

## Evolution of patients with bipolar disorder according to pharmacological treatment Pediatric Hospital "Juan Manuel Márquez" 2009-2011

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### Abstract

To know the evolution, according to the pharmacological treatment received, of the patients admitted to the Psychiatric Ward of the "Juan Manuel Márquez" Paediatric Hospital, with Bipolar Disorder (TB) in the period from January 2009 to December 2011, the present study. The objective is to identify the evolution of the patients three, six and twelve months after hospital discharge according to the pharmacological treatment used. A retrospective longitudinal descriptive study was carried out between May 2012 and May 2013. 81 hospitalized patients with TB were studied. The source of information was their medical records and a semi-structured interview. The data was processed in SPSS version 15 and the results are presented in statistical tables. Three months after hospital discharge, the highest percentage of patients with satisfactory clinical status had treatment with Haloperidol alone, in second place Risperdal and Carbamazepine and in third place the combination of Haloperidol and Magnesium Valproate (Mg), while Six months was Haloperidol alone, followed by the combination of Olanzapine and Lithium Carbonate, Risperdal and Mg Valproate, one year after hospital discharge the combination of Olanzapine and Lithium Carbonate was found first, followed by Risperdal with Carbamazepine and of quetiapine alone. The treatments most associated with satisfactory clinical status were: Haloperidol alone, Quetiapine alone, as well as the combinations of Risperdal and Carbamazepine, Risperdal and Mg Valproate, Olanzapine and Lithium Carbonate, and Haloperidol with Mg Valproate.

**Keywords:** Bipolar Disorder; Treatment; Evolution; Psychiatric

### 1. Introduction

Bipolar Affective Disorder (TAB) is considered a chronic disease, also called Bipolar Disorder (TB). It is responsible for 5% to 15% of new psychiatric hospital admissions for a long time, with considerable expenditure of resources for the country, mostly due to inadequate treatment (1, 2).

The disorder typically begins in adolescence or early adulthood, although it occasionally has an onset before the age of 13, with a higher incidence in males. It tends to be a lifelong condition characterized by high relapse rates, anxiety and other comorbidities, substance abuse, and premature mortality due especially to the high suicide rate. The incidence in children and adolescents treated for Bipolar Disorder increased forty-fold from 1994 to 2003 and has continued to increase (2, 3, 4).

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Its pharmacological treatment is based on the adaptation of the treatments used in adults with this condition.<sup>4</sup> The studies carried out on treatment in children and adolescents have been insufficient and not well designed, however, these studies have already begun to be carried out (5, 6, 7).

In clinical practice, three treatment phases are established depending on the clinical situation of the child or adolescent (1, 4, 5, 6, 7).

1st. Pharmacological treatment during the acute phase: The objective is to control the acute symptoms of the episode, whether manic, depressive or mixed, as well as the added symptoms of agitation or psychosis.

2nd Pharmacological treatment during the continuation phase: Aimed at consolidating the response obtained in the treatment of the acute phase and preventing relapses.

3rd Pharmacological treatment during the maintenance phase: Directed mainly towards the prevention of recurrences. The treatment will be the same used during the consolidation phase and the duration will depend on factors such as severity, frequency and type of TAB; difficulty to treat it, motivation of the patient and parents, as well as the response and adverse effects to treatment. The maintenance period must be at least five years.

The first-line drugs in the pharmacological treatment of BAD are lithium and anticonvulsants (Divalproate, Carbamazepine, Lamotrigine and Topiramate), which are considered effective in all phases of the disease (manic, depressive and symptom-free). without worsening or causing the transition from one to the other. Its use is also important to reduce the risk of relapse or recurrence of an acute episode (recurrence of acute episodes within two months free of symptoms after the last episode), which causes the patient's cognitive deterioration. More recently, other medications such as Gabapentin and Tiagabine have been added to BAD therapy. It is argued that these are the most commonly used drugs in practice today. With a significant improvement in manic symptoms( 4, 5, 6, 7, 8).

