

Medication Adherence among Patient with Bipolar Disorder: A Literature Review

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Abstract: Bipolar disorder is one of the chronic mental health disorders. It is ranked the seventh leading cause of non-fatal burden in the world. Patients with bipolar disorders encounter several disturbances in their moods, cognitions, and behaviours which express differently during mania and depressive episodes. These difficulties can affect a patient's life functionings, especially in regards to social functioning. Bipolar disorder can be treated and the patients can become productive and be able to live meaningfully. However, non-adherence with medication is common problem among patients with bipolar disorder that is associated with elevated rates of relapse, hospitalization, suicidal behaviour, greater cost of caring, and consequently a poor quality of life. Several factors contributed to medication adherence among patients with bipolar disorder have been discussed including age, gender, marital status, substance abuse, phase/stage of illness, medication knowledge, individual's beliefs, illness representation, social support, and medication side effects. This literature review aims to explore the importance of medication adherence to patients with bipolar disorder and several factors influencing to medication adherence. PubMed, CINAHL, Science Direct, Google Scholar were used to search the articles published from 2000 to 2013 in English that combined the search terms "bipolar disorder", "medication adherence", "medication non-adherence", and "medication adherence and bipolar disorder". In order in helping to enhance medication adherence in patients, health care providers indeed need to understand the phenomenon of medication adherence.

1 INTRODUCTION

Bipolar disorder is a chronic mental health disorder with periods of remission and relapse (Macneil, Hasty, Conus, Berk, & Scottt, 2009). It is estimated to be the seventh leading cause of non-fatal burden in the world (Ayuso-Mateos, 2001). Globally, the lifetime prevalence of bipolar spectrum disorder is approximately 3% to 7% of the population (Williams, Ruekert, & Lum, 2011) and approximately 0.5% to 5% for prevalence in any type of bipolar disorder (Vieta et al., 2011), with the average age of onset being 15 to 30 years (Williams et al., 2011). The prevalence of bipolar disorder in Indonesia is unknown yet. However, based on the Global Burden of Disease 2000 survey, the prevalence of bipolar disorder in the sub-region SearB (South-East Asia) in which Indonesia was included, showed the highest number per population in the 30-44 year

age group (Chisholm, van Ommeren, Ayuso-Mateos, & Saxena, 2005).

Despite not being ranked the first among mental health disorders, bipolar disorder causes a significant burden (Vieta, 2005), such as relapse, re-hospitalization, suicidal behavior, and a greater cost to caring (Adam & Scott, 2000; Colom, Vieta, Tacchi, Sanchez-Moreno, & Scott, 2005; Depp, Lebowits, Patterson, Lacro, & Jeste 2007; Sajatovic, Bauer, Kilbourne, Vertrees, & Williford, 2006; Scott & Tacchi, 2002) which ultimately affects functioning in everyday life (Nieng, 2011). Medication is one of the treatment approaches in bipolar disorder. Thus, if individuals get the proper medication, they would be able to regain a productive life like others (National Institute of Mental Health [NIMH], 2009). However, non-adherence with medication in bipolar disorder is a common problem (Lingam & Scott, 2002), with the

incident rate ranging from 20% to 60% (Berk, Berk & Castle, 2004; Colom & Lam, 2005; Lingam & Scott, 2002).

Medication non-adherence is associated with elevated rates of relapse, hospitalization, suicidal behavior, greater cost to caring (Adam & Scott, 2000; Colom, Vieta, Tacchi, Sanchez-Moreno, & Scott, 2005; Depp, Lebowits, Patterson, Lacro, & Jeste 2007; Sajatovic, Bauer, Kilbourne, Vertrees, & Williford, 2006; Scott & Tacchi, 2002), and consequently a poor quality of life (Crowe, Wilson, & Inder, 2011). Several factors contribute to medication non-adherence among patients with bipolar disorder including age (Baldessarini, Perry, & Pike, 2007; Berk et al., 2010; Hou, Cleak, & Peveler, 2010), gender, marital status, substance abuse (Berk et al., 2010; Clatworthy, Bowskill, Rank, Parham, & Horne, 2007; Sajatovic, Bauer, Kilbourne, Vertrees, & Williford, 2006; Sajatovic, Velligan, Weiden, Valenstein, & Ogedegbe, 2010), phase/stage of illness (Berk et al., 2010; Colom et al., 2005), medication knowledge (Berk et al., 2010; Rosa et al., 2009; Seo & Min, 2005), an individual's beliefs and attitude (Adams & Scott, 2000; Clatworthy et al., 2007; Clatworthy et al., 2009; Lan, Shiau & Lin, 2003; Scott & Pope, 2002), cognitive illness representation (Brown et al., 2001; Hou et al., 2010; Lobban et al., 2003; Sajatovic et al., 2009a), therapeutic alliance (Berk et al., 2004; Lingam & Scott, 2002), social support (Berk et al., 2010; Seo & Min, 2005), and medication side effects (Clatworthy et al., 2009; Patel & David, 2007; Sajatovic et al., 2011).

