Case Report

Combination treatment with carbamazepine and clonidine in a case of epilepsy with ADHD

Adhikari S, Upadhyaya S, Pant SB, Dhungana S, Tulachan P, Chapagai M, Ojha SP

Department of Psychiatry and Mental Health, Maharajgunj Medical Campus, Tribhuvan University Teaching Hospital, Kathmandu Nepal

Corresponding author: Dr. Sandarba Adhikari

Email: sandarba71@gmail.com

Abstract

In a child with epilepsy, Attention Deficit Hyperactivity Disorder (ADHD) is found to be more prevalent in comparison to general population. In western literature for the management of ADHD, stimulants like Methylphenidate and non-stimulant like Atomoxetine are considered the first line drugs. Although no any robust findings are found that support the use of such drugs in cases of epilepsy with ADHD, still they recommend using these drugs in such cases. In our scenario availability of such drugs is a major hindrance for which second line drugs like alpha agonists are the only options available to us. Here in this case report we have used Clonidine along with Carbamazepine in the management of a 12 years child presented in our centre with episodes of seizure and ADHD and had shown significant improvement with these medications.

Keywords: ADHD, Carbamazepine, Clonidine, Epilepsy

Introduction

Neurobehavioral comorbidities were present in 80% cases in a study of children with active epilepsy.[1] More observed in association with epilepsy are ADHD, autism, depression and anxiety.[2-4] Several studies have found prevalence rates of ADHD between 23% to 40% in patients with epilepsy.[1, 5, 6]

In addition to stimulants and atomoxetine, alpha-adrenergic agonists – clonidine and guanfacine – are used to treat ADHD. There are various concerns regarding efficacy and safety of standard medications in cases of ADHD with epilepsy. In contrast to the robust data for the use of stimulants in the child with ADHD alone, the data for the treatment of ADHD in children with Epilepsy(CWE) are much weaker. A persistent concern with the use of stimulant medication in CWE is the risk of increase in seizure frequency[7-9]and other concerns being effect on appetite, growth, and sleep. There are no reports of interaction between alpha adrenergics and anti epileptic drugs. Clonidine had been approved by the US FDA for the treatment of childhood ADHD in 2010 as monotherapy or as an adjunctive treatment to stimulants but there are no reports on alpha adrenergics in CWE.[10]

Case report

A 12-year female was brought to our setting with target symptoms of repetitive generalized tonic clonic seizure every 1-2 months for last 2 years.After few months of onset of seizure patient had difficult in giving and sustaining attention, not listening to when spoken, not following any instruction, losing her things at school, difficult at managing her things, sustained increase in psychomotor activity and running inappropriately, irritability and provoked anger and aggression towards others. There was no history of anxiety and depressive features, psychotic episodes and psychoactive substance use.There was no significant past and family history. Her birth and early childhood history was uneventful. Regarding premorbid temperament she was an easy child.

On examination her vitals were normal. Her psychomotor activity was increased, eye contact was not satisfactory and communication was difficult during interview. Her

self-care and hygiene were neglected. Her tone of voice was nasal and predominant mood was irritable.

Connor's Abbreviated Rating Scale(CARS) showed score of 23 which was above cut off (15)with scores high in domains of restlessness\overactive,excitability\ impulsive, short attention span and easily frustrated.

Routine blood examinations showed complete\ differential blood count(8290 mm3,N-56, L-30,E-12), hemoglobin 12.7 mg/dl, random blood sugar- 5.4 mmol/L, Na\k-138\4.5meq\L, bilirubin (total:11 direct: 2 micromol\L) SGOT: 35 U/L, SGPT: 19 U/L, urea: 4.8 mmol/L, creatinine: 56 micromol/L, Urine routine and microscopy was within normal limit. Thyroid function test was within normal limit (T3: 8.0 T4: 14.1 pmol\L and TSH:0.5microIU\ml). Ultrasonography of abdomen and pelvis showed normal findings. Electroencephalogram showed abnormal record suggesting interictal epileptiform activityin bilateral centroparietal region. Echocardiography and MRI brain was normal.

