

Critical Appraisal of the Use of Lamotrigine in Bipolar Disorder

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Introduction

Made topical with the recent NICE guideline changes following MHRA safety advice ⁽¹⁾, recommending caution in the use of valproate in the treatment of bipolar disorder for male and females under the age of 55 due to reproductive risks, the need for the exploration of alternative treatments for mania / long term maintenance in bipolar disorder, particularly in women of child-bearing age is relevant now more than ever before.

The aims of this systematic review were to: (1) assess the evidence for efficacy of lamotrigine, on its own or as an adjunct with lithium, in the treatment of adults with bipolar disorder, (a) in acute mania / hypomania episodes and (b) for long term maintenance treatment; (2) compare this with the evidence available for depakote to see if it is a suitable alternative for women of child-bearing age and (3) make recommendations for future research into the treatment of bipolar disorder

Methodology

SCOPUS and Medline were searched for randomised-controlled trials that using the keywords: "BIPOLAR DISORDER", "MANIA", "HYPOMANIA", "MANIC DEPRESSION", "DEPAKOTE", "VALPROIC ACID", "SODIUM VALPROATE", "LAMOTRIGINE", "LAMICTAL", "CONTROLLED CLINICAL TRIAL", "RANDOMISED CONTROLLED TRIAL" and "RCT". This search was limited to 2019 to present in SCOPUS due to a high number of results.

Eligible English records were then reviewed.

Final concept table used for refined search criteria

Concept 1 AND	Concept 2 AND	Concept 3 AND	Concept 4
BIPOLAR DISORDER (Article title) OR	DEPAKOTE OR	LAMOTRIGINE OR	CONTROLLED CLINICAL TRIAL OR
MANIA OR	VALPROIC ACID OR	LAMICTAL	RANDOMISED CONTROLLED TRIAL OR
HYPOMANIA OR	SODIUM VALPROATE		RCT
MANIC DEPRESSION			

Results & Conclusion

Three studies ⁽²⁻⁴⁾ were identified: (i) A randomised, double - blind control trial looking at the efficacy of lamotrigine as a monotherapy against placebo in the long term maintenance treatment of bipolar type I disorder, showed no statistically significant result in effectiveness (i.e. by decreasing time to relapse / symptom recurrence) or symptom severity (as subjectively reported by patient rating scales); (ii) A randomised open label study looking at the effectiveness of lamotrigine as a lithium adjunct vs lithium monotherapy in managing acute depressive episodes, showed a statistically significant decrease in suicide scores and (iii) A randomised open label showed that while lamotrigine as an adjunct does decrease the depression rated score of patients, lithium as monotherapy is more effective in doing so.

Lamotrigine is generally accepted to form part of the mainstay treatment for bipolar disorder. However, more robust evidence is needed to assess its effectiveness and efficacy. This review suggests there might be a role for it in the maintenance treatment of bipolar disorder as an adjunct; it also acknowledges its limitations, the need a more robust review, further studies particularly placebo-controlled and comparative studies to other interventions beside lithium.

Identification

Records identified from*: SCOPUS (n = 85) MEDLINE (n = 11)	Records removed before screening Duplicated records (n=0)
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Screening

Records screened (n=96); Reports sought for retrieval (n=5); Reports assessed for eligibility (n=5)	Records not relevant (n=91); Records not retrieved (n=0); Record does not fulfil criteria / would not allow aims to be met (n=2)
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Inclusion

Studies included in review (n=3)

Flowchart 1: Above - PRISMA Flow of information through stages of systematic review ⁽⁵⁾

Inclusion and Exclusion criteria

Inclusion:

- Any RCTs with adults with bipolar disorder
- Treatment with lamotrigine and / or depakote
- Comparison of lamotrigine to depakote

Exclusion:

- Unrelated e.g. about epilepsy, unipolar depression or other medical issues as main focus
- Duplicated
- Unavailable full text or abstract only papers
- Case report
- Case series
- Paediatric population
- Not in English despite filter
- Systematic reviews