onset of his aggression, it was difficult to engage him in any activities, including basic self-care. There was no evidence of a mood disorder or psychosis or of seizures either preceding or following the episodes of aggression. He was seizure-free for the past 4 years on carbamazepine 1,000 mg/d and diazepam 10 mg/d, and he had never exhibited postictal aggression in the past. He had already received trials of olanzapine (up to 15 mg/d for 6 weeks) and chlorpromazine (up to 400 mg/d for 3 months) without significant improvement and was currently on olanzapine 10 mg/d and chlorpromazine 300 mg/d in addition to his medications for epilepsy.

As his mother reported features of autonomic arousal—such as increased perspiration, motor agitation, and rapid breathing—during each episode, he was given a trial of propranolol, starting at 20 mg/d and increased by 20 mg every week. At 40 mg/d, there was a significant reduction in his aggression, and his food intake was better. On further increasing the dose to 60 mg/d, his mother reported that he was essentially "normal," with no significant episodes of aggression. Over the next year, olanzapine and chlorpromazine were tapered and stopped, and he remained stable. He has been well on carbamazepine 1,000 mg/d, propranolol 60 mg/d, and diazepam 10 mg/d for the past 3 months with no recurrence of either seizures or aggression, and it is now possible to engage him in household tasks and speech therapy.

The management of aggression in the intellectually disabled is a clinical challenge. The best evidence suggests that antipsychotics are of limited use, and the evidence for other medications is even more limited. Behavioral management is valuable, but may not be feasible in a very violent or uncooperative patient, and pharmacotherapy may be required initially in such cases.

Propranolol is effective in reducing aggression in a variety of neurologic and psychiatric conditions. Its exact mechanism of action is unknown, but may involve central β-adrenergic blockade,[15] peripheral effects on the sympathetic nervous system,[11,16] or serotonergic blockade.[17] It may be effective not only in aggression, but also in the self-injurious behavior commonly seen in the intellectually disabled.[18] Recent evidence suggests that it may improve some aspects of learning in patients with autism.[19] Given these properties, and the uncertainties surrounding other treatment options, low-dose propranolol may be a valuable treatment option in the management of aggression in intellectually disabled adults, even if they do not respond to other drugs.

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