Dopa-Responsive Dystonia subsequent to Lamotrigine Administration: Case Reports

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ABSTRACT

Epilepsy is a common neurologic disorder affecting approximately 1% of the population. The prevalence of active epilepsy in Kerman, Iran is 7.87/1000 individuals. The past decade has brought many advances to the treatment of epilepsy, including many new pharmacological agents. Lamotrigine is one of the new antiepileptic drugs. Lamotrigine has many side effects; the most important of which are allergic reactions. In this article, the author reports two cases of dopa-responsive dystonia (DRD) after few months of administration of lamotrigine for epilepsy. The cases are two girls (4 and 5 years old) who had seizures, and received lamotrigine 50 mg/day. They have been free of seizure after treatment but after some time the dystonic attacks developed. Lamotrigine administration discontinued, but dystonic attacks didn’t disappear. Levodopa/carbidopa was started. After a few days, the dystonic pastures disappeared. In conclusion, lamotrigine may introduce dystonia in susceptible patients. These dystonic attacks might be responsive to levodopa.

Keywords: ?????

Epilepsy is a common neurologic disorder affecting 42 other medications such as valproic acid. It’s about 1% of the population [1]. The prevalence of 43 predominantly metabolized in the liver by 44 active epilepsy in Kerman, Iran is 7.87/1000 individuals 45 glucuronidation [9]. Lamotrigine has many side effects, 46 [2]. Pharmacotherapy with antiepileptic drugs remains 47 most importantly allergic reactions. Gradual introducing of the treatment modality for epilepsy. This could 49 lamotrigine is one of the key factors to reduce the 50 occur as a result of decreased excitation concurrent with 51 and severity of allergic reactions [5]. Although the 52 increased inhibition [3]. Management of epilepsy differs 53 overall incidence of cutaneous reactions to lamotrigine 54 from the treatment of other chronic diseases in that a 55 high, the incidence of serious eruptions such as 56 single breakthrough event has a major negative effect 57 Stevens-Johnson syndrome, and 58 on quality of life. Complete control of seizures is 59 toxic epidermal necrolysis is low [10,11]. The revision necessary as a single seizure impacts negatively on 60 of La Roche and Helmers demonstrated that side-effects 61 patient quality of life and independence [4]. led to drug withdrawal in 10.2% of all patients under 62 The past decade has brought many advances to the 63 lamotrigine therapy. Rash was the main reason for 64 treatment of epilepsy, including many new 65 treatment discontinuation. It has been postulated that 66 pharmacological agents. Lamotrigine is one of the new 67 side-effects may be lessened by slow introduction and 68 antiepileptic drugs; it’s been used more than two 69 titration [12,13].

21 Lamotrigine is a broad-spectrum 68 The present study reports two cases of dopa- 69 antiepileptic drug of the phenyltriazine class chemically 70 responsive dystonia (DRD) after lamotrigine 71 unrelated to other anticonvulsants [8]. Lamotrigine has 72 administration for a few months due to epilepsy. DRD 73 an average elimination half-life of 33 hours, although 61 is a broad term used to described forms of dystonia 74 this can be influenced by concomitant therapy with 62 characterized by the onset dystonia in early childhood
with dramatic and sustained response to treatment with levodopa. This disorder was first described by Segawa [14]. The most common form of DRD is an autosomal-dominant condition (DYST) caused by mutation of the GTP cyclohydrolase I gene [20]. A study showed dizziness in 11%, and dysrhythmia in two cases [25]. Psychosis was one of the rare side effects of lamotrigine [13], oral ulcers [26], chorea [27], leucopenia and thrombocytopenia [28], anticonvulsant hypersensitivity syndrome [29], abnormal eye movements and hyper-sexuality [30]. This dystonic effect may be due to the lack of selectivity of lamotrigine to block glutamate release in susceptible individuals. In dystonic mutant hamsters when subsided, dystonia can be re-invoked when these animals receive sodium channel blockers such as lamotrigine [31-34]. The patients under discussion are two girls (4 and 5 years old) who had seizure and received lamotrigine for a time and were free of seizure attacks. Dystonic attacks disappeared after receiving 50 mg per day levodopa/carbidopa. In conclusion, lamotrigine may introduce dystonia in susceptible patients. The dystonic attacks are responsive to levodopa.

**Case Reports**

**Case 1**

A 5 years old girl who used lamotrigine 50 mg per day due to tonic-clonic seizure and had her first attack of seizure two months before her first visit. After starting lamotrigine, the patient was free from seizure for one year. Dystonic attacks worsened later in the day. Results of physical examinations, brain’s MRI scans and hematologic and serologic laboratory tests were normal. Dystonic pasture did not disappear after lamotrigine was discontinued. The dystonic attacks disappear after two days, when 50 mg per day levodopa/carbidopa was started.

**Case 2**

A 4 years old girl used lamotrigine 50 mg per day due to complex partial seizure. She had had her first attack of seizure a few months before her first visit. After receiving lamotrigine for two months, dystonic pasture developed in lower limb and then spread to lumbar spine. Dystonic pasture worsened later in the day. Physical examinations, brain’s MRI scans, hematologic and serologic laboratory tests were normal. Dystonic pasture did not disappear after lamotrigine was discontinued. The dystonic attacks disappear after three days, when 50 mg per day levodopa/carbidopa was started.

**Discussion**

DRDs are a group of disorders that show a good response to levodopa. The causes of these disorders are unknown, but the mutation of a gene is recognized in some studies. Onset of this disease usually happens in the first decade of life starting with foot dystonia, which progresses to involve other body parts, but typically remains more severe in the lower extremities. The severity increases progressively over the first two decades of life, but plateau with relatively few side effects and no long-term complication [16]. Untreated individuals developed diurnal fluctuations with marked improvement in the morning and worsening in the evening. DRDs are more frequent in female than in males, with a ratio varying from 1 to 4.3:1. Diagnosis of DRD can often be made on clinical grounds [17].

There are reports about DRD induction by diazepam [18], bupropion [19], cetirizine [20], riluzole [21], and tetrabenazine [22]. The authors, however, didn’t find any reports about post-lamotrigine conditions.

Lamotrigine is a new antiepileptic agent that is usually used in epileptic patients with a good tolerability and efficacy. Lamotrigine has side effects, the most important of which is exfoliative dermatitis [23]. A study showed dizziness in 11%, and doses, these events decreases [24]. Other side effects were also reported such as sudden death due to cardiac dysrhythmia in two cases [25]. Psychosis was one of the rare side effects of lamotrigine [13], oral ulcers [26], chorea [27], leucopenia and thrombocytopenia [28], anticonvulsant hypersensitivity syndrome [29], abnormal eye movements and hyper-sexuality [30]. This dystonic effect may be due to the lack of selectivity of lamotrigine to block glutamate release in susceptible individuals. In dystonic mutant hamsters when subsided, dystonia can be re-invoked when these animals receive sodium channel blockers such as lamotrigine [31-34]. The patients under discussion are two girls (4 and 5 years old) who had seizure and received lamotrigine for a time and were free of seizure attacks. Dystonic attacks disappeared after receiving 50 mg per day levodopa/carbidopa. In conclusion, lamotrigine may introduce dystonia in susceptible patients. The dystonic attacks are responsive to levodopa.

**References**


Dopa-responsive lamotrigine-induced dystonia


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