With the available history, psychometric assessment and investigations the child was diagnosed to have Epilepsy with ADHD. Pharmacological treatment was started with carbamazepine with dose gradually increasing upto 800mg per day in two divided doses for full control of seizure. Clonidine was started with 0.05mg twice daily after two weeks of starting carbamazepine when there was no significant improvement in hyperactivity and inattention as shown by the CARS score which was 21 and later dosage was increased upto 0.1mg twice daily. Patient was discharged on same doses of medications after 3 weeks of stay in psychiatry ward. Behavior modification through positive reinforcement and token economy was planned and initiated in care of her mother and reviewed on subsequent follow up visits. On subsequent follow up done at 2nd, 6th, 10thweek and every 2 months thereafter, she was seizure free and 50% improvement in her behavioral symptoms on 3rd follow up and 80% improvement on 5th follow up as reported by her mother along with improvement in daily functioning.No side effects were reported.The score of CARS was 18and 12 in respective follow ups.

Discussion

Stimulants are the most commonly prescribed pharmacological class of medication for ADHD. Nonstimulant treatments, including atomoxetine, guanfacine, and clonidine, have been found to be beneficial both as monotherapies and adjuncts to stimulant therapy.[11]Most of the studies favour the use of Stimulants like Methylphenidate in the treatment of CWE with ADHD.[12] Till now no any studies were done on the use of Clonidine in the treatment of ADHD with Epilepsy. As far as we know this is the first case report where use of Clonidine in the treatment of ADHD with epilepsy is found to be effective.

Studies have shown that CWE had predominantly inattentive presentation of ADHD than combined presentation in general population.[13-15]CWE and ADHD treated with carbamazepine and lamotrigine have shown better results on attention and behavioral problems than other anti-epileptics.[16] In the absence of guidelines in the management of ADHD in CWE, some authors from our sub-continent recommended that if inattention and hyperactivity symptoms persist for more than 6 months after the last epileptic seizure, one can go for a stimulant medication trial.[17] Use of stimulants and even non-stimulants like Atomoxetine is not possible in our country because of unavailability of these medications. In order not to treat or undertreat CWE and ADHD we chose to use Carbamazepine and Clonidine. The result from this case study showed that such a combination of second line drugs for the management of ADHD is beneficial in a CWE and needs further study.

Animal study showed that Clonidine at medium to high dose increases the seizure threshold.[18]Other studies in experimental animals found that Clonidine acts as proconvulsant at high dose and anti-convulsant at low dose.In human study, as evidenced by the use of Clonidine and Chlormethiazole for the management of Alcohol withdrawal seizure was found to be observed only in patients who were on Clonidine but not on Chlormethiazole.[19]One case report showed that a child developed new onset convulsive status epilepticus two weeks after starting treatment with Clonidine and was later successfully treated with Methylphenidate without any episodes of seizure.[20]But in our case report child did not have any episodes of seizure following use of clonidine and carbamazepine.

Concomitant use of Clonidine with Carbamazepine had not shown any significant interactions and can safely be used in CWE and ADHD. To support the use of the combination treatment of CWE and ADHD with Clonidine and Carbamazepine further study is warranted.

Conclusion

In the management of CWE and ADHD, drugs should be chosen considering the availability, affordability and accessibility to treatment. In resource limited setting like ours, second line drugs like Clonidine can be used safely and effectively in CWE and ADHD.

Conflict of interest: None declared.

