Self-Injurious Behavior Associated With Clonidine Withdrawal in a Child With Tourette's Disorder

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Abstract

A 7-year-old boy with Tourette's disorder, atypical pervasive developmental disorder, borderline mental retardation, and a history of self-injurious behavior was treated for 21 months with clonidine transdermal patches at doses ranging from 0.1 to 0.5 mg weekly. When withdrawn from clonidine over 4 weeks to assess the need for continued therapy, the patient developed multiple self-destructive behaviors involving the theme of suffocation. The importance of careful clinical monitoring of the behavior of patients undergoing withdrawal from prolonged treatment with high doses of clonidine is emphasized. (*J Child Neurol* 1990;5:308–310).

Tourette's disorder, a syndrome usually beginning in childhood and characterized by chronic motor and phonic tics, occasionally is associated with self-injurious behavior.[1,2] Clonidine has been proposed as a treatment for Tourette's disorder and for self-injurious behavior occurring in the context of Tourette's disorder.[3] Few data are available, however, to indicate when clonidine treatment might be discontinued or the possible consequences of discontinuation of treatment.

Withdrawal from clonidine can cause rebound hypertension and tachycardia in adult hypertensives[4] and can aggravate motor restlessness and tics in children undergoing therapy for Tourette's disorder.[5] The following is apparently the first report linking clonidine withdrawal to self-injurious behavior in patients with Tourette's disorder.

Case Report

A 7½-year-old white boy was referred to the Behavior Disorders Clinic of the Child and Adolescent Psychiatric Hospital, University of Michigan Medical Center, for treatment of Tourette's disorder.

The patient was the 4350-g product of an induced delivery following 43 weeks gestation complicated by hyperemesis and a prolapsed umbilical cord. In his first year, the infant suffered continual vomiting and had gained no weight by 11 months of age. Fine motor skills and language acquisition were delayed. Gross motor milestones reportedly were normal. Language at age 4 years was characterized by poor articulation, pronoun reversals, and echolalia.

The patient was noted to be hyperactive in his second year and by age 2½ displayed severe hyperactivity, head-banging, self-biting, hair-pulling, touching hot appliances, and tantrums. He also exhibited mannerisms such as toe-walking, hand-flapping, and rocking. Hypoxanthine guanine phosphoribosyltransferase was in the low-normal range. At age 5 years, the patient began to exhibit simple motor tics including eye-blinking, mouth-opening, and shoulder jerks, and complex tics such as light-switching and touching other children. Phonic tics included grunts, simple words, and profanity.

Family history was noteworthy for Tourette's disorder in two siblings, tic disorders in two maternal uncles, and learning disabilities in 16 of 32 maternal second cousins. Family history was negative for mental retardation, epilepsy, psychiatric hospitalization, affective disorder, or suicide.

At age 6 years, the patient was placed on clonidine transdermal patches (Catapres TTS) at doses gradually increasing over the next 21 months to a maximum of 0.5 mg (20 μg/kg) weekly. This resulted in marked reduction in motoric overactivity, according to parent and clinician reports. Self-injurious behaviors disappeared during the period of treatment, while tics showed a modest improvement.

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The patient was referred to the author at age 7.5 because of increasingly severe tics and behavioral problems unresponsive to clonidine.

On examination, the blood pressure was 100/70 mm Hg and the pulse 72 beats/min. General physical and neurologic examinations were normal except for mild hypertelorism and multiple nonlocalizing neurologic soft signs consistent with developmental delay. The patient established rapport readily. Speech articulation was impaired. Gross activity level and ability to persist in tasks were normal for developmental age. Mood was normal, and psychotic manifestations were absent. Recent psychological testing demonstrated borderline mental functioning.

The patient met *Diagnostic and Statistical Manual of Mental Disorders*, 3rd ed revised,[6] criteria for Tourette's disorder, pervasive developmental disorder not otherwise specified, and borderline mental retardation.

The patient was placed on fluoxetine in doses up to 20 mg daily, with the effect of extinguishing severe tantrums that had hitherto occurred several times daily.