In the following article, we review the literature on medication adherence among patient with bipolar disorder and discuss the small research based on how the concepts are linked.

2 FINDINGS

2.1 Definition and Nomenclature

In the literature review, there are three terms related to a patient's medication taking behavior; compliance, adherence, and concordance. In terms of compliance and adherence, these terms reflect different meanings in a patient's action in taking medication. However, some authors have often used compliance and adherence interchangeably because they want to shift away from negative connotation of compliance which is coercion. Even though they used adherence to replace compliance, however, they may

use the same measurement. For instance, in Berk's literature review (as cited in Berk et al., 2010), some studies used adherence and the others used compliance. However, among those studies, the same measurement to measure variables of taking medication was used.

Currently, since compliance and adherence have different meanings, some authors have defined these two terms. In terms of compliance, Vukovich (2010) defined that compliance is a patient's acceptance of medication and other psychiatric treatment because he/she is forced, persuaded, or pressured to take his/her medication. In compliance, patients yield to or obey to physicians' instructions. It implies conformity to medical defined goals only. Based on Seo and Min (2005), compliance is more likely a person's behavior of taking medication in the correct dose, and time as prescribed by the doctor. Based on Mullen (as cited in Cohen, 2009), compliance implies obedience and the expectation that patients will passively follow the order. It refers to behavior characterized by the extent to which people obey, follow the instructions, or use the prescriptions assigned by a health-care provider (Brawley & Culos-Reed, 2000). Meanwhile, Patel and David (2007) defined compliance is the extent to which a person's behavior coincides with medical advice. From these definitions, it shows that compliance occurs because of control or force by other people to follow the prescriptions (external control), therefore, in this condition, the patient is a passive patient.

Adherence, on the other hand, refers to patients' voluntary behaviors to take their recommended medication from their own commitment (Vukovich, 2010). Adherence is the patients' choice to take their medication under their own responsibility and they can interpret their medication correctly because of their understanding (Patel & David, 2007). It implies that patients have their own choice to plan their behavior to take medication and implement their medication by their own motivation and action (Brawley & Culos-Reed, 2000). Adherence is the patient's agreement to take medication and continue to use it for a period of time (Velligan et al., 2006). Patients' attempts to maintain health behavior related to behaviors to take their medication are based on their active participation and agreement (Cohen, 2009). Based on Lutfey and Whisner (1999), adherence is the patients' behavior to take their medication as independent, intelligent, and autonomous people, therefore, the patients are voluntary and become active participants in their medical treatment. Furthermore, Horne (2006) defined adherence as "the extent to which the patient's

behavior matches agreed recommendations from the prescriber” (p. 66S).

Nevertheless, to achieve adherence, adherence needs concordance that is emphasized on patient decision-making and patient agreement. Vukovich (2010) defined concordance as the agreement between the patient and the treatment team on the goals and means of the treatment. It implies that concordance is a necessary way to achieve adherence.

Medication adherence involves quite complex behaviors reflecting an integration of a person's mental state such as a person's willingness as well as external behaviors such as the actual actions of medication taking. Those refers to (1) patients' behavior in taking their medication by their own commitment/agreement (voluntarily), (2) taking medication from their own responsibility/plan/action/active participation as a result of their understanding (actively), (3) taking medication continuously for a period of time (continuously), and (4) taking medication matching the recommendation (taking medication correctly as prescribed).

