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Dexamathasone Pulse Therapy In Refractory Childhood Seizure Disorders

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Abstract

15 children with variable intractable seizure disorders who were on multiple anti-convulsant medications were treated with pulse monthly doses of parentral dexamethsone varying from 4 – 7 months. EEG and clinical response were assessed periodically as well at the end of the study. 53% of the patients showed clinical response and EEG response. Hypertension was noted in 6, hypokalemia in 3 and hyperglycaemia in 1 patient. The ultimate compliance from the parents for this treatment was seen among 12 patients because of its proven efficacy and parents of seven patients insisted to continue the treatment for long duration.

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Introduction

Epilepsy is a common problem in children which is treatable. However some patients are difficult to treat which was previously called intractable epilepsy and it varies from 6- 40% in many studies. [1,2] International League Against Epilepsy (ILAE-2010) defines drug resistant epilepsy (DRE) as *failure of adequate trial of two tolerated and appropriately chosen and used anti epileptic drugs schedules (whether as monotherapy or combination) to achieve sustained seizure freedom*.[1]

Corticosteroids, either as adrenocortciotrophic hormone (ACTH) or synthetic preparations of steroids have been used widely for the treatment of intractable epileptic disorders of childhood since long time. Livingston and Sorel reported the benefits of ACTH in West syndrome , an infantile form of epileptic encephalopathy.[4,5] Since then, numerous studies have been done regarding wide usage of corticosteroid in different preparations in therapy-resistant epilepsies of childhood although there is no consensus opinion regarding their efficacy.[4,5]. Moreover there is no regional or national strategy recommendations of uniformity in dosing, duration and choice of steroids.[5]. There were few reports of pulsatile corticosteroid, as an alternative to ACTH in such intractable seizure disorders in children and its efficacy as well safety.[7,8].We report here a retrospective study of efficacy and adverse side effects of pulsatile dexamethasone in the treatment of childhood intractable epileptic disorders.

Methods

15 patients were enrolled (9males and 6 females) on a retrospective basis and charts were analyzed between 2012 and 2015; all these patients had intractable epilepsies and on several medications. The patients included in this study had the diagnosis, as classified according to International criteria of diagnosis of epilepsies as follows: West syndrome, Lennox-Gastaut syndrome, Dravet syndrome, myoclonic atonic epilepsy of infancy and electrical status epilepticus of slow wave sleep. Informal written consent was obtained from parents prior to treatment regarding mode of administration of steroids, possible side effects and they were advised to report, if any. Baseline electroencephalogram were done prior to starting treatment and at the end of the study period of seven months. All of them were admitted to the ward and base line investigations to rule outacute or chronic infections were done. Patients received 20 mg/m2 of intravenous dexamethasone daily early morning for 3 days and subsequently on monthly basis for at least seven cycles. 12 patients adhered to the strict regime of 7 cycles of treatment and the rest could not complete. The defaulters were mostly non-responders to initial treatment. Routine biochemical investigations namely electrolytes and random blood sugar were done and no antibiotic prophylaxis was given. Blood pressure was monitored during the admissions and steroid administration was withheld, if high. No oral steroids were prescribed to the patients at time of discharge. Clinical response in the form of seizure frequency, response were graded into complete seizure freedom (100%) partial response (more than 50% but less than 100%) and poor response with no change in seizure frequency (0-50%). Similarly EEG response was also graded as good (100%) moderate (50%) and poor (0%). [3]

Results

Treatment response was assessed as per the classification and noted that no patient had total response to treatment (100%) but moderate response was noted in 8 out of 15 patients (53%) and poor response in the rest of 7 (0%). The non responders were 4 patients of Dravet syndrome, 2 with Lennox-Gestaut and one with infantile spasm (West syndrome). All other patients, (3) with electrical status epilepticus in slow wave sleep and myoclonic atonic epilepsy of infancy (2) showed moderate response (50% reduction in seizure frequency) and 2 patients of West syndrome and I with LGS showed similar response as above . The time of onset of response was noted in 1 patient with West syndrome soon after the first pulse therapy period with 50% reduction in seizure frequency by the time of discharge but the rest showed the response in varying periods within the completion of the study period. EEG response was concurrent to that of clinical response in terms of sharp wave paroxysmal frequency and evidence was much appreciated in patients with West syndrome and electrical status epilepticus of slow wave sleep. The commonest adverse

event noted was hypertension in 6 patients, low potassium in 3 and 1 patient had high blood sugar. All these side effects were transient, not needing intervention and did not persist after the completion of cycles of treatment. 12 patients were compliant to this pulse therapy treatment schedule with proven efficacy and parents of seven patients insisted to continue the treatment for longer duration.

Discussion

Intractable childhood epileptic syndrome forms a spectrum of therapy resistant epilepsies where conventional and new 'ant- epileptic' medications do not prove much benefit. Corticosteroids, used in various forms, appear to influence the seizure outcome both in short-term as well as long-term, in a few patients to a greater extent in various studies but the exact mechanism of their influence is still unknown.[8,9,10].

