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# Combination of Lamotrigine with Quetiapine in a Case with Treatment-Resistant Obsessive-Compulsive Disorder with Comorbid Depression

Abdullah N. A. Al-Qifari

Qassim University College of medicine, Buridah, Qassim, Saudi Arabia

***Abstract:*** **Obsessive-compulsive disorder (OCD) with comorbid depression is relatively common, often chronic and disabling disorder with high rates of partial and/or absent response to standard, recommended treatments. This is a report for a case of treatment-resistant OCD with comorbid depression that was successfully treated with a pharmacological combination of Quetiapine plus Lamotrigine. The patient, a 49-year-old woman, had partial response to antidepressant treatment. She was prescribed lamotrigine (up to 100 mg/day) in combination with Quetiapine ( up to 100mg/day). After three weeks of this treatment, her clinical condition remarkably improved. This case suggests some preliminary evidence that the addition of glutamatergic agent Lamotrigine in combination with Quetiapine may be useful in treatment-resistant OCD with comorbid depression. However, further studies are needed to support this finding.**

***Keywords:*** **OCD, depression, lamotrigine, quetiapine.**

## I. INTRODUCTION

Obsessive-compulsive disorder (OCD) is a common condition that affects individuals of all ages. This disorder has been listed as one of the 10 most disabling illnesses by the World Health Organization. [1] Approximately 2% to 3% of the world's population will suffer from OCD at some point in their lives. [2][3]

The serotonin reuptake inhibitors represent the first line pharmacotherapy intervention for OCD. [4] Meta-analysis have generally found that 40 – 60% of patients with OCD achieve response when treated with SRIs. [5] However, up to 40–60% of patients do not have a satisfactory outcome and these patients have significant disability and morbidity. [6] [7]

Augmentation strategies with antipsychotic medications, psychotherapies such as cognitive behavioral therapy (CBT) and others [8], as well as switching to newer classes of drugs such as the selective serotonin norepinephrine reuptake inhibitors (SNRIs) [9] have all been considered. Indeed, OCD management remains a debated issue essentially due to a still not fully understood etiopathology and to a number of eventually concomitant clinical features. [3]

One of the hypotheses that have been proposed in the pathophysiology of obsessive-compulsive disorder is glutamatergic dysfunction. This case report highlights the possible efficacy of Lamotrigine, a glutamatergic agent in combination with Quetiapine, atypical antipsychotic in Serotonin reuptake inhibitors-resistant patients with obsessive-compulsive disorder.

## II. CASE STUDY

This is a 49 years old lady presented to our OPD for refilling medication, as it was out of stock in the pharmacy of the private hospital that she is following with.

She had no medical illness and no family history of psychiatric disorder.

She had been diagnosed with OCD since 13 years and she had received several SSRIs with no satisfactory response. Her OCD symptoms include thoughts related to insulting god and fear that her prayer will not be accepted and god would punish her. Her symptoms increased in approximately 2 months prior to the presentation at our clinic. In addition, she had become depressed with decreased interest in socialization, having fatigue and death wishes but no suicidal ideas.

One month prior to her presentation, She was prescribed Quetaipine tapered to 50 mg bid and Lamotrigine tapered to 50 mg bid at the private hospital.

After 3 weeks, she reported that she had a remarkable improvement in comparison with the response to previous medications.

Detail of the history showed that there was nothing to suggest that she had bipolar illness, psychosis, or substance abuse. It was difficult to role out previous inadequate trials, however she mentioned that she used several antidepressants including SSRIs for more than 6 weeks. Laboratory tests, including complete blood count, complete serum chemistries, urinalysis, and thyroid function tests, were normal.

## III. DISCUSSION

Because refractory cases of OCD are common, having treatment strategies beyond the initial approach is necessary. Current recommendations involve switching between SSRIs once before initiating a trial of clomipramine. While a number of patients may fail mono-therapy, augmentation with an atypical antipsychotic agent may boost response. [10] [11]

However, some patients fail to respond or have only a partial response to antipsychotic augmentation. Therefore, clinicians lead to search for other potential augmentation strategies to improve outcomes. [12] In this case, Lamotrigine in combination with Quetiapine was used in the treatment of resistant OCD with comorbid depression. The psychotropic properties of Lamotrigine may probably come from its stabilisation of neural membranes and inhibition of the release of excitatory neuro- transmitters, such as glutamate and aspartate. [13] [14] [12] A small placebo-controlled study found that lamotrigine (Lamictal®) augmentation of serotonin reuptake inhibitors reduced OCD symptoms. [15]

Substantial recent interest has focused on the role of glutamate imbalance in OCD. [16] Polymorphisms in the gene for the major neuronal glutamate transporter have been associated with OCD, although the nature of any causative polymorphism remains unclear. [17] Several magnetic resonance spectroscopy studies have indicated abnormalities in glutamate and related molecules, although again the specific nature of the hypothesized disruption remains unclear. [18] Finally, a pair of studies examining cerebrospinal fluid in unmedicated adults with OCD has found elevated glutamate levels. [19] These findings have spurred interest in the use of glutamate modulators for pharmacological augmentation in SRI-refractory disease. [20]

Agents targeting the N-methyl-d-aspartate (NMDA) class of glutamate receptor have received particular attention. For example, a series of small-uncontrolled studies of Memantine have suggested benefit in both adults and children with OCD. [21] And a pair of open-label studies in profoundly refractory patients suggests benefit from the glutamate modulator riluzole. [22] [20]

Lamotrigine like riluzole, it reduces glutamate outflow through inhibition of certain presynaptic voltage-gated sodium channels. (It is not thought to potentiate glutamate reuptake, as riluzole does.) Early work showed no improvement from Lamotrigine treatment in OCD,[23] but a recent controlled trial suggested clear benefit.[24] More work is needed. [25]

As our patient developed comorbid depression, it is worth mentioning that the studies, which have examined the effectiveness of Lamotrigine in unipolar depression in adult cohorts, have produced inconsistent results. [26]

However In unipolar and bipolar depression, studies consistently found quetiapine to be effective versus placebo, at doses of approximately 150–300 and 300–600 mg per day, respectively.[27] a 6-week trial that compared monotherapy of MDD with three doses of quetiapine XR (50 or 150, or 300 mg/day) showed that all doses significantly decreased MADRS total scores at endpoint, relative to placebo. [28]

Contradictory results have been obtained from open label [29] and single-blind [30] studies of quetiapine augmentation in OCD patients. Three double-blind, placebo-controlled studies also yielded inconsistent results. [31]

## IV. CONCLUSION

The response of the patient to Lamotrigine combined with Quetiapine is consistent with a hypothesised role for glutamatergic dysfunction as contributing factor to resistant OCD symptoms. In addition, it give further evidence of effectiveness of qutiapine in unipolar depression. The case suggested that Lamotrigine may be effective when combined with Quetiapine in treating resistant OCD with comorbid depression, although further research required.

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