3.2 The Importance of Medication Adherence

Relapse prevention. Patients with bipolar disorder who are on maintenance medication, especially Lithium, but discontinue their medication, almost always result in relapse, usually in weeks to months after stopping (Peet & Harvey, 1991). A study by Adam and Scott (2000) showed that patients who are partially adherent are more likely to be relapsing compared than those who are highly adherent.

Hospitalization prevention. Likewise, high adherence to medication among patients with bipolar disorder is more likely to result in a smaller number of hospitalizations (Lage & Hassan, 2009; Sajatovic et al., 2006). A study by Scott and Pope (2002) about self-reported adherence in which psychiatric hospitalization was one of the outcomes among bipolar disorder patients showed that patients who were partially adherent to medication had had a higher number of psychiatric hospitalizations compared to those who were fully adherent.

Reducing of symptoms severity. Taking medication as prescribed can reduce symptoms severity. A study by Adam and Scott (2002) showed that patients with stronger beliefs about the benefits of treatment were highly adherent compared with the partially adherent subjects who had higher perceived severity of illness scores. Moreover, individuals who were non-adherent with prescribed medication

experienced more severe symptoms. (Sajatovic et al, 2009).

3.2 Factors Contributed to Medication Adherence

Age. Younger aged patients were more non-adherent than older patients, they have more negative views of medicines, they perceive that their medicines can harm them, and they perceive that they have more personal control over managing themselves in relation to their illness (Hou et al., 2010). A survey study of 429 patients with bipolar disorder related to treatment adherence (Baldessarini et al., 2007) showed that younger patients were more non-adherent. Moreover, patients who received either lithium or anticonvulsant medication were more likely to be younger in non-adherence to medication. To sum up, younger aged patients are more non-adherent than older aged patients (Berk et al., 2010).

Gender. Females are more likely to be non-adherent than males. Bipolar disorder in women is a challenging disorder to treat because it differs with male in various aspects, such as; women reproductive cycle particularly postpartum, premenstrual phase of menstrual cycle, peri-menopause, and menopause (Parial, 2015). Sajatovic et al. (2010) in their study about illness experience and reason for non adherence showed that females were more likely to be non-adherent. Similarly, Clatworthy et al. (2007) also reported higher numbers of females for non adherence. In addition, Kessing (as cited in Berk et al., 2010) reported that females were significantly more likely to have poorer adherence to lithium in a naturalistic study in Denmark.

Marital status. There are differences results in regards to marital status as a factor of medication adherence. Clatworthy et al. (2007) reported that there were no significant differences in marital status for non adherence or adherence. Meanwhile, based on Connely as cited in Berk et al., (2010) it appears that marital status is a protective factor that increases adherence. Similarly with Connely's study, Sajatovic (as cited in Berk et al., 2010) showed the results that non-adherent patients were more likely to be in the single status group. Individuals who get married are less frequent to suffer bipolar disorder than those who have divorced or never been married. (Aubry et al., 2007).

Substance abuse. Individuals with bipolar disorder who have any current substance abuse disorder will be more likely to be non-adherent and individuals who have any past substance use disorder showed no significant difference between the adherence and

non-adherence group. The most common substance abuse was alcohol (Sajatovic et al., 2006). Moreover, Sajatovic, et al. (2010) reported that a high number (65 % of 13 participants with bipolar disorder) of substance use dependents are non-adherent in regards to prescribed medication.

Phase/Stage of illness. Adherence problems also can happen in different phases and stages of the illness. For example, people who have an increasing severity of manic symptoms are at risk for adherence problems (Keck as cited in Berk et al., 2010). Related to this problem, Colom et al. (2005) stated that adherence problems may be prevalent at specific stages in the course of the illness, for example late adherence and late non-adherence. In late adherence, patients were in adherence after experiencing repeated relapses. Meanwhile in late non-adherence, patients will be in non-adherence in long-term treatment and they will feel that their treatment is not working well.