References

1. Reilly C, Atkinson P, Das KB, Chin RF, Aylett SE, Burch V, et al. Neurobehavioral comorbidities in children with active epilepsy: a population-based study. Pediatrics. 2014; 133(6):e1586-e93.
2. Torres AR, Whitney J, Gonzalez-Heydrich J. Attention-deficit/hyperactivity disorder in pediatric patients with epilepsy: review of pharmacological treatment. Epilepsy & Behavior. 2008; 12(2):217-33.
3. Dunn DW, Austin JK. Differential diagnosis and treatment of psychiatric disorders in children and adolescents with epilepsy. Epilepsy & Behavior. 2004; 5:10-7.
4. Aldenkamp AP, Arzimanoglou A, Reijs R, Van Mil S. Optimizing therapy of seizures in children and adolescents with ADHD. Neurology. 2006; 67(12 suppl 4): S49-S51.
5. Russ SA, Larson K, Halfon N. A national profile of childhood epilepsy and seizure disorder. Pediatrics. 2012; 129(2):256-64.
6. Cohen R, Senecky Y, Shuper A, Inbar D, Chodick G, Shalev V, et al. Prevalence of epilepsy and attention-deficit hyperactivity (ADHD) disorder: a population-based study. Journal of child neurology. 2013; 28(1):120-3.
7. Gonzalez-Heydrich J, Whitney J, Waber D, Forbes P, Hsin O, Faraone SV, et al. Adaptive phase I study of OROS methylphenidate treatment of attention deficit hyperactivity disorder with epilepsy. Epilepsy & behavior. 2010;18(3): 229-37.
8. Gucuyener K, Erdemoglu AK, Senol S, Serdaroglu A, Soysal S, Kockar I. Use of methylphenidate for attention-deficit hyperactivity disorder in patients with epilepsy or electroencephalographic abnormalities. Journal of child neurology. 2003; 18(2):109-12.
9. Koneski JA, Casella EB. Attention deficit and hyperactivity disorder in people with epilepsy: diagnosis and implications to the treatment. Arquivos de neuro-psiquiatria. 2010; 68(1):107-14.
10. Williams AE, Giust JM, Kronenberger WG, Dunn DW. Epilepsy and attention-deficit hyperactivity disorder: links, risks, and challenges. Neuropsychiatric disease and treatment. 2016; 12:287.
11. Wigal SB. Attention-deficit/Hyperactivity disorder. In: Gabbard GO, editor. Gabbard's treatments of Psychiatric disorders. 5th edition. 2016; New Delhi, India: American Psychiatric Association. p. 57-76.
12. Jensen PS. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. Archives of general psychiatry. 1999; 56(12):1073-86.
13. Dunn DW, Austin JK, Harezlak J, Ambrosius WT. ADHD and epilepsy in childhood. Developmental medicine and child neurology. 2003; 45(1):50-4.
14. Hermann B, Jones J, Dabbs K, Allen CA, Sheth R, Fine J, et al. The frequency, complications and aetiology of ADHD in new onset paediatric epilepsy. Brain. 2007; 130(12):3135-48.
15. Sherman E, Slick DJ, Connolly MB, Eyrl KL. ADHD, Neurological Correlates and Health related Quality of Life in Severe Pediatric Epilepsy. Epilepsia. 2007; 48(6):1083-91.
16. Schubert R. Attention deficit disorder and epilepsy. Pediatric neurology. 2005; 32(1):1-10.
17. Kattimani S, Mahadevan S. Treating children with attention-deficit/hyperactivity disorder and comorbid epilepsy. Annals of Indian Academy of Neurology. 2011; 14(1):9.
18. Shouse MN, Bier M, Langer J, Alcalde O, Richkind M, Szymusiak R. The α 2-agonist clonidine suppresses seizures, whereas the α 2-antagonist idazoxan promotes seizures-a microinfusion study in amygdala-kindled kittens. Brain research. 1994; 648(2):352-6.
19. Robinson B, Robinson G, Maling T, Johnson R. Is clonidine useful in the treatment of alcohol withdrawal? Alcoholism: Clinical and Experimental Research. 1989; 13(1):95-8.
20. Feron FJ, Hendriksen JG, Nicolai J, Vles JS. New-onset seizures: a possible association with clonidine? Pediatric neurology. 2008; 38(2):147-9.