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Comparative Between The Effectiveness Of Different Approaches For The Treatment of Bipolar Disorder (Pharmacological And Psychological) Systematic Review of Meta-analysis

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Abstract

This research is a systematic review of the available data concerning the psychological and pharmacological treatment of bipolar disorder (BD), the aim of this review was to compare the effectiveness of psychotherapy and pharmacotherapy for bipolar disorder, it yielded 1620 publications between 2005 to 2020. About 482 articles were repeated in more than one database. Also, we excluded 520 articles that did not assess the BD interventions. Then 579 articles were excluded because they were not a trial study. finally, the remaining 19 articles were included in this systematic review that met inclusion criteria, The literature suggests that the pharmacological intervention (Quetiapine) is the most effective pharmacological intervention in the treatment of BD, and that the psychological intervention (cognitive behavioral therapy (CBT)) is the most effective psychological intervention in the treatment of bipolar disorder, also noted that the pharmacological intervention (probiotics) is the least effective pharmacological intervention in the treatment of BD and that the psychological intervention (anxiety intervention to individuals with BD(AIBD)) is the least effective psychological intervention in the treatment of bipolar disorder.

keywords: Depression, Anxiety, Psychological Interventions, Pharmacological Interventions.

Introduction

Bipolar disorder (BD) is an inveterate, periodic disorder described as persistent changes in mood and energy. It affects widely less than 2% of the world's population indifferent to race, socioeconomic or nationality status. Bipolar disorder is a major cause of disability among young adults, resulting in cognitive and functional impairment and increased mortality, particularly death by suicide (Grandy,2016).

Scientists and physicians view the course of bipolar disorder as a disorder characterized by extreme mood swings between mania and depression. The patient's emotions oscillate between episodes of severe or hypomanic episodes of depression and accompanying feelings of malaise, distress, loss of energy and desire to enjoy various activities, but another pathway is

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increasingly challenging this view through clinical and epidemiological studies documenting the course of the chronic and disabling disorder, for example Disability and unemployment rates among individuals with bipolar disorder are much higher than the average population (Deckersbach, 2010).

(BD) disease is passed down genetically, with rates of up to 80% in identical twins and 6% in first-degree relatives. Although symptoms of bipolar disorder usually appear at a young age, parents often attribute changes to their children during episodes of Obsession leads to behavioral problems, not mental illness. The risk of unipolar depression (and to a lesser extent psychosis) is also increased in family members, and the genetic basis can be considered complex with many common and small-effect genetic variants contributing to risk, onset and course of injury. The disease is likely the result of trauma in early life. Severe life events and abuse of alcohol and other drugs (Goodwin,2016).

1.1 BD State

BD is a mental health condition that causes significant mood swings, with the upper limit of these emotional and mood disturbances amounting to mania or hypomania, while the lower limit to depression, which affects energy, sleep, activity, behavior, and the ability to think. Besides, the patients cannot decision making (Al-Shafei, 2019).

(Phillips, 2013) points out that BD in particular is a good example of a group of mental illnesses that are difficult to accurately diagnose. People with bipolar disorder may not accurately report their symptoms because they don't think they have a problem, so doctors often need to get information from patients' family members, even though the disorder is one of the ten most common illnesses. Debilitating non-infectious as well as other mental illnesses. In a survey of more than 10 countries, the prevalence of bipolar spectrum disorders was 2.4%, with a prevalence of 0.6% for bipolar I disorder and 0.4% for bipolar II disorder. Low prevalence of types I and II bipolar disorder (Roland, 2018).

Although bipolar disorder can occur at any age, it is usually diagnosed during the teenage years or early twenties, and symptoms may vary from person to person, as well as over time, in a large, population-based cohort study. There are two peaks in life for bipolar disorder starting at 15-24 years and 45-54 years, however, it is very difficult to accurately determine the prone ages for bipolar disorder, by looking at long periods of untreated and undiagnosed illness, as Symptoms appear or appear without diagnosis. Individual access to therapeutic services, which is often used as a starting point (Roland, 2018).