Medication knowledge. Having a good level of knowledge about their illness and treatment is one of important factors among patients with bipolar disorder. This condition can help patients in making decisions about illness management and negative beliefs about medications (Berk et al., 2010). Good knowledge about medication was found to directly improve medication compliance (Seo & Min, 2005). Moreover, a correlation study by Rosa et al. (2009) that assessed medication adherence and its related factors in patients with bipolar disorder showed that patients' knowledge about their disorder and medication positively correlated with treatment adherence to lithium prophylaxis.

Individuals' attitude. Attitude toward medication had a significant positive effect on medication compliance (Lan, Shiau & Lin, 2003). A study of Clatworthy et al. (2009) focused on patients' attitudes to medication showed that about 30% of patients were reported with low adherence because of greater doubts about personal need for treatment and stronger concern about potential negative effects. According to Scott and Pope (2002), not easy to accept the illness may also influence medication non adherence.

Individual's beliefs and cognitive illness representation. Adams and Scott (2000) reported that highly adherent and partially adherent subjects are significantly different in their perception of illness severity, their beliefs about themselves and their control over the disorder, and their concerns about future hospitalization. Moreover, Clatworthy et al. (2007) assumed that patients can make decisions about taking medication or not based on their perceptions of

the illness and treatment. A study by Hou et al. (2010) showed that participants who were in the non-adherence group believed that their illness caused more negative effects on their life (consequences) and would have a longer-term impact (timeline). In a preliminary investigation by Brown et al. (2001), Brown stated that a patient's illness cognition (i.g. timeline, consequences, and cause) were associated with medication adherence. In their study, they also found that poor adherence associated with interpersonal difficulties was a cause of depressive symptoms. In addition, patients who perceived their illness as a mental health identity, with negative consequences, and high levels of belief in treatment to control symptoms were more likely to take medication as prescribed (Lobban, Barrowclough & Jones, 2003). An individual's perception of risks and benefits of medication treatment were more likely to affect treatment adherence in bipolar populations (Scott as cited in Sajatovic et al., 2009b).

Therapeutic alliance. Therapeutic alliance is important for affective disorder patients (Lingam & Scott, 2002). Lingam and Scott reported that poor interaction between the clinician and patient was four times more common with non-adherent patients compared to those who were adherent. Moreover, in Zeber's study (as cited in Berk et al., 2010) among veteran patients with bipolar disorder, it showed that therapeutic alliance was positively connected to medication adherence.

Social support. Social support has been identified as a factor to medication adherence. Seo and Min study (2005) found that social support is the strongest direct effect on medication compliance. This social support can come from family, friends and health care professionals. Family members will also influence the patient's attitudes and beliefs about the illness and its treatment, and it also can affect adherence (Cochran as cited in Berk et al., 2009). High expressed emotions and particularly over involvement in the family is considered being associated with poorer adherence and poorer overall outcomes in bipolar patients (Miklowitz as cited in Berk et al., 2010).

Medication side effects. Medication side effects are a common reason for non-adherence in psychiatric patients (Scott as cited in Patel & David, 2007). Clatworthy et al. (2009) reported that about 30% of the participants that were in low adherence was predicted by greater doubts about personal need for treatment and stronger concern about potential negative effects. Then, Sajatovic et al. (2011) reported that the side effects of a drug were main reason for deciding not to take the medication.

3 DISCUSSION

As medication is important for patients with bipolar disorder, many research studies had been conducted for bipolar disorder to see how non-adherent to medication can have the negative effects to patients with bipolar disorder. Nurses and health care professionals usually use routine care procedures in the hospital to enhance a patient's medication adherence. Usually routine care focuses on the patient's problems, especially problems related to symptom management, providing education about the patient's medication, the frequency of taking medication, and indications and side effects of the medication. In the psychiatric hospital, patients follow this routine care and take medication because of the order from the nurse or another health care professional. There is no known specific study that can enhance medication adherence, especially in patients with bipolar disorder.

4 CONCLUSIONS

Medication adherence is important for patient with bipolar disorder, to prevent relapse and re-hospitalization, to reduce symptoms severity, to gain a better control of mood swings and to improve functioning and quality of life. However, in fact, non-adherence to medication is a common problem in the psychiatric area including patients with bipolar disorder. Prior to helping to enhance medication adherence in patients, health care providers indeed need to understand the phenomenon of medication adherence.