Atypical antipsychotics (Quetiapine, Olanzapine, Risperidone, Aripiprazole, Ziprasidone, and Asenapine) are being increasingly used in paediatrics to control BAD, displacing the typical ones, among other reasons due to their better tolerance, fewer adverse effects and greater adherence to treatment. . There is an improvement in affective and cognitive symptoms with the use of Quetiapine and Risperidone, they also reduce aggressiveness and the improvement occurs more quickly than with mood stabilizers. They have been used in monotherapy to control the acute phase and eliminate psychotic symptoms, with effectiveness also in the maintenance phase, and properties such as mood stabilizers are attributed to them and may be effective in preventing manic relapses (1, 4.5, 6, 7, 8).

Valproate is a first-line drug for maintenance monotherapy in patients with BAD. Other drugs included in this level are Lithium, Quetiapine, Lamotrigine, and Asenapine. Aripiprazole is also considered a first-line drug, although its efficacy for the prevention of depressive episodes has not been demonstrated. Lithium is effective for the prevention of new manic or depressive episodes and will decrease the risk of suicide. Quetiapine is useful for maintenance therapy, especially in patients with mixed symptoms. Asenapine is more effective in preventing manic episodes, although it would also be useful in the presence of depression. Carbamazepine, the response was superior in patients with atypical symptoms or BAD type II.

Regarding the combined treatment, the usefulness of Valproate in combination with Quetiapine or Aripiprazole is highlighted. Finally, the combined use of Lithium with Quetiapine or Aripiprazole can be opted for. It is recommended to optimize the dose and ensure compliance with first-line treatment before considering its lack of efficacy. Second-line options for maintenance therapy in patients with BAD (which should only take place in patients who do not respond adequately to the use of different first-line drugs) include the use of Olanzapine, and Risperidone alone or as complement treatment with other substances. Paliperidone, Lurasidone and Ziprasidone are recommended for use in combination with mood stabilizers such as Valproate. In the absence of a response to the aforementioned therapeutic options, the use of third-line agents should be chosen. In this case, complementary treatment with Lamotrigine, Aripiprazole, Clozapine or Gabapentin is included. The success of the treatment depends on several factors that are not dependent on the drug, such as therapeutic compliance, social support, and the absence of rapid cycling or comorbidities. Of course, if an insufficient treatment scheme is used, this is also a cause of failure (5, 6, 7, 8).

In the Child Psychiatry Service of the "Juan Manuel Márquez" Paediatric Hospital, due to the economic situation and market limitations imposed by the blockade, which prevents certain medications from entering the country and prevents an adequate supply from others in time and frequently, it has forced, according to the general lines of Treatment Protocol in the world, to make modifications according to the real possibilities of disposition of the drugs. Despite what has been stated, there are few research works that characterize the treatment used and its results in

patients treated in this hospital, which motivated the realization of this work that had as its objective: to identify the evolution of patients at three, six and twelve months from hospital discharge, according to the pharmacological treatment in the evolutionary phase of the disease.

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## 2. Material and methods

A retrospective longitudinal descriptive study was carried out in the period from May 2012 to May 2013, at the "Juan Manuel Márquez" Paediatric Hospital in the Mariano municipality in Havana.

The study universe consisted of 117 patients who were admitted to the Mental Health Service of the said institution with a diagnosis of Bipolar Disorder (TB), from January 2009 to December 2011. A sample was selected from them, consisting of 81 patients who met the following inclusion criteria:

- Admitted to the Mental Health Service of a said institution with a Diagnosis of Bipolar Disorder, from January 2009 to December 2011, aged up to 18 years 11 months and 29 days at the time of the study.

A total of 36 patients were excluded for the following reasons: 19 years of age or older at the time of the study (24 patients). Various difficulties with medical records (12 patients)

Of the 81 selected patients, thirteen did not continue to attend the consultation after three months, so the group was reduced to 68 patients who evolved after three months. After 6 months, another five patients stopped attending follow-ups, so the group was reduced to 63 for the evolution at 6 and 12 months.