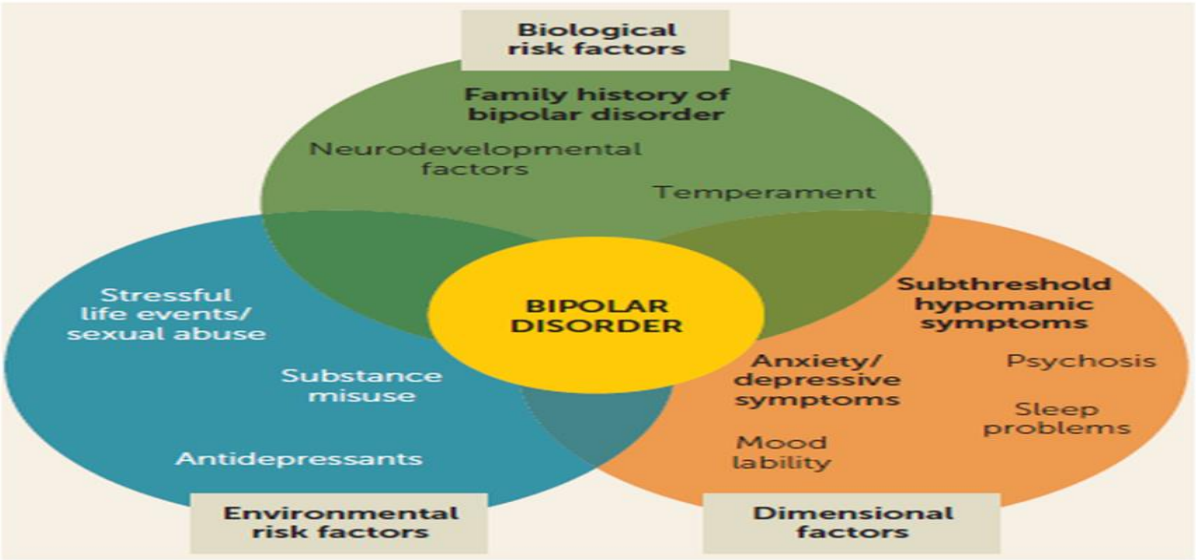
Identification of risk factors or prodromal symptoms that define the stage at risk has important therapeutic implications, as delays in diagnosis and treatment can lead to personal, social, and financial problems that make the disorder more difficult to treat for those who suffer from it and for those around them, and the early stages are usually more responsive for treatment thus may require fewer complex interventions (Faurholt, 2014), as we see in Figure 1 (Vieta, 2018), we can mention these points:

- Several environmental risk factors for bipolar disorder, such as stressful life events including sexual abuse, antidepressant use, or substance misuse like cocaine or alcohol misuse .

- Biological risk factors include family history of bipolar disorder or neurodevelopmental factors such as child developmental delay. Family history of bipolar disorder is one of the strongest risk factors for bipolar disorder, while sexual abuse has been consistently related to a worse illness course.
- Dimensional factors predictive of bipolar disorder include anxiety and depressive symptoms, mood lability, and psychosis or subjective sleep problems, but the most robust predictive factor is the presence of subthreshold (hypo)manic symptoms.

figure 1: Putative Risk Factors and Prodromal Symptoms of Bipolar Disorder

1.2 Psychological and Pharmacological Intervention



Increasingly, according to clinical and psychological studies, there is indication that optimal management of BD disease requires the integration of pharmacological treatment with psychotherapy of the target patient (Geddes,2013).

Psychological interventions for BD, recommended by the National Institute for Health and Care Excellence (NICE), have been shown to be effective in reducing relapse and hospitalization and improving functioning (Todd, 2014), the main goals of psychotherapy for BD disease revolve around educating patients and caregivers as much as possible about stress management strategies, identifying and interfering with early signs of bipolar disorder, and how to maintain regular healthy lifestyle habits (such as sleep and exercise) (Geddes, 2013).

Individual psychotherapy may help patients learn to better cope with the problems of daily life, Although the evidence was not strong, group psychoeducation has also shown beneficial effects of reducing the risk of relapse and relapse of bipolar disorder, and possibly some improvement in symptoms. It also found significant reductions in relapse rates for people who had bipolar disorder. Psychological education through the family despite good evidence. The score was also low (Oud, 2016).

The increasingly pronounced chronicity of bipolar disorder, bipolar type I and bipolar II disorder, has important implications for treatment. The initial treatment offered for BD disease

is acute treatment, given to achieve acute episodic remission of the current episode, and the primary treatment for the acute phase of bipolar disorder, for both episodes of depression and mania, is mood stabilizers, usually lithium or sodium valproate. In addition to atypical antipsychotics. Most patients will, at some point, require combination therapy, eg, a classic mood stabilizer and an antipsychotic during episodes of mania (Fagiolini, 2013).

