

Cyproheptadine adverse drug interaction with anti-epileptic drugs**Ankit Bhardwaj*, Anand Shukla, Sunita Singh, Anil Kem**

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ABSTRACT

Cyproheptadine is a H1 and 5-HT_{1/2} receptor antagonists, impairing the anticonvulsant activity of antiepileptic drugs and reduces threshold, increases severity of seizures, when administered chronically. Anuj a 13 years old male from Delhi, known case of SSPE stage-III with epilepsy, on oral anti-epileptic drug has seizure induction followed the use of oral cyproheptadine. Stopping cyproheptadine, patient didn't sustain any further seizures.

Keywords: Antiepileptic drugs and H1 and 5-HT_{1/2} receptor antagonist, Cyproheptadine and seizure, H1 and 5-HT_{1/2} receptor antagonists and seizure

INTRODUCTION

Histamine is found to take part in the inhibition of seizures via H₁ and 5-HT_{1/2} histamine receptors. In past epileptic patients were frequently prescribed cyproheptadine, as an appetite stimulant for the treatment of anorexia associated with anti-epileptic drugs and for the management of 'serotonin syndrome' in depressed epileptic patients. Cyproheptadine antagonizing subtypes of 5-HT_{1/2} receptors and H₁ receptor and decreases neurotransmission of serotonin, which in turn reduces seizures threshold.

If used chronically it is found to increase the severity of seizure and decreases efficacy of antiepileptic drugs in animal study.¹

CASE REPORT

A 13 years old male, resident of Khajuri, Delhi, presented to us with history of multiple episodes of General tonic seizures from last 3 days. Patients is known case of sub-acute sclerosing pan encephalitis stage III with quadriplegia and seizure disorder. Old MRI imaging suggestive of T₁/T₂ prolongation and mild restricted diffusion seen in bilateral basal ganglia region, suggestive of gliosis/metabolic etiology. The patient was conscious at the time of hospital visit. At admission at our health care facility, child was sick looking and mild pallor. On Primary survey: Airway: Patent.

Bilateral chest rises present, bilateral air entry equal, respiratory rate of 22/min, SPO₂: 98% on room air. GCS-

E4V2M6, pupils 2mm BERL, moving all four limb, no external injuries noted. ECG was within normal range.

Peripheries were cold and peripheral pulses well felt, CRT less than 2sec, HR-96/min, BP- 114/86mm Hg, Inj. Levetiracetam 1.35gm given IV bolus. Blood sample collected. Investigations revealed anemia (Hb 9g/dL), (TLC: $9.9 \times 10^9/L$), Normal liver and renal function tests. Blood culture and Widal test were negative. Urine routine and microscopy was normal. RBS random 134mg/dl. Sr. Calcium 8.8mg/dl and sr. magnesium 1.6meq/l. MRI brain: showed symmetric area of prolongation and mild restricted diffusion seen in bilateral basal ganglia region suggestive of gliosis of metabolic etiology.

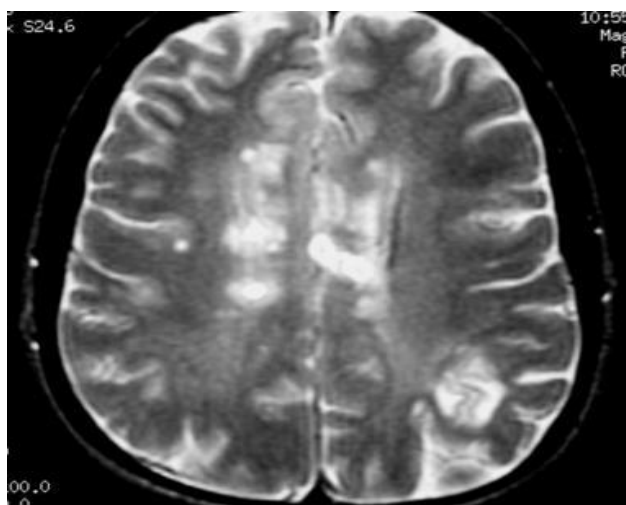


Figure 1: Axial T2-weighted MRI brain in a patient with multiple sclerosis demonstrates numerous white matter plaques in a callosal and pericallosal white matter distribution.

Patients kept under observation for three days, Cyproheptadine stopped and treated with Devaloprex sodium extended release 500mg twice daily.

PAST MEDICAL AND SURGICAL HISTORY

Patient is known case of SSPE with stage III with seizures and quadriplegia diagnosed at R.M.L hospital Delhi where patient was treated with Interferon alpha-2b intrathecal followed with subcutaneous doses. Tab Isoprinosine 500mg B.I.D. Patient become bed ridden gradually. Birth history: Cried immediately after birth and immunized till date. There is no significant family history. Patients was non-smoker or had any type of addiction.

CSF analysis shows IgG Measles titers elevated in CSF and Serum. Patient was kept under observation for three days. During hospital stay no episode of seizure been recorded, and later discharged with same dose of anti-epileptic drugs he was taking earlier.

DISCUSSION

Cyproheptadine is a H1 receptor and 5-HT_{1/2} antagonist. The study of serotonergic and histaminergic pathway shows that the decreased neurotransmission of serotonin and histamine in the brain reduces seizure threshold. Since, cyproheptadine interferes with these pathways via antagonizing subtypes of H1 and 5-HT_{1/2} receptors, impairing the anticonvulsant activity of some antiepileptic drugs and reduces threshold, increases severity of seizures and decreases the efficacy of clinically used antiepileptic drugs, especially when administered chronically.² Example of antiepileptic drugs whose activities are impaired by H1 and 5-HT_{1/2} receptor antagonists are phenobarbital, phenytoin, valproic acid and devaloprex sodium in maximal electroshock induced convulsions in mice.¹ Few days back he started taking Syp. Cyproheptadine over the counter for increasing his appetite. Later he had 2 episodes of convulsions. He was kept under observation for 3 days. Syp Cyproheptadine was stopped. MRI brain showed symmetric area of prolongation and mild restricted diffusion seen in bilateral basal ganglia region suggestive of gliomas of metabolic etiology. Blood, CSF and urine culture showed no growth. CSF analysis showed positive IgG for measles. All other causes of seizure were ruled out. After stopping cyproheptadine, patient didn't sustain any further seizures. Later patient was discharged on same epileptic drugs.

CONCLUSION

Cyproheptadine can cause seizures in epileptic and in non-epileptic patients. Cyproheptadine reduces threshold, increases severity of seizures and decreases the efficacy of clinically used anti-epileptic drugs.

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