REFERENCES

Adams, J., & Scott, J. (2000). Predicting medication adherence in severe mental disorders. *Acta Psychiatrica Scandinavica*, 101, 119–124.

American Psychiatric Association [APA]. (2000). *Diagnostic statistical manual of mental disorder fourth edition text revision (DSM-IV-TR)*. Washington, DC: American Psychiatric Association.

Aubry, J., Ferrero, F., Schaad, N., & Bauer, M. S. (2007). *Pharmacotherapy of bipolar disorder*. West Sussex: John Wiley & Sons.

Ayuso-Mateos, J. L. (2001). Global burden of bipolar disorder in the year 2000. *World Health Organization: Global program on evidence for health policy (GPE), global burden of disease*. Retrieved from http://www.who.int/healthinfo/statistics/bod_bipolar.pdf

Baldessarini, R. J., Perry, R., & Pike, J. (2007). Factors associated with treatment nonadherence among US bipolar disorder patients. *Human Psychopharmacology: Clinical and Experimental*, 23, 95–105.

Berk, M., Berk, L., & Castle, D. (2004). A collaborative approach to the treatment alliance in bipolar disorder. *Bipolar Disorders*, 6, 504–518.

Berk, L., Hallam, K. T., Colom, F., Vieta, E., Hasty, M., Macneil, C., & Berk, M. (2010). Enhancing medication adherence in patients with bipolar disorder. *Human Psychopharmacology: Clinical and Experimental*, 25, 1–16.

Brawley, L. R., & Culos-Reed, S. N. (2000). Studying adherence to therapeutic regimens: Overview, theories, recommendations. *Controlled Clinical Trials*, 21, S156–S163.

Brown, C., Dunbar-Jacob, J., Palenchar, D. R., Kelleher, K. J., Bruehlman, R. D., Sereika, S., & Thase, M. E. (2001). Primary care patient's personal illness model: A preliminary investigation. *Family Practice*, 18, 314–320.

Chisholm, D., van Ommeren, M., Ayuso-Mateos, J. L., & Saxena, S. (2005). Cost effectiveness of clinical intervention for reducing the global burden of bipolar disorder. *The British Journal of Psychiatry*, 187, 559–567. doi: 10.1192/bjp.187.6.559

Clatworthy, J., Bowskill, R., Parham, R., Rank, T., Scott, J., & Horne, R. (2009). Understanding medication non-adherence in bipolar disorders using a Necessity-Concerns Framework. *Journal of Affective Disorders*, 116, 51–55.

Clatworthy, J., Bowskill, R., Rank, T., Parham, R., & Horne, R. (2007). Adherence to medication in bipolar disorder: A qualitative study exploring the role of patients' beliefs about the condition and its treatment. *Bipolar Disorders*, 9, 656–664.

Cohen, S. M. (2009). Concept analysis of adherence in the context of cardiovascular risk reduction. *Nursing Forum*, 44, 25–36.

Colom, F., & Lam, D. (2005). Psychoeducation: Improving outcomes in bipolar disorder. *European Psychiatry*, 20, 359–364.

Colom, F., Vieta, E., Tacchi, M. J., Sanchez-Moreno, J., & Scott, J. (2005). Identifying and improving non-adherence in bipolar disorders. *Bipolar Disorder*, 7, 24–31.

Depp, C. A., Lebowitz, B. D., Patterson, T. L., Lacro, J. P., & Jeste, D. V. (2007). Medication adherence skills training for middle aged and elderly adults with bipolar disorder, development and pilot study. *Bipolar Disorder*, 9, 636–645.

Dogan, S., & Sabanciogullari, S. (2003). The effects of patient education in lithium therapy on quality of life and compliance. *Archives of Psychiatric Nursing*, 17, 270–275.

Horne, R. (2006). Compliance, adherence, and concordance: Implication for asthma treatment. *Chest*, 130, 65S–72S.