1.3 Aims of Reviews

Psychological and pharmacological interventions is one of the main therapeutic methods that play a critical role in psychological treatment conditions especially anxiety symptoms emerging from bipolar disorder. The present systematic review, aims to investigate and compare the effectiveness of the psychological and pharmacological interventions on anxiety symptoms in patients with BD and highlight the benefits of psychological and pharmacological interventions in treating anxiety symptoms in patients with bipolar disorder.

2. Material and Methods

2.1 Search Strategy

The present systematic review is dependent on the relevant article that detected and identified through the following libraries and journals databases: Springer, PMC, NIH, Wiley, Sage pub in addition to a search was achieved by using the specific subject keywords terms depression, depression therapy, and psychological interventions.

All articles were published between the year 2005 to 2020 (around 15 years ago). No limit of population age that targeting. We depend on hand searched method to research of journals that included papers and references in electronic database, so any study did not publish in electronic was missed in this systematic review. A review was conducted using the subject words *bipolar disorder, psychological intervention OR Therapy, pharmacological intervention.*

2.2 Inclusion Criteria

A selected paper that builds the structure form of the present study by depended on screening of the articles titles from electronic database.

In addition to, all related papers were reviewed to confirm from eligibility to this systematic review, because many of papers not clearly appeared where it is compatible to used. We judge the article to be compatible if they include the following criteria:

- The studies are specialized with a patient with bipolar disorder.
- The studies dealt with psychological and pharmacological interventions.
- Studies being achieved over the past 15 years (from 2005 to 2020).
- The articles were written by English language.

By used keywords in electronic database libraries the present study yielded 1620 publications between 2005 to 2020. About 482 articles were repeated in more than one database. Also, we excluded 520 articles that did not assess the BD interventions. Then 579 articles were excluded

because they were not a trial study. finally, the remaining 19 articles were included in this systematic review that met inclusion criteria listed below, bearing in mind, that all the 1620 studies that were monitored did not address the treatment of bipolar disorder, and according to the above, studies that dealt with drug treatments and psychological treatments for BD were extracted.

2.3 Data analysis and collection

By searched into an electronic database, all identified articles were imported to investigate their titles and abstracts to assessment if each paper might meet the selection criteria. Based on some primary instruments, as Program of the Critical Appraisal Skills (Public Health Resource Unit, 2006), a novel checklist, and compatible for our purposes, For more information please check the appendix.

4. Discussion

Our systematic review on studies of the effectiveness of psychological and pharmacological interventions on anxiety symptoms in patients with BD 19 studies, all studies concluded many of results, we'll highlight the benefits of psychological and pharmacological interventions on anxiety symptoms in patients with BD treated by the selected studies, as shown below:

1- There are many and varied countries where the studies were selected for the systematic review, as Iran, Turkey, United Kingdom, Spain, United States of America, Canada, Australia, as shown in Table1:

Table1, Percentage of Research Studies by Country

Country	Number of studies	Year of studies	Percentage
Iran	5	2009,2011,2015,2020	26.3%
Turkey	4	2005.2009.2010	21.0%
United Kingdom	4	2006.2008,2011,2013	21.0%
Spain	2	2010,2013	10.5%
United States of America	2	2010.2012	10.5%
Canada	1	2013	5.35%
Australia	1	2013	5.35%
Total	**19**		**100%**

2. Most of the studies applied experimental design, with double-blind, parallel-group design around (11 studies), while (4 studies) applied quasi-experimental design, with measurements, and only study applied A multigroup experimental design with repeated assessment, and another one applied case studies design, and one applied Single blind randomized controlled trials design, and one applied multicenter, randomized, rater-blind outpatient trial, as shown in Table2:

Table2, Percentage of Research Studies by Methodology

Methodology	Number of studies	Year of studies	Percentage
Experimental design, with double-blind, parallel-group	11	2005, 2006, 2008, 2009, 2010, 2011, 2013, 2015, 2020	57.8%
Quasi-experimental design, with measurements	4	2009. 2010 ,2012, 2013	21.0%
Multigroup experimental design with repeated assessment	1	2010	5.3%
Case studies	1	2011	5.3%
Single blind randomized controlled trials	1	2013	5.3%
Multicenter, randomized, rater-blind outpatient trial	1	2013	5.3%
Total	**19**		**100%**

