Cartas aos editores

Treatment emergent affective switch with topiramate

Indução de mania associada ao tratamento com topiramato

Dear Editor,

Topiramate is a novel anticonvulsant that has been used for bipolar disorder. However, no clear evidence of efficacy was found in clinical trials. More recently, topiramate has been used for the management of weight gain associated with the use of mood stabilizer and atypical antipsychotics.

There are only two reported cases of treatment emergent affective switch (TEAS) to mania or hypomania associated with the use of topiramate.[1-2] These patients were using topiramate for treatment of epilepsy and had no previous diagnosis of bipolar disorder. In this letter we report the emergence of manic symptoms within a period of one month after the introduction of topiramate in the pharmacological treatment of two euthymic patients previously diagnosed with bipolar disorder.

The medical records of all outpatients treated in our Bipolar Disorder Research Program from 1997 to 2004 were retrospectively analyzed. Out of a total of 123 outpatients, 34 received topiramate combined with mood stabilizers and/or atypical antipsychotics. For the diagnosis of topiramate-associated TEAS it was required the fulfillment of DSM-IV criteria for a manic or hypomanic episode and a Young Mania Rating Scale (YMRS) total score equal to or greater than 12.

Four patients (11.7%) presented TEAS but only two (5.8%) during the first month of treatment with topiramate, which represents a more rigorous criterion for TEAS.[3]

Case 1: A 56-year-old female was in remission for two months, on lithium carbonate 900 mg/day, carbamazepine 600 mg/day and olanzapine 20 mg/day. One week after introducing topiramate for weight loss, the patient presented insomnia, irritability, increased rate of speech and motor agitation, fulfilling criteria for a hypomanic episode. Her YMRS score changed from 1 (before topiramate introduction) to 14 points. Topiramate was discontinued and olanzapine was increased up to 25 mg/day, with remission of the episode after two weeks.

Case 2: A 40-year-old male was in remission for 12 months, on lithium carbonate 2100 mg/day. Topiramate was introduced for treatment of obesity. The patient lost 7 kg in the course of one month of treatment, but presented insomnia, racing thoughts, irritability, aggressiveness, talkativeness and motor excitement, fulfilling criteria for a manic episode. His YMRS score increased from 2 (before topiramate introduction) to 29 points. Topiramate was discontinued, and olanzapine plus clonazepam were introduced. The patient and his family decided to seek treatment in a different service and he was lost to follow-up.

Topiramate has been used mainly as an add-on drug in acute and prophylactic treatment of bipolar disorder, especially for weight loss. To our knowledge this is the first report of bipolar patients taking topiramate who presented TEAS. We detected a 5.8% incidence of TEAS in our sample, using a strict diagnosis criterion. Since topiramate has been widely used for weight loss, we think it is very important to study its safety and tolerability, specially the incidence of TEAS. Data from placebo controlled double-blind topiramate studies should be analyzed. Prospective trials may help to shed light in this issue.

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Financing: None
Conflict of interests: None

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Association study between the 1287 A/G exonic polymorphism of the norepinephrine transporter (NET) gene and obsessive-compulsive disorder in a Brazilian sample

Estudo da associação entre o polimorfismo exônico 1287 A/G do gene transportador da norepinefrina e o transtorno obsessivo-compulsivo em uma amostra brasileira

Dear Editor,

Obsessive-compulsive disorder (OCD) is a chronic, severely debilitating anxiety disorder, characterized by intrusive and senseless thoughts and impulses (obsessions) and by repetitive behaviors or mental acts (compulsions), with a lifetime prevalence of 2 to 3%. Data from family, twin and segregation studies have shown that genetic factors contribute to the expression of the disorder.[1] An essential step to understanding the genetics of OCD is the localization and characterization of the genes that confer susceptibility to the disorder.

Since there are reports that some drugs used in the treatment of OCD, like clomipramine and venlafaxine, act on the noradrenergic system among other systems[2] and that young unmedicated OCD subjects excrete in the urine more adrenaline and homovanillic acid than healthy controls,[3] it is hypothesized that the noradrenergic system may be related to the pathophysiology of OCD. Therefore, the norepinephrine transporter (NET) gene became a candidate target for genetic studies of this disorder. To our knowledge, there is no previous investigation of the NET gene as a susceptibility gene for OCD.

NET is a 617-amino acid protein and its gene (SLC6A2) is located on chromosome 16q.12.2, consisting of 14 exons