At age 7 years 11 months, arm-throwing and bruxism become functionally incapacitating, and tolerance to clonidine was suspected. Medication was tapered by 0.1 mg weekly. At doses of 0 to 0.2 mg weekly, ratings on the Abbreviated Teacher's Questionnaire[7] rose from a previous baseline of 1.4 to 2.6 (of a possible maximum of 3.0). Multiple self-destructive behaviors occurred during the next 3 weeks. Following a disagreement with his mother, in a fit of anger, the patient attempted to suffocate himself with a pillow. On another occasion he placed a plastic bag over his head and likely would have expired had his mother not found him stumbling down the stairs frantically grasping the bag. At school, he turned blue strangling himself with an elastic lanyard. At home, he made a similar gesture with a rubber band. Finally, he fell or jumped from the roof of a garage, sustaining minor bruises and abrasions. All but the first of these acts were spontaneous and unaccompanied by depressed or angry affect. Between episodes, his mood, appetite, and interest in friends and activities were stable.

One week following discontinuation of clonidine, the patient displayed a supine blood pressure of 142/84 mm Hg, with a pulse of 100 beats/min. He was markedly overactive. His mood was cheerful and his affect somewhat brighter than observed on previous occasions. He denied suicidal ideation.

The patient was placed on haloperidol, 1 mg twice daily. Tics decreased by 23%, and his score on the Abbreviated Teacher Questionnaire fell to 1.8. In the fourth week of haloperidol treatment, another episode of self-strangling with a lanyard occurred. Haloperidol was discontinued, and the clonidine patch was reinstated at a dose increasing to 0.3 mg/week. The Abbreviated Teacher Questionnaire score dropped to 0.7, and teacher-rated stereotypies dropped by 55%. On examination, blood pressure was 95/65 mm Hg, pulse 72 beats/min, and mental status had returned to the baseline established prior to discontinuing clonidine therapy. No further self-injurious behavior has been reported during 6 months of continuing clonidine therapy.

Discussion

This case illustrates the risk that self-injurious behavior may develop or be aggravated during clonidine withdrawal. It also raises several questions of potential theoretical and practical significance.

The attempts at self-suffocation, which were not associated with dysphoric mood, intent to die, or thought disorder, were evidently not suicide gestures in the classic sense. They may have represented complex tics associated with Tourette's disorder or a phenomenon distinct from Tourette's disorder.

The present study used the patient as his own control in a single-case A-B-A design. The appearance of self-injurious behavior when clonidine was discontinued, the rapid normalization of behavior when clonidine was reinstated, and the parallel changes in sympathetic tone, provide support for a noradrenergic mechanism. It is of interest in this connection that pain and asphyxia both are potent stimuli of sympathetic discharge (Dillon JE, unpublished data). Clonidine may have interrupted a positive feedback loop in which increased sympathetic tone promoted behavior that in turn provoked sympathetic discharge. Previous reports, implicating a role for opiate systems in self-injurious behavior[8] and in the modulation of sympathetic activity in the locus coeruleus,[9] peripheral ganglia, and adrenals,[10] are consistent with the present data supporting a possible noradrenergic mechanism in some forms of self-injury.

In a study by Leckman et al[5] of clonidine withdrawal in Tourette's disorder, patients were treated with lower doses, up to 0.3 mg/day orally, over 12 weeks. These patients demonstrated increased motor activity, tics, blood pressure, pulse rate, urinary catecholamines, and urinary and plasma 3-methoxy-4-hydroxyphenylglycol. Motor restlessness, but not tics, remitted dramatically on reinstitution of clonidine. The 20-μg/kg/week dose of transdermal clonidine used in the present case is apparently higher than the 3- to 7.5-μg/kg/day by mouth recommended by Leckman et al,[11] though it is compatible with doses employed by others.[12]

This case illustrates the importance of close clinical monitoring in patients being withdrawn from clonidine following prolonged treatment at high doses. It further suggests that in patients developing tolerance to clonidine, a brief interlude of no treatment or alternative treatment may permit reinstitution of clonidine at a lower dose.

Finally, the possibility is raised that adrenergic dysregulation may play a mechanistic role in some

patients with self-injurious behavior and that clonidine might be useful in the treatment of self-injurious behavior unrelated to Tourette's disorder. Paradoxically, rodent studies suggest that clonidine can induce automutilation.[13,14] While this provides support for the hypothesis that adrenergic dysregulation (perhaps especially associated with α_2 presynaptic receptors) might be linked with self-injurious behavior, it recommends caution in the employment of clonidine in clinical research trials. Further study of the possible role of noradrenergic mechanisms in self-injurious behavior is warranted.

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