Role of Naltrexone in Treatment of Refractory Self-Injurious Behavior in a Child with Intellectual Disability: A Case Report

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Introduction

The prevalence of self-injurious behavior (SIB) in persons with intellectual and developmental disabilities varies widely, from 3% to 30%.¹,² SIB can lead to lacerations, tissue loss, and permanent scarring.³,⁴ Various pharmacological agents have been studied to treat SIB, most of which have been antipsychotics.⁵ Drug refractory SIB has been defined as SIBs requiring medication adjustment despite previous trials of risperidone and aripiprazole or previous trials of 3 psychotropic drugs, one of which was risperidone or aripiprazole.⁶ The current literature shows conflicting evidence about the efficacy of naltrexone in SIB with small controlled studies. There are very few studies on the use of naltrexone for the management of SIB in children.⁷ Most of the cases in literature mention the use of either antipsychotics or a combination of medications for management of SIB. This case focuses on the management of SIB using naltrexone as a single pharmacotherapy if the SIB is appropriately classified.

Case Details

An 8-year-old male child, a diagnosed case of seizure disorder with moderate ID, presented with complaints of biting on hands, forearms, and lips for the past 16 to 18 months, which increased in the last 3 to 4 months. The self-biting episodes were severe and had increased from 6 to 7/day to 14 to 15/day, and were at different locations over hands, forearm, and lips. The child also had episodes of headbanging for the last 4 months with a frequency of 3 to 4/day. There was no difference in frequency or severity of SIB based on the type of setting or time of the day. There was no history suggestive of any noninjurious motor or vocal stereotypies or other compulsive behavior. The reason for current consultation was a poor response to previously prescribed medications and thus an increase in severity of SIBs.

Birth and developmental history were suggestive of delayed cry after birth and global developmental delay with a birth weight of 2.2 kg. The child had seizure disorder (left focal seizure with no generalization) from 5 years of age, and the SIBs did not occur during these seizure episodes. There was no aura preceding SIB, no lack of awareness, and no behaviors like picking at clothes or any other behavior suggestive of automatism during SIB. Also, there were no focal or generalized motor seizures observed during the episodes of SIBs. He was taking 600 mg of oxcarbazepine (prescribed by a pediatrician) from the age of 5½ years, and though a repeat electroencephalography (EEG) was not done, no episode of seizure was noted by the family since. The child had been previously prescribed risperidone, clonidine, aripiprazole, fluoxetine (all of these were prescribed for SIBs), valproate, levetiracetam, oxcarbazepine (prescribed for seizure and SIB) by a private practitioner but there was minimal improvement. There were no other indications for prescribing the above medications. Each of the above medications was prescribed for a minimum of 6 to 8 weeks at optimum dose. There was no significant family history, no history of consanguinity, failure to thrive, and frequent hospitalizations for a medical crises like hypoglycemia, severe dehydration, and acidosis. There was no major physical anomaly or dysmorphism or any significant findings in local or systemic examination. Considering all these factors and the age of onset of SIBs, the possibilities of genetic syndromes and inborn metabolism errors were clinically ruled out.

On local examination, there were multiple abrasions on hands, forearms, lips, and right side of the head and some lacerations on both forearms and dorsum of hands. 3 lacerated wounds on forearms were of size >3 × 3 cm. The height of the child was 127 cm, and he weighed 27 kg. Blood pressure and pulse were within normal limits.

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Considering worsening SIBs and minimum response to medications, the child was admitted to the child psychiatry ward. Immediate medical and surgical aid was given for the wounds. Hemogram, serum chemistry (sodium, potassium, chloride, creatinine, and blood urea nitrogen), liver function test, and thyroid function tests were within normal limits. Magnetic resonance imaging (MRI), EEG, and intelligence quotient (IQ) testing, previously done (at age of 5½ and 6 years, respectively and not repeated), were suggestive of periventricular leukomalacia, right temporal epileptiform discharges with background slowing, and moderate ID (score of 40 on Binet–Kamat test of intelligence$^9$ and score of 38 on Vineland Social Maturity Scale$^6$, respectively). MRI, EEG, and IQ testing were done at a government tertiary care center in the city. Because of financial concerns, they were not repeated at our center. There was no specific antecedent on functional behavioral assessment (FBA) of SIBs. SIB was present in all environmental situations and not associated with any distress on the infliction of injury, agitation, screaming, or sweating, and the episode would continue for 25 min to 30 min and stop on its own. There was no change in onset or termination of SIB on modifying environmental stimulation. There was no seizure episode observed during the ward stay.

A minimally restrictive environment was provided, but adequate safety measures were taken. Protective gowns and gloves were used to reduce the harm, followed by fading use of protective equipment. Naltrexone was started at 12.5 mg/day and increased to 25 mg/day after 10 days. The nonpharmacological interventions used were blocking and occasional least restrictive restraint along with reinforcement techniques. Oxcarbazepine was continued at 600 mg/day. The child showed significant improvement in terms of frequency and severity of self-biting and headbanging. The child was discharged on naltrexone 25 mg and oxcarbazepine 600 mg. The child improved significantly over a period of 4 weeks. Headbanging disappeared completely. Self-biting episodes decreased from 1 to 2 per 15 days. The child has been on regular follow-up for 8 months and maintaining improvement. Currently, there are no SIBs. The liver function tests done in follow-up are also within normal limits.