To comply with the proposed objective, the medical records of the patients were used as a source of information. The data collected was recorded in a form prepared for this purpose and were as follows:

- Age and sex.
- Psychoactive drugs are used according to the phase of treatment and form of use of the medications (in combination or alone, depending on the phase of treatment)
- Evolution of the patient at 3, 6 and 12 months after hospital discharge from the first admission (presence or absence of psychotic and/or affective symptoms, quality of interpersonal relationships, adequate incorporation into study, work and active social life)

A total of 10 patients who completed the year of evolution in the last months of 2012, were summoned to consult on the date they fulfilled it and they underwent a psychiatric examination and a semi-structured interview, with the patient and the family member who attended. accompanied. In the interview, answers to the following questions were sought:

- How have you been in that period if recurrences have occurred in the period from 6 months to a year?
- At the time of the relapse or recurrence, what medications were you taking?
- How have you incorporated it into social, school or work life?
- Are you currently on treatment or not?
- What is it if it is fulfilled?
- Do you currently have symptoms of the disease?

In the reviewed bibliography, no standardized parameters were found to assess the clinical status of the patients in the different phases of treatment, so a nominal group of experts<sup>9</sup> was created, made up of 6 Child and Adolescent Psychiatry specialists from the same hospital, with category teacher, who had the task of determining the parameters that were taken into account to define the clinical status of the patients in said phases. In the meeting of the nominal group, the main author of the work acted as moderator and to begin the activity, she explained the objective of the consultation and the need for the criteria expressed in her answers to be based on her knowledge and, above all, on her work experience. Practical in the speciality, they were later asked to say what they considered the parameters to determine if the patient's clinical status was satisfactory at 3, 6, and 12 months of evolution. The nominal group developed the following criteria:

They considered satisfactory clinical status:

- After 3 months of treatment:

- State 1: Without psychotic symptoms and with a reduction of affective symptoms by more than 50.0% or euthymic.
- State 2: Without psychotic symptoms and with a reduction in affective symptoms by more than 50.0% or euthymic and incorporated into school or work activity for his age.
- At 6 months of treatment:
  - State 3: Without psychotic symptoms and with a reduction in affective symptoms by more than 50.0% or euthymic and incorporated into school or work activity for his age.
  - State 4: Without psychotic symptoms and with a reduction in affective symptoms by more than 50.0% or euthymic, incorporated into school or work activity and his social life according to his age.
- At 12 months of treatment
  - State 5: Without psychotic symptoms, reduction of affective symptoms by more than 50.0% or euthymic, performs the usual social activities for his age, incorporated into school or work activities and adequately incorporated into his usual life

An unsatisfactory clinical state was considered if the aforementioned requirements were not met in each evaluation phase or if the patient was alone, without psychotic symptoms and/or without psychotic symptoms and with a reduction in affective symptoms of 25.0% in each phase.

For information processing, an automated database was created in Windows Excel. The primary data was processed using the benefits of the SPSS software in version 15. The qualitative variables were statistically described by absolute and relative frequencies (%). To determine the statistical association of variables, the chi-square test was used, and the estimates were made with a reliability of 95%. The results are presented in statistical tables.

### 3. Results

Table 1 shows that the most frequently found diagnosis was Bipolar Manic Episode Disorder (BD I Manic), in both sexes, with a slight predominance of males and in the age group of 15 to 18 years. It was followed by Mixed Episode Bipolar Disorder (TB I Mixed) similarly in both sexes, there was only a discreet predominance in females and ages 10 to 14 years. One male patient aged 5 to 9 was diagnosed with Bipolar Depressive Episode Disorder (BD II Depressive), and the other two were diagnosed with BD I Manic episodes. A fact to highlight is that only one male patient was diagnosed with Bipolar Disorder Hypomanic Episode (TB II Hypomanic), his age was between 15 and 18 years. The differences found were not statistically significant.

