

# Original Article

## Seasonal Affective Disorder (SAD): Role of Lamotrigine Augmentation to Anti-Depressant Medication in Winter Depression

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### ABSTRACT

**Background:** Many therapeutic options have been evaluated and tried for seasonal affective disorder (SAD) including bright light therapy (BLT), anti-depressants, beta-blockers and psychotherapy, but the data supporting use of mood-stabilizing agents is just handful in spite of this condition being understood most frequently to be associated with bipolar affective disorder II (BPAD II). So we planned to study role of Lamotrigine (Mood stabilizing agent) in SAD. **Materials and Methods:** 30 patients of SAD who were prescribed lamotrigine in addition to antidepressant medications for a minimum of 8 weeks and were assessed for severity using HAM-D were selected retrospectively from the hospital records for this study. HAM-D scores at 2, 4 and 8 weeks were compared to baseline scores. **Statistics Analysis:** Single tailed t-test was used to study the difference of means to assess the therapeutic response and pre/post analysis of change. Statistical significance was set at  $P < 0.05$ . **Results:** Though no significant difference was seen in HAM-D Scores at 2 weeks of treatment compared to baseline, but results were statistically significant at 4 and 8 weeks of treatment with lamotrigine augmentation of antidepressant medications. **Conclusion:** We conclude that lamotrigine augmentation was found to be effective treatment strategy for managing winter depression phase of Seasonal Affective Disorder.

**Key words:** Anti-depressant, Lamotrigine, mood-stabilizer, seasonal affective disorder

### INTRODUCTION


Seasonal affective disorder (SAD) was first time described as syndrome of recurrent episodes of depression that occur annually (usually in winter season at same time each year) by Rosenthal *et al.* in 1984.<sup>[1]</sup>

Diagnostic and Statistical Manual of Mental Disorders,

4<sup>th</sup> Edition, Text Revision (DSM-IV-TR) describes SAD not as a separate mood disorder but as ‘Specifier’ referring to the seasonal pattern of major depressive episodes that can occur within major depression or bipolar disorders. The specifier within seasonal pattern can be applied to pattern of major depressive episodes in bipolar affective disorders I, bipolar affective disorders II and major depressive disorder (recurrent).<sup>[2]</sup> It still remains a ‘Specifier’ in DSM-5.<sup>[3]</sup>

The International Classification of Diseases, 10th Revision (ICD-10) gives only provisional diagnostic criteria for SAD on the grounds that its status is best regarded as uncertain, and its diagnostic criteria available in research domain of ICD-10 manual are three or more episodes of mood (affective) disorder must occur with onset within same 90-day period of

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year, for three or more consecutive years. Remission also occurs within a particular 90-day period of the year and seasonal episodes substantially outnumber any non-seasonal episodes that may occur'.<sup>[4]</sup>

Although original description of SAD included most people with diagnosis of bipolar affective disorder (BPAD; most common BPAD II) rather than recurrent major depressive disorder, who used to switch into hypomania (or mania) in summer season.<sup>[1,5,6]</sup> However, subsequent research into treatment strategies for SAD almost exclusively focused on it as a subtype of recurrent depressive disorder as most of clinical trials involving SAD focused on either bright light therapy (BLT),<sup>[1,7-9]</sup> anti-depressant drug treatments,<sup>[10-14]</sup> beta-blockers,<sup>[15,16]</sup> vitamins<sup>[17-19]</sup> and psychotherapy.<sup>[20-23]</sup>

There is negligible data on role of mood stabilizers in management of SAD (winter depression). Here, we describe response of 30 patients of recurrent major depressive disorder (seasonal pattern — winter) (winter SAD) to Lamotrigine, who failed to respond to different anti-depressant treatment previously.

## MATERIALS AND METHODS

Patients of SAD (winter depression) fulfilling DSM-IV-TR criteria for major depressive disorder, recurrent, with seasonal pattern (winter season), who failed to respond or responded partially to different anti-depressants were assessed from hospital records. The case records and assessment was done by different members of the resident staff, but most of them were recorded by two of the authors. They had already been assessed for mania/hypomania symptoms in current episode or in past (particularly mania/hypomania in summer season) using routine clinical interview and Mini-International Neuropsychiatric Interview (MINI). Those having history of mania or hypomania and other Axis I disorders were not taken up for this study. Treatment records of such patients from last three years were assessed.

