A Retrospective Observational Study of Long Term Response to Mood Stabilizers in Patients with Bipolar Disorders

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Author Note

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 A Bipolar disorder (BD) refers to a chronic psychiatric illness characterized by a combination of depressive and manic episodes. A range of clinical guidelines for the pharmacotherapy are available, however, long-term response in BD patients receiving care under these guidelines still remain insufficiently explored (Sadock, Kaplan, & Sadock, 2011). Long-term BD studies are complex and challenging owing to the difficulty researchers encounter in defining outcomes, especially because individuals experience a substantial variation in the manifestation of BD-associated symptoms. In this regard, previous studies have attempted to investigate the predictors and effects of prophylactic lithium treatment for BD patients, but offer no substantial conclusions on what the patient's long-term response to these treatments could be. Furthermore, it is difficult to generalize the effects of a single form of pharmacotherapy to BD treatment as a whole. Therefore, a detailed investigation was required to gain a wider view of the long-term outcomes of BD-associated treatments.

 In order to explore the utility and efficacy of prophylactic treatment in BD patients over the long-term, I will discuss the research study and findings as described in the article by Ahn and colleagues (2017). Their study aimed to estimate the long-term effects and responses of BD patients undergoing mood stabilizer treatment and to investigate the association of other clinical factors to that response. The study was based on other studies which established that the most common mood stabilizers, lithium, and valproate, are appropriate prescriptions for the task, and thus chose it for the treatment (Kleindienst, Engel, & Greil, 2005). To simulate a naturalistic clinical setting, the study also used combinations of other mood stabilizers during the primary treatment in order to assess the long term response more accurately.

# Methods

Participants

To study the long-term effects of a combination of BD treatments, the researchers selected 80 participants that had either bipolar I or II disorder (BDI or BDII). The participants had already been receiving valproate and/or lithium for over 2 years in a clinical setting. Patients selected for inclusion in the study were those who fit the DSM-IV criteria for Bipolar disorder type I or II. Further inclusion criteria included age, which was set between 18 to 55 years. However, any patients that exhibited symptoms of other mental illnesses, or had other physiological or neurological disorders were also part of the exclusion criteria. The final number of patients who met the inclusion criteria numbered 80 and gave informed consent to participate in the study. A number of these patients had also participated in various other genetic and clinical studies, however, it was ensured that their participation did not impact the course of the current study.

## Materials and Procedures

The participants selected for the study were provided treatment following established clinical treatment guidelines. A retrospective chart review was used to evaluate the long-term response of the treatments. The Alda scale was used for the evaluation besides obtaining data form their other previous clinical visits. The Alda scale was used to evaluate the association between the treatment and clinical improvement, and to establish any potential causal relationship between prophylactic treatment and the patient’s improvement. The treatment algorithms which were implemented were provided by the best-established treatment options in earlier studies, in order to obtain an accurate assessment of the long-term responses of patients.

Furthermore, the clinical characteristics of the patients were obtained from their entire life’s health record. They were subsequently separated into two main response groups based on the total Alda scale score they would receive. The bipolar illness clinical global impressions scale (CGI-BP) was used to evaluate the current mood of the participants before the course of the study. Since 60 out of the 80 subjects were already evaluated for any potential physiological or neurological diseases by the other studies they participated in, the researchers already had information about comprehensive disease characteristics for most participants. Other study variables include the age of the participants when they first experienced bipolar episodes, alongside any comorbid conditions and other manifested symptoms. Based on the Alda scores, they were classified into two groups; the poor responders and the good responders, relying upon frequentist mixture analysis. According to the analysis, the cut-point was 4.5, therefore any participants with a good response were those who scored 5 or higher, while those who scored 4 and lower were classified as poor responders to the treatment.

