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Case Report

Fortuitous Results with Hydroxyzine in Autistic Child: A Case Report

Dr. Versha Deepankar
P.G. Resident, Department of Psychiatry
Pacific Medical College and Hospital
Bhilon Ka Bedla, Udaipur (Raj.)

Dr. S. G. Mehta
Professor and Head, Department of Psychiatry
Pacific Medical College and Hospital
Bhilon Ka Bedla, Udaipur (Raj.)

Dr. Bhakti Murkey Sisodia
Assistant Professor, Department of Psychiatry
Pacific Medical College and Hospital
Bhilon Ka Bedla, Udaipur (Raj.)

Dr. Harmandeep Kaur
P.G. Resident, Department of Psychiatry
Pacific Medical College and Hospital
Bhilon Ka Bedla, Udaipur (Raj.)

Dr. Sangamjyot Kaur
P.G. Resident, Department of Psychiatry
Pacific Medical College and Hospital
Bhilon Ka Bedla, Udaipur (Raj.)

Address for Correspondence
Dr Bhakti Murkey Sisodia
doctor.bhaktii@gmail.com

ABSTRACT

Autism is a neuro-developmental disorder characterized by impairment in communication, social interaction and with restricted and repetitive behavior. Autism spectrum disorder is frequently associated with, attention deficit/ hyperactivity disorder (ADHD) and also other symptoms that become the primary focus of psychiatric treatment, such as aggression, anxiety, irritability or self-injury. These complaints often subside on pharmacotherapy with low dose antipsychotics. In this report we describe accidental benefit of Hydroxyzine in the treatment of hyperactivity in a 4 year old autistic boy. This child had presented with severe and persistent irritability and hyperactivity, which apparently worsened on use of titrated Atomoxetine doses. He was later initiated on a trial of Risperidone which demonstrated adequate response on the presenting behavioral complaints and clarified the diagnostic formulation of Autism with secondary hyperactivity, not primary ADHD.

KEYWORDS: Neuro-developmental disorder, Autism, ADHD, Treatment

INTRODUCTION

In India, Autism Spectrum Disorder (ASD) is prevalent in age less than ten years of age is one in hundred children. The absolute cause remaining unknown, approximately 1 in 8 of these children have at least one comorbid neuro-developmental disorder.[1] Many patients diagnosed with ASD, show signs of behavioral disabilities, insomnia, psychomotor activity disability, anxiety and communication issues. ASD and attention deficit/hyperactivity disorder (ADHD) are both seen to increasingly co-occur with their shared genetic heritability and social and cognitive impairments. Majority of individuals with ASD have ADHD symptoms and nearly 15–25% of children with ADHD demonstrate ASD symptoms. Hence, comorbid ADHD symptoms need to be considered for attaining maximal efficacy in ASD interventions.[2,3] The current treatment standards aim at both behavioral and medical treatment modalities for these symptoms, including medications such as antidepressants or anti psychotics and methylphenidate or atomoxetine. All these medicines have showed comparable efficacy although with lower effect sizes and increased side effects, in relation to patients with primary ADHD (without ASD).[3]

Social deficits in ASD are seen in the form of lack of sustained eye contact, facial expression deficits and atypical pattern of social responsiveness. These children often experience difficulty having peer relationships due to lack of empathy (awareness of others' thoughts and feelings) and poor communication skills.[4] However, there is little scope of medication use in treating these symptoms and one can rely more on special educators, occupational therapists, speech therapists and child psychologists for a team-approach to teaching adequate life skills to the child and conducting parent management and training

programmes for the cargivers. So far, only Risperidone and Aripiprazole have received approval by the Food and Drug Administration (FDA, United States) for the treatment of behavioral symptoms in ASD.[5] Although effective, these molecules are occasionally associated with adverse effects like excess sleep, weight gain, metabolic disturbances or mild cognitive impairment[6]. In this case, we present the unexpected response to behavioral symptoms in an autistic child, with the accidental use of hydroxyzine. Perhaps direct reduction of neuro-inflammation by the antihistaminic effect of hydroxyzine might have been an underlying mechanism for the response. However, since it is not approved as standard treatment protocol for ASD, it was replaced with another medicine (Risperidone) and a desirable response to the presenting complaints was further obtained.