Selection criteria for this study:

1. Patients having the onset of depression in autumn/winter lasting for whole of winter season and early spring.
2. Patients in whom progress was routinely monitored using Hamilton depression rating scale (HAM-D).
3. Patients whose treatment was augmented with Lamotrigine in addition to their routine anti-depressant medications.
4. Patients having minimum of three consecutive seasonal mood episodes.
5. Patient having a stable dose of other medications for minimum of 8 weeks and these doses were not

changed during Lamotrigine augmentation.

These patients had been treated with Lamotrigine augmentation for their partially responding or non-responding depressive episode. They were assessed routinely at baseline, at 2 weeks, at 4 weeks and at 8 weeks of Lamotrigine augmentation. More than 50% decrease in HAM-D score from baseline was taken as response and a final score of less than 8 was taken as remission.<sup>[24]</sup>

Lamotrigine was started at dose of 25 mg per day and gradually increased to 200 mg by 8 weeks with weekly increment of 25 mg. Lamotrigine was stopped in some patients owing to development of rash. In total, 30 patients who had completed follow-up for minimum of 8 weeks were assessed for this study. This study included in-patients as well as out-door patients.

The data was tabulated and the individual results of the cases were studied statistically. Mean/average and the deviations were calculated using Statistical Package for Social Sciences version 16 (SPSS-16). Single tailed t-test was used to study the difference of means to assess the therapeutic response and pre/post analysis of change. Statistical significance was set at  $P < 0.05$ .

## RESULTS

Thirty patients met the selection criteria, having a complete follow-up with fully maintained case sheets. The sample included 9 males and 21 females with a mean age of  $37.14 \pm 11.31$  years (22 to 56 years). Before the initiation of Lamotrigine, the mean HAM-D score was  $20.93 \pm 4.93$ , suggesting an ill state of most of these patients. Other variables, treatment history and treatment response are noted in Table 1.

The mean HAM-D scores with standard deviation at start of treatment at 2 weeks, at 4 weeks and, at 8 weeks are  $20.93 \pm 4.93$  (range = 14-35),  $19.63 \pm 5.82$  (range = 9-36),  $11.27 \pm 5.32$  (range = 3-23) and  $9.57 \pm 6.16$  (range = 2-23), respectively.

The difference in HAM-D scores at 2 weeks of treatment was not significant compared to scores at baseline ( $t = 0.93$ ,  $df = 58$ ,  $P = 0.177$ ). However, there was significant difference in treatment outcome as per HAM-D scores at 4 weeks of treatment compared to baseline scores ( $t = 7.29$ ,  $df = 58$ ,  $P < 0.01$ ) and this significant difference was maintained at 8 weeks of treatment ( $t = 7.88$ ,  $df = 58$ ,  $P < 0.01$ ) compared to start of treatment (zero weeks).

An average decrease of 46.25% in HAM-D score was achieved around 4<sup>th</sup> week and it was sustained to a

**Table 1: Sociodemographic and clinical variables**

| Score at zero weeks (HAM-D) | Score 2 weeks (HAM-D) | Score 4 weeks (HAM-D) | Score 8 weeks (HAM-D) | Gender | Age (Years) | Other medications along with Lamotrigine (currently) |
|-----------------------------|-----------------------|-----------------------|-----------------------|--------|-------------|--|
| 15                          | 16                    | 7                     | 3                     | F      | 22          | SSRI   |
| 15                          | 12                    | 9                     | 5                     | F      | 30          | Mirtazapine  |
| 18                          | 22                    | 15                    | 7                     | F      | 43          | BZD + Bupropion                                      |
| 16                          | 16                    | 13                    | 12                    | M      | 26          | Bupropion  |
| 18                          | 15                    | 11                    | 6                     | F      | 37          | TCA  |
| 14                          | 12                    | 9                     | 4                     | M      | 56          | None   |
| 17                          | 15                    | 14                    | 10                    | F      | 39          | BZD + Bupropion                                      |
| 17                          | 16                    | 13                    | 11                    | F      | 35          | SSRI + BZD   |
| 18                          | 9                     | 3                     | 4                     | F      | 29          | Bupropion  |
| 19                          | 19                    | 13                    | 12                    | F      | 44          | Mirtazapine  |
| 21                          | 19                    | 17                    | 18                    | M      | 39          | Bupropion  |
| 21                          | 16                    | 23                    | 22                    | M      | 41          | SSRI   |
| 22                          | 24                    | 10                    | 8                     | F      | 29          | Bupropion  |
| 20                          | 21                    | 7                     | 6                     | F      | 29          | SSRI   |
| 19                          | 18                    | 6                     | 4                     | F      | 33          | Mirtazapine  |
| 20                          | 17                    | 4                     | 2                     | F      | 38          | SNRI   |
| 22                          | 23                    | 14                    | 15                    | M      | 51          | TCA  |
| 21                          | 17                    | 12                    | 9                     | F      | 49          | BZD + Bupropion                                      |
| 21                          | 19                    | 5                     | 6                     | F      | 35          | Bupropion  |
| 22                          | 20                    | 15                    | 16                    | M      | 28          | SSRI + BZD   |
| 22                          | 23                    | 6                     | 8                     | F      | 42          | SNRI   |
| 20                          | 15                    | 9                     | 6                     | F      | 48          | Bupropion + BZD                                      |
| 21                          | 25                    | 18                    | 21                    | F      | 29          | BZD + SSRI   |
| 20                          | 17                    | 7                     | 7                     | F      | 25          | Mirtazapine  |
| 19                          | 19                    | 4                     | 2                     | M      | 56          | BZD + SSRI   |
| 25                          | 26                    | 20                    | 19                    | F      | 44          | SSRI   |
| 27                          | 29                    | 22                    | 23                    | M      | 26          | BZD  |
| 29                          | 22                    | 7                     | 6                     | M      | 46          | Mirtazapine  |
| 35                          | 36                    | 13                    | 10                    | F      | 27          | SNRI   |
| 34                          | 31                    | 12                    | 5                     | F      | 38          | SSRI   |

