UMEÅ UNIVERSITET

Umeå University Medical Dissertations, New Series No 2078

Factors affecting the pharmacological treatment of bipolar disorder

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av filosofie/medicine doktorsexamen framläggs till offentligt försvar i Aulan, Konferenscentrum, Sunderby sjukhus.
Fredagen den 29 maj, kl. 13:00.
Avhandlingen kommer att försvaras på engelska.

Fakultetsopponent: Professor, Allan Young,
Institute of Psychiatry, King's College, London, Storbritannien.

Department of Clinical Sciences
Umeå University, Umeå 2020

Organization
Umeå University
Department of Clinical Sciences

Document type
Doctoral thesis

Date of publication
8 May 2020

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Title
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Abstract
In patients with bipolar disorder, long-term treatment with mood-stabilisers is often required to prevent manic and depressive episodes. Lithium is a first-line treatment of bipolar disorder, thought to be superior regarding the prevention of acute relapse, self-harm and suicide. However, patients may find it difficult to take lithium long-term. The reasons why patients discontinue lithium remain largely unknown. Neither do we know whether lithium is equally effective in patients with bipolar I and bipolar II disorder. Finally, there is only little evidence on how patients with a dual diagnosis of bipolar disorder and adult attention-deficit hyperactivity disorder (ADHD) should be treated. In this patient group, central stimulant treatment may be of benefit. However, there are no studies that have explored the impact of central stimulants on suicidal behaviour in patients with such a dual diagnosis.

This thesis is based on LiSIE (Lithium – Study into Effects and Side Effects), a retrospective cohort study exploring effects and side-effects of lithium and other mood-stabilisers. In the first study, we identified and assessed reasons for lithium discontinuation in 468 patients with bipolar disorder or schizoaffective disorder. We found that more than half of all patients discontinued lithium at some point and that lithium was discontinued mainly because of adverse effects. More patients with bipolar II or other bipolar disorder than patients with bipolar I or schizoaffective disorder discontinued lithium because of a perceived lack of effect. Men were more likely to discontinue lithium when feeling well. They were also less likely to consult with a doctor prior discontinuation. In the second study, we examined the clinical course and need for hospital admission in 194 patients with either bipolar I or schizoaffective disorder or bipolar II or other bipolar disorder within two years before and after lithium discontinuation. For the whole sample, the number of hospital admissions and bed-days doubled after lithium discontinuation. This increase was exclusively attributable to patients with bipolar I or schizoaffective disorder. In the third study, we assessed occurrence of suicidal or non-suicidal self-injurious behaviour in 206 patients with a dual diagnosis of bipolar disorder or schizoaffective disorder and ADHD, within six months and two years before and after central stimulant initiation. Our results showed, that suicide attempts and non-suicidal self-injury events decreased after central stimulant treatment start.

Our results indicate the importance of discussing and managing potential adverse effects before and continuously during lithium treatment. Particularly men may require proactive follow-up. Further, it is important that patients who may benefit from lithium can continue their treatment. Particularly, the higher relapse risk in patients with bipolar I or schizoaffective disorder points towards a need to apply a higher threshold for discontinuing lithium in this patient group. In patients with both bipolar disorder and ADHD, addition of central stimulant treatment may reduce the risk of suicidal and non-suicidal self-injurious behaviour.

Keywords
Lithium, Bipolar Disorder, Schizoaffective Disorder, Physical Health, Compliance, Medication Adherence, Side Effects, Long Term Adverse Effects, Mood Stabiliser, Admission, Hospitalisation, Attention Deficit Disorder with Hyperactivity, Central Nervous System Stimulants, Self-Injurious Behaviour, Non-Suicidal Self Injury, Suicide Attempted, Suicide.

Language
English

ISBN
978-91-7855-251-1 (tryck)
978-91-7855-252-8 (PDF)

ISSN
0346-6612

Number of pages
113 + 3 papers