# Results

The findings suggested that nearly 34% of the total participants scored higher than 5 on the Alda scale and were thus classified as good responders. As regards the treatment combinations, the response rates of the participants remained largely the same between valproate and lithium only groups. However, the groups that received a combination therapy exhibited poorer response compared to the former. Among poor responders, increased appetite during the depressive phase and delusions during the manic phase were more common. Additionally, the poor responders' group also exhibited more tendencies to have co-morbid anxiety disorders.

In addition, poor responders were more likely to use other combinations of adjunct pharmacotherapy treatments such as antidepressants, mood stabilizers, and antipsychotics, alongside the main course of treatments. Compared to good responders, the former group had received a higher number of adjunctive medication, yet certain mood stabilizer combinations remained in use with both good and poor responders (Ahn, et al., 2017).

The study also compared disease and demographic course characteristics among all types of responders. Poor responders with lower Alda scores exhibited significantly larger episodes of manic and depressive moods before they used mood stabilizer medication. When comparing individual symptom profiles of both types of responders, delusion was found to have been experienced among a substantially higher number of poor responders during manic episodes, compared to good responders.

The analysis of depressive episodes among the responders demonstrated that good responders generally experienced more instances of appetite loss compared to moderate responders and poor responders. Thus, poor responders were more likely to deal with depressive symptoms by increasing their diets. Furthermore, when the responders were evaluated for any comorbid conditions and psychiatric disorders, very few anxiety disorders were observed among the good responders compared to nearly 25% poor responders experiencing a lifetime co-morbidity.

# Discussion

In the study, the researchers attempted to investigate the various clinical responses of patients belonging to one of the two categories of bipolar disorder (I and II) according to the DSM-IV criteria. The patients included in the study were those who had been receiving lithium and/or valproate treatment for their condition. The Alda scale was used to measure their response to medication over a period of 2 years and was classified as poor responders and good responders based on whether their scores were below 4 or above 5, respectively. Among patients who received both lithium and valproate, there were not many differences experienced by patients in the long-term. The earlier findings regarding lithium and valproate were corroborated by Ahn et al (2017) who found nearly similar long-term responses for the two drugs. Additionally, the analysis of the collected data demonstrated that participants with baseline clinical and demographic features experienced similar effects from both drugs, except in the case of BD II patients who generally exhibited a preference for Valproate. Thus, the study confirmed the efficacy of current clinical guidelines, in the case of long-term response, when it came to prescribing medications for treating BD conditions.

Furthermore, Ahn et al (2017) identified the various clinical factors that were linked to mood stabilizer treatment. These clinical factors included certain baseline characteristics, the onset of the disease and its course, comorbidities, and individual symptoms of episodes. Among subjects that did not respond effectively to treatment and had experienced mixed episodes earlier, typical long-term responses included appetite increase with depressive episodes, delusions during manic episodes. Moreover, BD I patients also experienced increased appetite during the depressive phase, however, the study’s findings cannot be easily generalized owing to a smaller sample of BD I patients. In addition, the study found out that poor responders to treatment also exhibited anxiety disorders and generally also experienced a greater frequency of psychotic episodes and delusions. This tendency along with their tendency to have increased appetites during depressive episodes indicate that they are at a higher risk of developing psychiatric comorbidities. It indicates that a poor response may correlate with suicidal ideation, distress, and disability, and lead to further negative clinical outcomes.

The study has several strengths and limitations. One key limitation in the study is the small sample size which makes it more prone to false positives and false negatives. Additionally, the statistical analysis methods to detect differences among valproate and lithium treatments may not be precise enough to detect small changes. The retrospective nature of the study also did not allow the researchers to draw a causal link between poor response rates and the various clinical factors under investigation. Additionally, all of the patients were from Korea and thus a number of other confounding factors that were ignored may limit the generalizability of the study.

One of the key findings of the study was that patients with psychotic features who experience mixed BD episodes, along with anxiety disorders, are more likely to exhibit a poor response to mood-stabilizing medication in the long term. Furthermore, it provides a specific list of symptoms that patients experience when the response to the treatment is poor. These symptoms can be utilized as important predictors for evaluating mood stabilizer treatment in the long-term.

# References

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