Dysfunction of brain adrenal axis is said to play an important role in seizures evolution and propagation [9,15,16]. Increase in serum levels of cortisols and suppression of corticotrophin releasing hormone levels by the steroids could be the one of the possible effect of its benefit[11,13]. Reduction in cerebral blood circulation, reduced cerebral oedema, increased enzymatic activity if brain, increase in cerebral glucose levels were other probable mechanisms of alleviation of seizure activity[11,12] Although complete response (100%) to steroid therapy were not achievable in our group of patients, a 50% reduction in seizure frequency in 8 patients (53%) is well appreciated by the parents and the parents of six patients sought advice from us to re start or continue the therapy. Pulsatile steroids either in the form of adrenocorticotrophic hormone (ACTH) or steroids were found to be beneficial in West syndrome as first line therapy and the responder within the first pulse therapy of such patient was an expected outcome.

Our study proved that pulsatile steroid therapy was beneficial and probably a treatment option in patients with West syndrome, Lennox Gastaut syndrome, myoclonic atonic epilepsy of infancy and electric status epilepticus[6]. of slow wave sleep. Adverse events namely hypertension, electrolyte disturbances, hyperglycemia as described above were transient and did not require any long term follow up. Complete response (100%) to treatment, which could not be achievable in any of our patients could not be explained; possibly the comorbidity of developmental delay, starting pulsatile steroid therapy late after significant delay with trial of combination of other anti epileptic medications and their possible interaction could be the possible reason. Thus it is postulated by us that earlier administration of pulsatile therapy of steroids in the above epileptic encephalopathy of childhood, once the diagnosis is made, could avoid the unnecessary, inadvertent usage of many anti convulsant medications as well better treatment response.

Conclusion

In this pilot study, pulsatile steroid therapy, in the form of dexamethasone injections, is an effective therapeutic option in patients with childhood onset epileptic encephalopathy. Earlier administration of this mode of treatment could not only alleviate the problem of seizure severity and frequency but also the usage of multiple anti epileptic medications and their side effects. It is well known that the major drawbacks of steroid use are seizure recurrence after discontinuation and the significant side effects from long-term use. Dravert syndrome, a form of severe myoclonic epilepsy of infancy may not respond to this treatment.

References

1. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia. 2010 Sep;51(9):1922.
2. Ramos LJ, Rodriguez LMI, Angiler LP, Aguirre RJ, Cassinello GE. A study of drug-resistant epilepsy testing the new ILAE criteria. Seizure. 2012:266–72
3. Murray DM, Boylan GB, Ryan CA. Early EEG findings in hypoxic-ischemic encephalopathy predict outcomes at 2 years. Pediatrics 2009; 124(3): 459-57.
4. Klein R., Livingston S.: The effect of adrenocorticotrophic hormone in epilepsy. J Pediatr 35.733-742.1950
5. Sorel L, Dusaucy- Bauloye A. A propos de 21 cas d'hypsarrhythmia de Gibbs. Son traitment spectaculaire par L'ACTH. Acta Neurol Psychiatr Berg 1958; 58: 130-141.

6. Jayakar P.B; Seshia S.S: Electrical status epilepticus during slow wave sleep: a review. J Clin Neurophysiology 8.299-311.1991.
7. Snead OC, 3rd, Benton JW, Myers GJ. ACTH and prednisone in childhood seizure disorders. Neurology 1983; 33: 966-970
8. Bobele G.B., Bodensteiner J.B: The treatment of infantile spasms by child neurologists. J Child Neurol 9.432-435;1994; Abstract
9. Karenfurt M., Wilken B., Hanefed F.: Pulsatile dexamethasone pulse therapy in symptomatic infantile spasms (Abstract) Neuropediatrics 6.A52.2002.
10. Lux AL, Edwards SW, Hancock E. United Kingdom Infantile Spasm Study (UKISS) Lancet Neurol. 2005 Nov;4(11):712-7.
11. Inui T, Kobayashi T, Kobayashi S. Efficacy of long term weekly ACTH therapy for intractable epilepsy. Brain Dev. 2015 Apr;37(4):449-54.
12. Haberlandt E, Weger C, Sigl SB et al. Adrenocorticotropic hormone versus pulsatile dexamethasone in the treatment of infantile epilepsy syndromes. Pediatr Neurol 2010; 42: 21-27
13. Sinclair DB. Prednisone therapy in pediatric epilepsy. Pediatr Neurol 2003; 28: 194-198
14. Liu J.L., He B., Fang F., Tang C.Y,. Zou L.P., Analysis of single nucleotide polymorphisms in the melanocortin-4 receptor promoter in infantile spasms. Neuropediatrics 38. 304-309. 2007; Abstract.
15. Baram T.Z.: Pathophysiology of massive infantils spasms: perspective on the putative role of the brain adrenal axis. Ann Neurol 33. 231-236. 1993; Abstract.
16. Riikonen R.: Infantile spasms: some new theoretical aspects. Epilepsia 24.159-168. 1983.