

Safety and Efficacy of Lamotrigine for Pediatric and Adolescent Bipolar Disorder Patients

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ABSTRACT

Objective

To assess the effectiveness and safety of lamotrigine in the treatment of pediatric patients with bipolar disorder.

Methods

Chart reviews of 92 children and adolescents aged 7-17 years with DSM-IV bipolar disorder and treated with lamotrigine were conducted (mean age 15.2±2.0 years; 66.3% female; 26.1% bipolar I, 42.4% bipolar II, 31.5% bipolar not otherwise specified). Charts of subjects who received lamotrigine in a private practice setting (LDG, Red Oak Psychiatry Associates, Houston, TX) between October 1998 and May 2004 were reviewed. Treatment response was assessed with the Clinical Global Impressions-Improvement (CGI-I) scale (1 = marked improvement, 2 = moderate improvement). Relapse was defined as a mood change that occurs 4 weeks after initiation of treatment medication or the return of symptoms from the original episode.

Results

Fifty-five subjects (59.8%) taking lamotrigine had marked to moderate improvement (CGI-I scores: 1, 16.3%; 2, 43.5%). Thirty-two patients (34.8%) relapsed during lamotrigine treatment (mean time to relapse = 143 days). The mean final lamotrigine dose was 100.54±78.79 mg/d. Rash (14.1%) and headache (5.4%) were the most frequently reported side effects.

Conclusion

Lamotrigine appears effective in the treatment of pediatric patients with bipolar disorder and was well tolerated.

INTRODUCTION

- Up to 65% of adults with bipolar disorder experience an initial mood episode before 18 years of age,¹ and about 30% of adults with bipolar disorder report that the onset of mood symptoms occurred before age 15.²
- In adults with bipolar I disorder, lamotrigine has been shown to improve manic³ and depressive⁴ symptoms and prolong the time to relapse to a depressive episode.⁵⁻⁷
- Lamotrigine also reduces the risk of relapse over 6 months of monotherapy⁸ and improves depressive symptoms⁹ in adults with bipolar II disorder.
- Thus far, no prospective studies have evaluated the safety and effectiveness of lamotrigine in children and adolescents with bipolar disorder.
- The objective of this study was to assess the effectiveness and safety of lamotrigine in the treatment of pediatric and adolescent patients with bipolar disorder.

METHODS

- A retrospective chart review was conducted on 92 children and adolescents, 17 years of age or younger, with a DSM-IV diagnosis of bipolar disorder who received lamotrigine in a private practice setting (LDG, Red Oak Psychiatry Associates, Houston, TX) between October 1998 and May 2004.
- Charts were reviewed for relapse, adverse events, scores on the Clinical Global Impression-Severity (CGI-S) and Clinical Global Impression-Improvement (CGI-I) scales, and lamotrigine dosages.
- Treatment response was assessed with the CGI-I scale (1 = marked improvement, 2 = moderate improvement). Subjects were considered to have responded to therapy if they achieved a CGI-I score of ≤3. Subjects were considered to have relapsed if they experienced a mood change 4 weeks after initiation of medication or a return of symptoms from the original episode.

RESULTS

- Of the 92 subjects reviewed in this study, 66.3% were female, and ages ranged from 7-17 years, with a mean age of 15.2 years. The final mean lamotrigine dose ± SD was 100.5±78.8 mg/day (Table 1).
- 24 subjects (26.1%) were diagnosed with bipolar I disorder, 39 (42.4%) with bipolar II disorder, and 29 (31.5%) with bipolar disorder not otherwise specified (Figure 1).
- At the initiation of lamotrigine, 18.5% of subjects had a CGI-S score of 3, 47.8% a score of 4, 26.1% a score of 5, and 3.3% a score of 6. Of the 92 subjects in the study, 59.8% taking lamotrigine experienced marked-to-moderate improvement, with a CGI-I score of 1 observed in 16.3% of subjects and a CGI-I score of 2 in 43.5%.
- 77 subjects (83.7%) responded to lamotrigine. 61.0% of responders did not relapse, and 39.0% relapsed. The mean time to relapse was 142.6±153.3 days (Figure 2).
- Within each bipolar disorder type, patients' CGI-S scores were ≥3 at treatment initiation (Figure 3). The majority of subjects with each bipolar subtype had CGI-I scores of 1 or 2 at titration completion (Figure 4).
- The most frequently reported side effects were non-serious rash (14.1%) and headache (5.4%) (Table 2).

Table 1. Study Population

Patients	92
Gender (% female)	66.3
Mean age (y ± SD)	15.2±2.1
Age range (y)	7-17
Mean lamotrigine dose* (mg/d)	100.5±78.8

*Mean dose and blood levels are at patient's best CGI-I score.