3. A few of the studies (6 studies) had relatively small numbers of samples and short durations of follow-up, and do not allow robust conclusions about the efficacy of psychological or pharmacological intervention method to be drawn, (The sample size was divided into (large = 30, and small = 30) according to what is known in the scientific community), but the rest, however, was distinguished by large numbers of samples and long durations of follow-up, which allow robust conclusions about the efficacy of psychological or pharmacological intervention method to be drawn, as shown in Table3:

Table3, Percentage of Research Studies by sample size

Sample size	Number of studies	Year of studies	Percentage
A few ≤ 30	6	2005.2006,2008,2009,2010,2011,2013,2015,2020	31.5%
A large ≥ 30	13	2009.2010,2012,2013	68.5%
Total	**19**	**100%**	

4. There are a few studies that applied pharmacological interventions (7 studies), which are, and the following table (Table.5) shows the size of the pharmacological intervention effect for each study separately, as the researcher used the Cohen equation, which states:

Cohen's d = (M2 - M1)/SD pooled

where:

SD pooled = √ ((SD12 + SD22)/2)

Through applying Cohan's equation to find out the value of the effect, where:

Namely, h = 0.2 is a "Few" differences, h = 0.5 is an "average" difference, h = 0.8 is a "big" difference, h = 1.10 is a "very big", and h = 1.50 is a "huge".

Table 4, Size of the pharmacological intervention effect

Study	pharmacological Intervention	Treatment duration	Effect size		Effect value	Rank
			Post-test	Follow-up		
Bowden, 2005	Quetiapine (flexibly dosed up to 800 mg/day)	12 weeks	3.14	11.28	Huge	1
Tohen, 2005	olanzapine and lithium olanzapine, 15 mg/day, and lithium, 600 mg/day.	12 weeks	0.5	1.0	Average	4
Behzadi, 2009	folic acid 3 mg of folic acid/day	3 weeks	7.4	9.6	Huge	3
McIntyre, 2010	Asenapine 10 mg Asenapine twice daily (BID) on day 1 of the 3-week efficacy trials and was flexible (5 or 10 mg BID) thereafter.	52 weeks	0.3	2.8	Huge	2
Amrollahi,2011	Tamoxifen The starting dose of tamoxifen citrate was 20 mg twice daily (40 mg/day). Thereafter, daily doses were adjusted upward by 10 mg to achieve 80 mg/day in twice-daily divided doses for all subjects.	6 weeks	0.20	0.68	Average	5
Zeinoddini, 2015	Pioglitazone 15 mg pioglitazone daily for the first week followed by 30 mg pioglitazone (15 mg tablet, twice daily) for the rest of the trial	6 weeks	1.14	1.60	A few	6
Shahrbabaki, 2020	Probiotics a probiotic capsule (containing 1.8×109 CFU/capsule Bifidobacterium bifidum, Bifidobacterium lactis, Bifidobacterium langum, and Lactobacillus acidophilus)	8 weeks	0.03	0.01	-	7
Total			2.05		Huge	

Referring to the previous table, it appears that the average effect of pharmacological interventions treatment is “Huge”, Quetiapine was ranked first, and this can be attributed to the

versatility of its uses. Quetiapine is an antipsychotic medicine that is used to treat schizophrenia in adults and children who are at least 13 years old, Quetiapine is used to treat BD (manic depression) in adults and children who are at least 10 years old, Quetiapine is also used together with antidepressant medications to treat major depressive disorder in adults, While the treatment with Probiotics ranked last, this can be attributed to a few evidence that mood disorders may be related to overall inflammation and to changes in the microbiome, the bacteria that live in our digestive tract. We have learned that probiotics may help improve a variety of health conditions, in part due to an anti-inflammatory effect, but not in bipolar disorder.