CASE PROFILE

A 4 years old boy weighing 21 kgs, presented to the OPD along with his parents, with complaints of preference to remain alone and untouched, increased physical activity, rocking body movements when excited, temper tantrums, eating chalk, breath-holding spells and not following verbal commands. He could point to pictures and words in times of need. He was irritable, intolerant of noise and crowds, and had anger outbursts with frequent destruction to objects at home. He had a particular preference for certain foods or toys. He was described as always overactive child by his mother. His conceptual understanding seemed to be good. He was delivered by Caesarean section at term, with birth weight of more than 3.5 kgs following an uneventful pregnancy. Perinatal asphyxia was noted by delayed cry at birth, followed by NICU admission for 15 days in view of neonatal sepsis, kernicterus and acute respiratory distress (ARDS). Patient is youngest of four siblings, but was conceived after demise of two elder siblings at birth; one by sudden infant death syndrome (SIDS) and another by probable meningomyelocele lesion. Developmentally, most milestones were attained normally, except for language and social. There were occasional incidents of head banging, eating of chalk (pica) and breath holding spells, which made the parents hesitant to start his normal schooling. On examination, the history was corroborated adequately and additional observations of echolalia and concomitant squint were noted. Physical examination, laboratory tests to rule out autoimmune disorders and MRI scan of the brain revealed no significant findings. Other investigations such as 2D Echo, BERA & Karyotyping couldn't be conducted due to financial constraints. The complete assessment of the child prompted a diagnostic formulation of ASD with additional hyperactivity, perhaps primary or secondary in nature.

From therapeutic aspect, his hyperactivity and irritability were considered as predominant symptoms for initial management and he was prescribed tablet Atomoxetine 5 mg per day along with relaxation & behavioral therapy exercises explained to his mother. Over two weeks, parents reported significant improvement in the symptoms (nearly 50%) and no adverse effects. It was decided to now titrate the doses of Atomoxetine as per the child's weight to 10 mg per day (0.1 mg/kg). However, within 2-3 days of doing so, the mother hurriedly reported back to the OPD with worsening of psychomotor symptoms and poor oral intake by the child following drug dose titration. Following this turn of events, the mother was asked to bring all the prescribed medication strips for review, which revealed a surprising finding. In the initial two weeks of treatment, the child has accidentally been offered Tablet Atarax (Hydroxyzine) 10 mg half tablet instead of Tablet Axepta (Atomoxetine) 10 mg half tablet by the mother. The apparent response to treatment was thus, not owing to the expected response to Atomoxetine, rather to the unexpected response to Hydroxyzine.

The treatment was immediately changed at this point of time, due to poor tolerability to Atomoxetine and lack of standard protocols for use of Hydroxyzine in treatment of hyperactivity. Moreover, lack of availability and affordability for Methylphenidate left us with not much choice, but to consider the use of low dose Risperidone for the presenting complaints. The child was then prescribed Syrup Risperidone 0.25 mg per night, slowly titrated up to 0.5 mg per night. Over next one month, the mother reported satisfactory improvement in her child's mood, activity levels, temperament, sleep and energy levels. She however had more expectations of response from these medicines in his eye contact, socializing and understanding abilities, for which further psycho-educational inputs and parent training was offered.

DISCUSSION

During the era of the previous millennial century, the medical fraternity of the world considered self- regulation and maintenance of orderly social relations as qualities of a model child. Contrarily, a' troubled child' would display a broad range of behaviors depicting misconduct. As per problem severity, these children were managed with either psychotherapy and/ or medications in various clinical settings.[7] ASD is distinguished by social and communication difficulties, and restricted patterns of behaviors [8]. Treatment of social deficits in ASD has always been difficult, and only selected psychotropic medications having established evidence base for the management of behavioral difficulties. [9]

An increasing body of evidence suggests the role of active inflammation in the central nervous system (CNS) in ASD patients. There is evidence that blood brain barrier functioning is altered in ASD children due to inflammation of neurons and dysregulation of its immune mechanisms by inflammatory cytokines [10]. It is known that the antihistaminic molecule 'hydroxyzine' reduces proinflammatory cytokines and increases serotonin and GABA levels in the brain. This can in turn decrease the experienced anxiety and improve the child's overt behavior. With its anti-inflammatory and immunomodulatory effects and relative shortage of adverse effects in the long-term, there is a modernized interest in hydroxyzine for the treatment of neuro-developmental disorder such as ASD.[11] The historical use of hydroxyzinein treating behavioral symptoms of children has come its full circle and has perhaps made its way back into off-label treatments, albeit sporadically.

CONCLUSION

While being an anecdotal case study, the dearth of effective interventions for core ASD deficits with comorbid ADHD-like symptoms, makes the accidentally demonstrated

improvement with hydroxyzine in this case noteworthy.

CONFLICTS OF INTEREST: None

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