- Hou, R., Cleak, V., & Peveler, R. (2010). Do treatment and illness beliefs influence adherence to medication in patients with bipolar affective disorder? A preliminary cross-sectional study. *European Psychiatry*, 25, 216-219.
- Kessing, L. V., Agerbo, E., & Mortensen, P. B. (2004). Major life events and other risk factors for first admission with mania. *Bipolar Disorder*, 6, 122-129.
- Lage, M. J., & Hassan, M. K. (2009). The relationship between antipsychotic medication adherence and patient outcomes among individuals diagnosed with bipolar disorder: a retrospective study. *Annals of General Psychiatry*, 8, 1-9. doi:10.1186/1744-859X-8-7
- Lan, C., M., Shiao, S. J., & Lin, L. C. (2003). Knowledge, beliefs, attitudes, and drug compliance in schizophrenic patients. *Tzu Chi Medical Journal*, 15, 369-375.
- Lingam, R., & Scott, J. (2002). Treatment non-adherence in affective disorders. *Acta Psychiatrica Scandinavica*, 105, 164-172.
- Lobban, F., Barrowclough, C., & Jones, S. (2003). A review of the role of illness models in severe mental illness. *Clinical Psychology Review*, 23, 171-196.
- National Institute of Mental Health. (2009). *Bipolar disorder*. NIH Publication: U.S Department of Health and Human Services.
- Nieng, C. H. (2011). Overview of bipolar disorder. *The Singapore Family Physician*, 37, 13-16.
- Parial, S. (2015). Bipolar disorder in women. *Indian Journal of Psychiatry*, 57, S252-S263.
- Patel, M. X., & David, A. S. (2007). Medication adherence: Predictive factors and enhancement strategies. *Psychiatry*, 6, 357-361.
- Rosa, A. R., Marco, M., Fachel, J. M. G., Kapczinski, F., Stein, A. T., & Barros, H. M. T. (2009). Correlation between drug treatment adherence and lithium treatment attitudes and knowledge by bipolar patients. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 31, 217-224.
- Sajatovic, M., Bauer, M. S., Kilbourne, A. M., Vertrees, J. E., & Williford, W. (2006). Self-reported medication treatment adherence among veterans with bipolar disorder. *Psychiatric Services*, 57, 56-62.
- Sajatovic, M., Jenkins, J., Cassidy, K., & Muzina, D. (2009). Medication treatment perceptions, concerns and expectations among depressed individuals with Type I Bipolar Disorder. *Journal of Affective Disorders*, 115, 360-366.
- Sajatovic, M., Velligan, D. I., Weiden, P. J., Valenstein, M. A., & Ogedegbe, G. (2010). Measurement of psychiatric treatment adherence. *Journal of Psychosomatic Research*, 69, 591-599.
- Scott, J., & Pope, M. (2002). Self-reported adherence to treatment with mood stabilizers, plasma levels, and psychiatric hospitalization. *American Journal of Psychiatry*, 159, 1927-1929.
- Scott, J., & Tacchi, M. J. (2002). A pilot study of concordance therapy for individuals with bipolar disorder who are non-adherent with lithium prophylaxis. *Bipolar Disorder*, 4, 386-392.
- Seo, M. A., & Min, S. K. (2005). Development of a structural model explaining medication compliance of persons with schizophrenia. *Yonsei Medical Journal*, 46, 331-340.
- Velligan, D. I., Lam, Y. F., Glahn, D. C., Barret, J. A., Maples, N. J., Ereshefsky, L., & Miller, A. L. (2006). Defining and assessing adherence to oral antipsychotics: A review of the literature. *Schizophrenia Bulletin*, 32, 724-742.
- Vieta, E. (2005). Improving treatment adherence in bipolar disorder through psychoeducation. *Journal Clinical Psychiatry*, 66, 24-29.
- Vieta, E., Blasco-Colmenares, E., Figueira, M. L., Langosch, J. M., Moreno-Manzanaro, & M., Medina, E. (2011). Clinical management and burden of bipolar disorder: A multinational longitudinal study (WAVE-bd study). *BMC Psychiatry*, 11, 1-8. doi: 10.1186/1471-244X-11-58
- Vuckovich, P. K. (2010). Compliance versus adherence in serious and persistent mental illness. *Nursing Ethics*, 17, 77-85.
- Williams, K. L., Ruekert, L., & Lum, C. (2011). Treatment of bipolar disorder: A focus on medication therapy for mania. *Formulary Journal*, 46, 82-97