NICE National Institute for Health and Care Excellence

Surveillance report 2017 – Bipolar disorder: assessment and management (2014) NICE guideline CG185

Surveillance report
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Contents

Surveillance decision

We will not update the guideline on bipolar disorder at this time.

During surveillance editorial or factual corrections were identified. Details are included in appendix A: summary of evidence from surveillance.

Reason for the decision

Assessing the evidence

We found 32 studies through surveillance of this guideline.

This included evidence on case identification and assessment, pharmacological treatments of mania in adults, and pharmacological treatments of bipolar depression in children and young people that supports current recommendations.

We also identified evidence that was not consistent with current recommendations on pharmacological treatments of bipolar depression in adults, long-term management in adults, psychological interventions for bipolar disorder, and pharmacological treatments for mania in children and young people. This evidence was considered to be insufficient in volume and the results insufficiently conclusive to change recommendations in these areas at this time.

We did not find any evidence related to improving the experience of carers or management of physical health in adults.

Additionally, we identified relevant ongoing studies or research due to be published in the next 3 to 5 years. There are 5 ongoing trials investigating the effects of psychological interventions for bipolar disorder. A further study is investigating the effects of pharmacological interventions for bipolar disorder in children and young people. The progress of the ongoing studies will be monitored and any published results will be considered at the next surveillance review.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

After considering all the evidence and views of topic experts and stakeholders, we decided that an update is not necessary for this guideline.

See how we made the decision for further information.

Commentary on selected evidence

With advice from topic experts we selected 1 study for further commentary.

Managing bipolar disorder in children and young people – Pharmacological interventions

We selected the randomised controlled trial of lithium in paediatric bipolar disorder by Findling et al. (2015) for a full commentary. This study was selected as pharmacological studies in young people are not as common as those in adults. A full commentary may be beneficial as recommendations for children and young people are generally based on evidence and trials from an adult population.

What the guideline recommends

NICE guideline CG185 recommends (see recommendations 1.11.9 and 1.11.15) the use of aripiprazole for the management of moderate to severe manic episodes. For the management of moderate to severe bipolar depression, it advises considering a pharmacological intervention in addition to a psychological intervention.

It is also advises that prescribers follow the recommendations for pharmacological interventions for adults and refer to the BNF for children when making treatment decisions. Routine antipsychotic treatment in children and young people should not continue for longer than 12 weeks.

Methods

The Findling et al. (2015) randomised controlled trial investigated the effects of lithium in the acute treatment of bipolar I disorder in a paediatric population. Participants were recruited from academic medical centres in the US.

Eligible participants were aged 7 to 17, met Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) criteria for current manic or mixed episode, and scored 20 or more on the Young Mania Rating Scale (YMRS). Participants were also required to be drug-free at baseline and during the study. Before participation, psychotropic medications were

removed during a washout period. However, to aid recruitment, following 4 weeks of double-blind therapy the treating physician could use their discretion to prescribe psychostimulants to participants with comorbid attention deficit hyperactivity disorder.

Children were excluded from the study if they were clinically stable on a medication regimen for bipolar I disorder or if they were diagnosed with any of the following:

- Schizophrenia or schizoaffective disorder.
- A pervasive developmental disorder.
- Anorexia nervosa.
- Bulimia nervosa.
- Obsessive compulsive disorder.
- Substance dependence.
- Symptoms of mania attributable to a general medical condition or secondary to use of medications.
- Any general medical condition or abnormal laboratory assessments that could affect the use of lithium.
- Serious homicidal/suicidal ideation or hallucinations/delusions causing concerns for safety.
- Any concomitant medications that would interact with lithium or affect the participant's physical or mental status.

Participants were randomised in an unblinded data coordinating centre, which provided the assignments to unblinded site staff through an electronic format. Randomisation to the treatment groups was allocated in a 2 (lithium) to 1 (placebo) ratio and stratified according to study site, age and sex. The lithium group received either 600 mg daily if weighing less than 30 kg or 900 mg daily if more than 30 kg.

The primary outcome of the trial investigated the effects of lithium using changes in scores from baseline to the end of study (week 8) on the YMRS. Secondary outcomes were measured with the Children's Depression Rating Scale-Revised (CDRS-R), Clinical Global Impression-Severity (CGI-S), and Clinical Global Impression-Improvement (CGI-I) scales.

Results

A total of 81 participants were randomised with 53 in the lithium group and 28 in the placebo group. Analyses were based on last observation carried forward values.

A significant difference in YMRS score mean change from baseline to week 8 was found in favour of lithium compared to placebo (p=0.03). The results do not present any further statistical data for this comparison.

