

**Lamotrigine in treatment of Writer's cramp (Focal dystonia) in unspecified bipolar and related disorder****Rajnish Raj<sup>1\*</sup>, Raj Kumar<sup>2</sup>**

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**Received:** 23 October 2015**Accepted:** 16 November 2015**\*Correspondence to:**

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**ABSTRACT**

Writer's cramp is a focal dystonia and its non-response to a standard treatment regimen prompts review of the diagnosis as unspecified bipolar and related disorder. Mr. X, aged 44 years male, showed a symptom of writer's cramp and his condition worsened on augmentation with antidepressant and antipsychotic drugs. The diagnosis of unspecified bipolar and related disorder is applied when it clinically impairs social, occupational, or other important areas of functioning that do not meet the full criteria for any of the disorders in bipolar class or when a clinician chooses not to specify the reason that the criteria are not met, and there is insufficient information to make the specific diagnosis. In our case, lamotrigine has shown effectiveness in unraveling writer's cramp and is suggested as an alternate treatment in unmet need for bipolar disorders because of its pleiotropic actions on the nervous system, e.g., membrane stabilizing, neuronal plasticity, and inhibition of glutamate release.

**Keywords:** Writer's cramp, Unspecified bipolar and related disorders, Lamotrigine, Diagnostic and statistical manual of mental disorders

**INTRODUCTION**

Writer's cramp the most common occurs in an upper limb, also called task-specific tremors. Men and women are equally affected, most often between the ages of 20-50 years.<sup>1</sup> On attempting to write, the muscles of the thumb and fingers either go into spasm or inhibited by stiffness and pain that interferes with the execution of fluid, cursive movements. The similarity has been reported with others activities such as playing golf, throwing dart, shooting, and playing musical instrument. The cause is unclear though some conclude that it is a variant of focal dystonia, although studies of reciprocal inhibition are normal.<sup>2</sup> Electromyography (EMG) shows an alternating agonist-antagonist burst.<sup>3</sup> At present, it is unclear whether primary writing tremor is related to dystonia,

essential tremor or a separate disorder. In term of response to drug therapy the task-specific and essential tremor respond to propranolol or primidone, others improve with anticholinergic medication;<sup>4</sup> Botulinum toxin;<sup>5</sup> thalotomy,<sup>6</sup> and deep brain stimulation.<sup>7</sup>

Bipolar II disorder is clinically distinct from the bipolar I as reported in diagnostic and statistical manual of mental disorders (DSM-5).<sup>8</sup> The pharmacological response also helps in delineating the depressive phase of the disorder. The worsening of mood, non-response on increase of antidepressant warrants review of the diagnosis. Bipolar II is not a "milder form" of bipolar I disorder. It is more chronic; patient spends more time in the depressive phase, which can be severe and disabling. There is a higher preponderance

for female gender, suicide risk, binge eating disorder and alcohol-related substance use disorder. Though the most common age of onset is 18 years but extremes of age are not uncommon, and there are reports of middle age onset of the first episode bipolar disorder after ruling out precipitation of symptoms by medical or substance.<sup>8-10</sup>

We report a case of non-responding writer's cramp "quid pro quo" as one of the symptoms of psychomotor retardation in unspecified bipolar and related disorder that was treated successfully by lamotrigine.

## CASE REPORT

Mr. X aged 44 years male, married, and working as a reader in District Court reported to the Department of Psychiatry, Government Medical College and Rajindra Hospital, Patiala with symptoms of difficulty in gripping pen and loss of felicity in writing for the last 3 months. These symptoms were gradual on onset and worsened after 15 mins of persistent writing. His sleep and appetite were normal. The past medical, substance or psychiatric illness, family, personal history, and premorbid personality were normal. These symptoms caused significant functional impairment. Various laboratory investigations, i.e., complete blood count, electrolytes, serum calcium, liver function test, urine analysis, thyroid, and diabetic profiles, etc., were within normal range. On magnetic resonance imaging (MRI) scan for brain and cervical spines, electroencephalogram, EMG and nerve conduction studies (NCS) for bilateral upper limbs, e.g., radial, median and ulnar nerves were normal. Mental status examination showed mood as normal; the speech was of low volume, at normal rate, rhythm, tone and prosody. Thought process was slow, goal-directed and content was normal. Higher mental function, judgment, abstract thinking, insight and contact with reality were normal.

The opinion of Neurologist was taken who diagnosed it as writer's cramp and treated with trihexyphenidyl 2 mg and clonazepam 0.5 mg twice daily for 2 weeks. There was no improvement. Subsequently, another consultation prompted augmentation with tianeptine 12.5 mg a day, tetrabenazine 50 mg per day, haloperidol 0.25 mg twice daily, tocopherol 400 mg a day and zolpidem 5 mg at night for the next 2 weeks. Again, there was no improvement rather specific symptom, i.e., psychomotor retardation worsened and treatment-related adverse effects emerged, e.g. increased sleepiness, low in mood, feeling lethargic and helplessness with suicidal ideations. Clinical Global Impression - Improvement (CGI-I) scale showed change in score from 2 baselines to 6 after 4 weeks; indicating much worse that could be attributed to medication.

The worsening of mood probably happened after tetrabenazine or low dose of haloperidol (conventional antipsychotic) which were stopped. Amantadine (dopamine agonist) was

added as per the treatment protocol for writer's cramp. The possibility of pharmacodynamic action with other antidepressants, e.g., amitriptyline, a tricyclic antidepressant and tianeptine, selective serotonin reuptake enhancer could not be ruled out. However, during the treatment mood further worsened as assessed on Hamilton rating scale for depression (HAM-D)<sup>11</sup> which showed a score change from 8 (mild) to 15 (moderate degree of severity).