5. Most studies applied psychological interventions (12 studies), the number of studies for which the effect of the psychological intervention will be measured is (6) studies, and the duration of treatment for each psychological intervention was also shown, to ensure the effectiveness of the treatment, although it is not a requirement, there are psychological interventions such Emotional Freedom Techniques (EFT), which leads to tangible therapeutic results within a few minutes as shown in Table 5:

Table 5, Size of the psychological intervention effect

Study	psychological intervention	Treatment duration	Effect size		Effect value	Rank
			Post-test	Follow-up		
Scott, 2006	cognitive behavioral therapy (CBT)	18 months	0.6	4.2	Huge	1

Table 5 (continued)

Williams, 2008	Mindfulness based Cognitive Therapy (MBCT)	2 months	3.6	5.6	Huge	3
Jones, McGrath, 2013	anxiety intervention to individuals with BD(AIBD), cognitive behavioural therapy (CBT)	18 months	0.1	0.6	Average	6
Torrent, 2013	Functional remediation (FR)	7 months	2.51	02.3	Average	5
Perich, 2013	Mindfulness based Cognitive Therapy (MBCT)	12 months	0.20	1.23	Big	4
Khoshnevisan,2020	anger management educational program Treatment	1 month	3.73	6.68	Huge	2
Total			1,58		Huge	

Referring to the previous table, it appears that the average effect of psychological interventions treatment is “Huge”, cognitive behavioural therapy (CBT) was ranked first, and this can be attributed to the CBT is used to treat BD by addressing depressive symptoms that occur as part of periods or episodes of depression, addressing feelings of guilt or other negative thoughts and

beliefs about manic episodes, addressing feelings of losing friends or relationships, While the treatment with anxiety intervention to individuals with BD(AIBD), ranked last, this can be attributed to this treatment has not been tested enough.

5. Conclusion

It is clear from the previous presentation, that psychological interventions, despite the large number of studies that relied on them, their results are not to the degree of the effect of the results of the pharmacological intervention, it is also noted that there is a difference between the treatment periods for each of them, as the pharmacological interventions take weeks, while the psychological interventions are long-term (they take months, perhaps years), it is also clear that the pharmacological intervention (Quetiapine) is the most effective pharmacological intervention in the treatment of bipolar disorder, and that the psychological intervention (cognitive behavioural therapy (CBT)) is the most effective psychological intervention in the treatment of bipolar disorder, also noted that the pharmacological intervention (probiotics) is the least effective pharmacological intervention in the treatment of BD and that the psychological intervention (anxiety intervention to individuals with BD(AIBD) is the least effective psychological intervention in the treatment of bipolar disorder.

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مقارنة بين فعالية الأساليب المختلفة لعلاج اضطراب ثنائي القطب (الدوائية والنفسية) مراجعة منهجية للتحليل البعدى

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المستخلص

هذا البحث عبارة عن مراجعة منهجية للبيانات المتاحة المتعلقة بالعلاج النفسي والدوائي لاضطراب ثنائي القطب، وكان الهدف من هذه المراجعة هو مقارنة فعالية العلاج النفسي والعلاج الدوائي لاضطراب ثنائي القطب، وقد أسفرت عن ١٦٢٠ منشورًا بين عامي ٢٠٠٥ و٢٠٢٠. تم تكرار حوالي ٤٨٢ مقالة في أكثر من قاعدة بيانات واحدة. أيضًا، استبعدنا ٥٢٠ مقالة لم تتناول علاج اضطراب ثنائي القطب. ثم تم استبعاد ٥٧٩ مقالة لأنها لم تكن دراسات تجريبية. أخيرًا ، تم تضمين المقالات الـ ١٩ المتبقية في هذه المراجعة المنهجية التي تفي بمعايير التضمين، وتشير الأدبيات إلى أن التدخل الدوائي(Quetiapine) هو العلاج الدوائي الأكثر فاعلية في علاج اضطراب ثنائي القطب، وأن العلاج النفسي العلاج السلوكي المعرفي(CBT) هو التدخل النفسي الأكثر فاعلية في علاج اضطراب ثنائي القطب، كما لوحظ أن العلاج الدوائي (Probiotics) هو أقل تدخل دوائي فعال في اضطراب ثنائي القطب وأن العلاج النفسي(تدخل القلق للأفراد المصابين باضطراب ثنائي القطب AIBD) هو التدخل النفسي الأقل فعالية في علاج اضطراب ثنائي القطب.

الكلمات المفتاحية: الاكتئاب، القلق، التدخلات النفسية، التدخلات الدوائية.

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