The treatment effect size is presented following adjustments for baseline factors (5.51, 95% Confidence Interval [95% CI] 0.51 to 10.50).

For secondary outcomes, only overall CGI-I scores were significantly different between groups and favoured lithium (p=0.03).

No significant differences were found for the secondary outcomes between groups for CDRS-R, CGAS or CGI-S scores. No significant differences between groups was found for response or remission rates.

Strengths and limitations

Strengths

The study population is relevant to the guideline with the inclusion of children with bipolar mania or mixed episodes. The primary and secondary outcomes are also relevant and included within the scope of the guideline.

Limitations

The study methodology is generally unclear with no details of how randomised lists were generated or allocated to participants. Blinding of participants and study personnel is not fully reported. It is also unclear whether outcome assessors were blinded to treatment allocation. These methodological limitations increase the risk of bias in the results.

Full statistical data is not presented in the results making it unclear how the effect sizes were calculated. The data on the primary outcome measure does not include mean change scores or confidence intervals. This data would be beneficial in determining the robustness of the effect sizes.

Impact on guideline

The results suggest a benefit of lithium in reducing mania symptoms for this population. Current guideline recommendations advise using aripiprazole for mania in young people. According to the recommendations for adults, lithium can be used in conjunction with an antipsychotic as a third-line treatment if alternatives are poorly tolerated.

The outcome of this study is unlikely to impact NICE guideline CG185 recommendations due to the methodological limitations. There remains sufficient uncertainty in the effectiveness of lithium in this population to warrant a challenge to the current recommendations.

How we made the decision

We check our guidelines regularly to ensure they remain up to date. We based the decision on surveillance 4 years after the publication of NICE's guideline on bipolar disorder (NICE guideline CG185) in 2014.

For details of the process and update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Evidence

We found 32 studies in a search for randomised controlled trials and systematic reviews published between 1 January 2014 and 5 April 2017.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See appendix A: summary of evidence from surveillance for details of all evidence considered, and references.

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline and other correspondence we have received since the publication of the guideline.

Views of stakeholders

Stakeholders commented on the decision not to update the guideline. Overall, 6 stakeholders commented. See appendix B for stakeholders' comments and our responses.

Of the stakeholders who commented on the proposal not to update the guideline:
3 agreed and 3 disagreed with the decision. One stakeholder who agreed with the decision commented that it is worth deferring the update until results of ongoing studies are known. Stakeholders who disagreed suggested that the evidence on psychological

therapies requires a review. The suggestions include consideration of cognitive analytic therapy to be included in the recommendations and reconsideration of the recommendations to offer cognitive behavioural therapy (CBT) and couples therapy as treatment options. However, another stakeholder commented that the use of bipolar specialist psychological therapies is not realistic and is costly. They suggest that generic CBT is appropriate and reasonable for this population. Evidence on psychological therapies was reviewed during the surveillance review and determined that inconsistencies in results were too great to impact current recommendations.

Two stakeholders commented on the use of pharmacological interventions for bipolar disorder. It was stated that aripiprazole is now generic and could be cost effective as a treatment option for mania. At the surveillance review, the evidence identified for aripiprazole provided inconclusive results for its effectiveness in an adult population with bipolar disorder. Aripiprazole is recommended for children and young people to treat mania and is included in NICE's technology appraisal guidance on aripiprazole for moderate to severe manic episodes in adolescents. However, without further robust evidence in adults, it is unlikely to impact recommendations at this time.

One stakeholder commented that lamotrigine is not mentioned in the recommendations though it has a license for the long-term treatment of bipolar disorder. Although lamotrigine is now licensed for use in long-term treatment, no evidence was found at all during the surveillance review for its use in a bipolar disorder population. Until evidence on its effectiveness is available, it is unlikely to impact recommendations at this time.

It was also stated that the recommendations on the use of lithium be reviewed. The suggestion is that if lithium is ineffective then it should be withdrawn. Also, if it has been partially effective then it should be used in combination with another maintenance agent as there is no randomised controlled trial evidence to support the addition of valproate. During the development of the guideline, the guideline committee considered lithium as the preferred choice of drug as it has a better profile than valproate in the long-term management of bipolar disorder. At the time, it was determined that individual medications can be used with clinical judgement and in some clinical circumstances other medications might be preferable to lithium. The guideline committee acknowledged the poor evidence base and suggested that prescribers use their expert judgement when considering treatment options.

A further stakeholder comment suggests the use of routine HIV testing due to the presence of mania and psychosis as features of HIV cognitive impairment. This area is not

covered in NICE guideline CG185 and no evidence to support this view was identified during the surveillance review.

See ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual for more details on our consultation processes.

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