Table 2. Treatment-Emergent Adverse Events on Lamotrigine

Event	Percentage	Event	Percentage
Non-serious rash	14.1%	Dry mouth	<1%
Headache	5.4%	Rhinitis	<1%
Somnolence	1.1%	Pharyngitis	<1%
Nausea	1.1%	Exacerbation of cough	<1%
Insomnia	1.1%	Constipation	<1%
Back pain	<1%	Abdominal pain	<1%
Vomiting	<1%	Fatigue	<1%
Diarrhea	<1%		

Fig 1. Distribution of Bipolar Subtypes

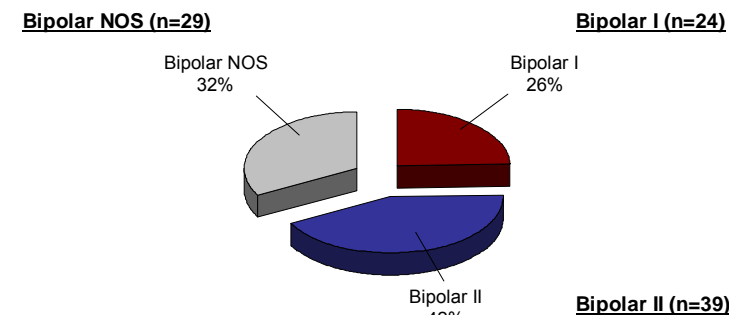
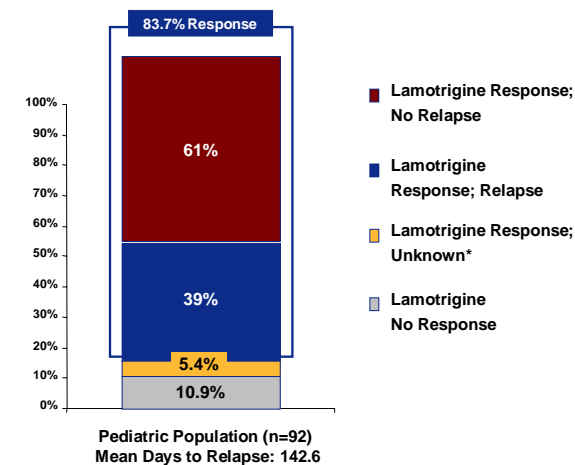


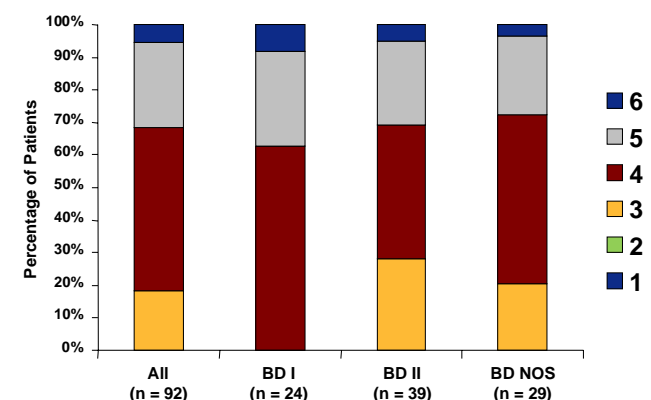
Fig 2. Relapse Rate of Pediatric Patients Treated With Lamotrigine



Lamotrigine response is defined as achieving a CGI-I ≤ 3. Relapse is defined by a change in CGI-I to ≥4 after an observed lamotrigine response, or return of episode.

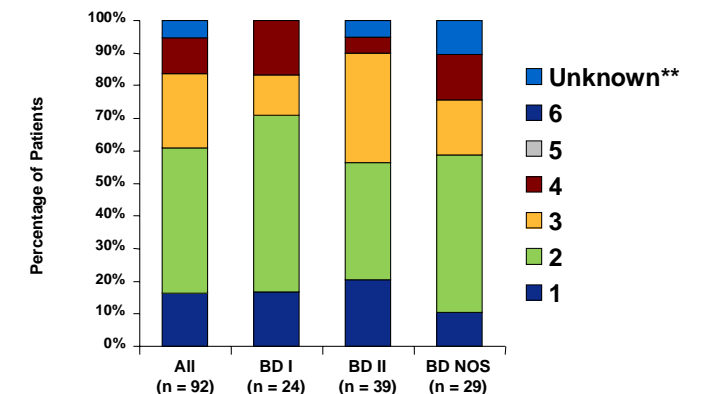
*Includes lost to follow-up, moved out of location; switched physicians, couldn't afford treatment, etc.

Fig 3. Across BD Subtypes, CGI-S Scores Were Mainly 4-6



BD = bipolar disorder; CGI-S = Clinical Global Impression of Severity; NOS = not otherwise specified.

Fig 4. After Lamotrigine Treatment, CGI-I Scores Were Mainly 1 and 2



BD = bipolar disorder; CGI-I = Clinical Global Impression of Improvement; NOS = not otherwise specified.

**Includes lost to follow-up or patient discontinued drug before assessment.

CONCLUSIONS

- These data suggest that lamotrigine produces marked-to-moderate improvement in pediatric and adolescent patients with bipolar disorder.
- Based on these data, placebo-controlled studies are warranted.
- Lamotrigine appears effective across the bipolar spectrum for children and adolescents.
- Lamotrigine was well tolerated, with a low incidence of side effects and no evidence of serious rash.

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