F – Female; M – Male; SSRI – Selective serotonin reuptake inhibitors; BZD – Benzodiazepines; TCA – Tricyclic anti-depressants; HAM-D – Hamilton depression rating scale; SAD – Seasonal affective disorder; BPAD – Bipolar affective disorder; BLT – Bright light therapy; HAM-D – Hamilton depression rating scale; SSRI – Selective serotonin reuptake inhibitors; SNRI – Serotonin norepinephrine reuptake inhibitors; TCA – Tricyclic anti-depressants; BZD – Benzodiazepines

further decrease in score by 54.27% by 8<sup>th</sup> week. The mean time for responders to achieve an approximate 50% reduction on HAM-D score was  $4.2 \pm 1.2$  weeks at a mean dose of 150 mg/day of Lamotrigine. The mean dose of Lamotrigine at 8 weeks was 200 mg/day with a 54.27% decline in HAM-D score and 15 (out 30) showed remission (less than 8 score). The difference in treatment response in different age-groups, gender groups and in groups of patients with different primary anti-depressant medication was not assessed because of small study group.

A few adverse effects were documented which included sedation (seven patients), headache eight patients), fatigue (one patient) and benign skin rash (one patient). These effects were generally mild and transient and did not force discontinuation.

## DISCUSSION

Although first descriptions of SAD presented it as more

prevalent condition associated with BPAD, however subsequent research into its therapeutics failed to focus it as such. Till now, most of the therapeutic research has failed to highlight it as BPAD and there only few studies focusing on use of mood stabilizers in this condition.<sup>[25]</sup> This retrospective, non-blinded, open-label, non-comparative study in natural settings is an attempt to highlight role of mood stabilizers in SAD. This study proved significant improvement in depressive symptoms of SAD patients (winter depression) with Lamotrigine augmentation. These were the patients who had previously shown poor response to anti-depressant (medication) alone treatment.

The role of early morning BLT in winter depression may be actually an intervention based on ‘Social Rhythm Therapy’ which has been proven as effective strategy to deal with bipolar disorder patients because early morning BLT in winter depression invariably promotes concept of chronotherapeutics in management of SAD.<sup>[26-29]</sup>

Lamotrigine approved for the maintenance treatment of BPAD I has also shown some efficacy for the treatment of bipolar depression. Different studies support the view that Lamotrigine mainly affects depressive phase of BPAD.<sup>[30-32]</sup>

Limited data is available suggesting efficacy of Lamotrigine in major depressive disorder (MDD) (unipolar depression) and these studies do not support Lamotrigine use in unipolar depression robustly.<sup>[33,34]</sup>

In view of above findings and results of our study, the nosology and therapeutics of winter depression (and other forms of depression not responding adequately to anti-depressant treatment) needs to be reviewed as SAD being a type of 'bipolar spectrum disorder' even in absence of hypomania or mania symptoms. Further, mood-stabilizing agents may have increased role in management of SAD. Future research should be directed on these lines.

The limitations of this study include the small sample size, lack of controls and randomization. In future, this study needs to be replicated with better scientific design and these limitations need to be addressed.

## CONCLUSION

Lamotrigine appeared to be useful in treatment of SAD with winter depression. This study brings to light the fact that SAD needs to be looked as type of bipolar disorder for therapeutic purposes.

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