**Discussion**

SIB is defined as a behavior that produces physical injury to the individual’s own body.$^{10}$ There is no suicidal intent or sexual arousal leading to these behaviors.$^{11}$ Different studies show variable prevalence rates of SIB.$^{12}$ One study found a 17% prevalence of SIB in children with severe ID.$^{13}$ An Indian study found the prevalence of SIB in children to be 80%.$^{14}$

The onset of SIBs in children with ID is seen in 50% of individuals before 3 years of age, 70% before 7 years of age, and up to 90% before 10 years of age.$^{15}$ Development of SIBs in neurodevelopmental disorders (NDD) depends on various risk factors like language deficits, deficiencies in daily living skills, sensory and motor impairments, concomitant overactivity and impulsivity, repetitive behaviors, and most significantly, the degree of intellectual disability. The severity of SIB is inversely related to IQ score.$^7$

Based on FBA, SIB can be divided into 2 categories: socially mediated SIB (influenced by task escape-avoidance, attention-seeking, and tangible reward) and automatic reinforced SIB (ASIB), which is more under biological control. ASIB can be further divided into 3 subtypes. Subtype 1 occurs because of deprivation of stimulus. Subtype 2 ASIB occurs irrespective of external stimulation, and the neurobiological factors hypothesized in this subtype are sensory-motor dysfunction, including nociception or central nervous system endogenous reinforcement by opioids. Subtype 3 of ASIB occurs in the presence of self-restraint.$^{15,16}$

SIB can also be classified topographically into 5 categories based on the wound site, the way the injury is caused, and various associated behaviors. Type 1 is extreme self-inflicted injury leading to extensive lacerations, bone injuries, and loss of consciousness. Type II is repetitive or stereotypic SIB. Type III is SIB along with agitation. In type IV SIB, the individual displays agitation when interrupted, and type V is SIB with multiple topographies.$^{17}$ The neurotransmitters implicated in type I, II, III, and IV SIBs are endogenous opiates, dopamine, norepinephrine, and serotonin, respectively.$^{18}$

An opiate hypothesis suggests that in SIB, there is a release of endogenous opiates (like endorphins) that results in a “high,” which can become addictive. Individuals with NDD may have less sensitivity to pain because of high circulating levels of endorphins.$^{19}$ Endorphin levels have been observed to be raised after SIB, leading to the maintenance hypothesis of endorphin reduction in self-injury.$^{12}$

Naltrexone is an opioid receptor (mu) antagonist. It may act in the reduction of SIB by blocking an individual’s “high” caused by release of endogenous opiates on SIB or by increasing pain sensitivity.$^{20}$ Common side effects are nausea, vomiting, and decreased appetite. Life-threatening side effect is hepatocellular injury.$^7$ The starting dose of oral naltrexone in self-mutilatory behavior is 0.5 mg/kg/day and increased to 1 mg/kg/day. The maximum recommended dose is 2 mg/kg/day.$^{21}$

Although the use of naltrexone for reducing SIB was of great interest in the 1980s and the 1990s, the available literature is limited to case reports and a series and small controlled trials. The current literature about naltrexone use in children with SIB is scant.$^7$ A Cochrane review concluded that there is conflicting evidence about the efficacy of naltrexone in the management of SIBs in individuals with ID.$^{22}$

The child, in our case, started having SIB at around 6½ years of age. Although the child was diagnosed to have moderate ID, his IQ was in the lower range. As the child could not communicate his issues because of his low IQ, this may have led to increase in the frequency of SIBs. This concurs with the inverse relation IQ score with the frequency of SIB.$^7$ Based on FBA and topographical classification, the SIB was classified as type 2 ASIB and type I SIB, respectively. Naltrexone was preferred in this child because endogenous opioids are hypothesized to be implicated in both type 2 ASIB (based on FBA) and type I SIB (based on topographical classification). The history also...
was suggestive of poor response to antipsychotics, selective serotonin reuptake inhibitors, alpha-2 adrenergic agonists, and mood stabilizers. Tablet naltrexone was started at 12.5 mg/day. The child tolerated it well, and the dose was increased to 25 mg/day after 10 days. He continues to maintain improvement on the same dose and is following up for 8 months. He did not develop any side effects, and liver function tests were within normal limits.

This case highlights the need for a detailed evaluation of SIBs, specially in children with ID. The classification of SIB using a combination of FBA and topographical evaluation may help understand the neurotransmitter(s) involved in SIB and decide the type of pharmacological intervention required. There is a need to conduct future studies to evaluate and understand the role of endogenous opiates in SIBs and the use of naltrexone for its management in children with neurodevelopmental disorders. There is also a need for these studies to have long follow-up periods to assess the role of naltrexone in long-term management of SIBs in children with ID.

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