According to DSM-5/ICD10, diagnosis was revised as 296.80 (F31.9) unspecified bipolar and related disorder. Though there were no previous episodes of depression or mania, period of observation was less, lack of family history of bipolarity, later age of onset of the first episode probably substance-induced mood disorder, e.g., worsening of psychomotor activity by antidepressant or extrapyramidal side-effects due to haloperidol. He was prescribed lamotrigine 25 mg once daily for 2 weeks and then increased to 50 mg for the next 2 weeks to a target level of 200 mg in 6 weeks. On HAM-D, his scores were 15 (baseline) and 7 (after 6 weeks); CGI - Severity (CGI-S) from 5 to 2 and CGI-I from 6 to 1, indicating very much improvement.

## DISCUSSION

Writer's cramp is related to focal dystonia or essential tremor and responds to propranolol, primidone, and anticholinergic medication.<sup>4</sup>

Byl et al., 1996 reported that sustained, rapid, and repetitive stereotypical movements expand the area of cortical representation of sensory information from the hand.<sup>12</sup> The degradation of sensory feedback to motor cortex was responsible for excessive and persistent motor activity, including dystonia. The volume of gray matter was decreased in sensorimotor cortex, thalamus, and cerebellum corresponding to affected hand as reported by Delmaire and coworkers.<sup>13</sup> However, none was reported in our case as his MRI scans, NCS etc., were within normal limits.

Dystonia can be interpreted as a disorder of abnormal synaptic plasticity in basal ganglia. The sensorimotor maps in the basal ganglia-thalamocortical circuits are less defined in focal dystonia. Evidence for disordered plasticity comes from the beneficial effects of treatment such as surgical lesioning and chronic electrical stimulation of the globus pallidus.<sup>14</sup> The indirect evidence of non-beneficial effects from dopamine agonist and anticholinergic drugs prompted that the disorder is not compatible with the aforementioned etiology. Botulinum toxin injection and Deep brain stimulation were not performed to ameliorate the symptoms as these facilities are not available in this institution.

Non-response to the already established treatment in writer's cramp and worsening of mood by antidepressants

warrants a review of the underlying bipolar disorder. They are delineated under the rubric of bipolar spectrum disorders.<sup>10</sup> DSM-5 has expanded the domain of bipolar disorders by encompassing various specifiers, e.g., mixed, anxious, peripartum, seasonal, catatonic, rapid cycling, mood congruent, or incongruent psychosis.<sup>8</sup> Although, antidepressant and substance abuse destabilizes the episodes of depression in bipolar disorder<sup>9,10</sup> and described as bipolar III and III<sup>1/2</sup> but has not yet found place in the current diagnostic criteria of DSM-5.<sup>8</sup>

In recent years, there occurred a paradigm shift in prevalence of mood disorders in terms of recognition and diagnosis from 2% bipolar I, 2% bipolar II, 10% bipolar not otherwise specific and 80% major depressive disorder to 2% bipolar I, 15% bipolar II, 33% bipolar not otherwise specific and 50% major depressive disorder.<sup>10</sup>

Should these be classified as substance-induced mood disorder? The onset of symptom, cessation after stoppage of the offending substance, re-challenge test to confirm the etiological cause and full recovery within 4 weeks, etc., highlight the need for not to over-diagnose bipolar disorder and on ethical issues, i.e., do no-harm. However, the severity of the symptoms, worsening of mood by antidepressant; risk/benefit ratio of suicidality and sub-threshold symptoms beyond the cut-off limit of 4 weeks; prompt an earlier treatment with mood stabilizer for first episode depression in absence of previous mood episodes and/or negative psychiatric family history or late age of onset these symptoms by delineating them as unspecified bipolar and related disorder.

Whether to consider this as co-morbid condition? But no response to writer's cramp with standard treatment protocol proves beyond doubt that this is not a case of writer's cramp with co-morbid mood disorder rather vice-versa is possible. The authors are of the considered view that loss of execution of fluid and cursive movements in writing can be a disorder of volition and a role of dorso-motor prefrontal cortex dm PFC, i.e., motoric acts and dorsolateral prefrontal cortex DLPFC, i.e., sustained attention and problem solving is due to dysregulation of dopamine D1 neurotransmitter that may attribute to the symptom of psychomotor retardation in bipolar spectrum disorders.

Further research is required to understand the mechanism of action of lamotrigine which blocks voltage-sensitive sodium channels and in turn decreases glutamate release<sup>15</sup> in modulation of mood disorder and its role as a pharmacological probe in delineating bipolar spectrum disorders. The other drugs recommended for treatment of bipolar depression are lurasidone, quetiapine, olanzapine and  $\pm$  fluoxetine, valproate, lithium and antidepressant, pramipexole and carbamazepine, etc., that open new vistas of pharmacogenomics in psychiatric care.<sup>16</sup>

## ACKNOWLEDGMENTS

We also thank Dr Harbag Singh, DM Neurologist, Associate Professor, Department of Neurology, Government Medical College and Rajindra Hospital, for his intellectual support.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

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**Cite this article as:** Raj R, Kumar R. Lamotrigine in treatment of Writer's cramp (Focal dystonia) in unspecified bipolar and related disorder. *Int J Basic Clin Pharmacol* 2015;4:1292-5.