**Table 1** Diagnosis of the type of Bipolar Disorder of the patients on admission according to their age and sex. HPJMM. 2009-2011

Age group and Sex	Diagnosis on admission										Total	
	TB I Maniac		TB I Depressive		TB I Mixed		TB Depressive II		TB Hypomaniac II		N	%
	N	%	N	%	N	%	N	%	N	%		
5-9 Male	2	66.7	0	0.0	0	0.0	0	0.0	1	33.3	3	100
10-14 Male	5	29.4	7	41.2	5	20.4	0	0.0	0	0.0	17	100
10-14 Female	4	30.0	4	30.3	5	38.6	0	0.0	0	0.0	13	100
15-18 Male	14	58.3	2	8.3	7	29.2	1	4.2	0	0.0	24	100
15-18 Female	11	45.8	7	29.2	6	25.0	0	0.0	0	0.0	24	100
Total	36	44.4	20	24.7	23	28.4	1	1.2	1	1.2	81	100

Source: Clinical History; Statistical Significance  $\chi^2 = 7.7$   $p=0.25$

Table 2 shows that, three months after hospital discharge, the most widely used treatment was the combination of Risperdal and Magnesium Valproate (Mg), followed by Haloperidol and Carbamazepine, Risperdal with Carbamazepine and Haloperidol with Mg Valproate. As monotherapy, the most used medication was Mg Valproate.

At 6 months after hospital discharge, the frequency of use of the drug combinations was similar and always in favour of Risperdal with Mg Valproate or with Carbamazepine. The use of anti-recurrent drugs alone increased, while the combinations decreased, being Mg Valproate the most widely used (14.3%). Risperdal continues to be the most widely used medication, but always in combination, and the anti-recurrent medication, both alone and in combination, is Mg Valproate.

At 12 months the combination of Risperdal and Mg Valproate continues to be the most widely used medication, in second place Magnesium Valproate alone was found and in third place Carbamazepine alone and both antirecurrence drugs the percentages of patients who used them were higher than those used. found in earlier periods.

**Table 2** Pharmacological treatment according to the evolutionary phase of the disease of the patients admitted with a diagnosis of Bipolar Disorder. HPJMM. 2009-2011

Treatment	Evolutive Phase					
	3 months		6 months		12 months	
	N	%	N	%	N	%
Risperdal	1	1.5	-	-	-	-
Quetiapine	2	2.9	1	1.6	3	4.8
Haloperidol	2	2.9	2	3.2	-	-
Magnesium Valproate	3	4.4	9	14.3	14	22.2
Carbamazepine	2	2.9	5	7.9	8	12.7
Risperdal and Magnesium Valproate	27	39.7	17	27.0	17	27.0
Risperdal and Carbamazepine	8	11.8	9	14.4	5	7.9
Quetiapine and Magnesium Valproate	1	1.5	1	1.6	1	1.6
Quetiapine and Carbamazepine	1	1.5	1	1.6	-	-
Olanzapine and Magnesium Valproate	2	2.9	1	1.6	-	-
Haloperidol and Magnesium Valproate	7	10.3	6	9.5	4	6.3
Haloperidol and Carbamazepine	9	13.2	5	7.9	2	3.2
Olanzapine and Lithium Carbonate	2	2.9	1	1.6	1	1.6
Haloperidol and Lithium Carbonate	-	-	1	1.6	1	1.6
Flufenazine	-	-	1	1.6	1	1.6
Flufenazine and Magnesium Valproate	-	-	-	-	1	1.6
None	1	1.5	3	4.8	5	7.9
Total	68	100.0	63	100.0	63	100.0

Source: Clinical History

Statistical Significance  $X^2 = 15,6$   $p=0,27$

Table 3 shows that three months after hospital discharge with satisfactory clinical status, 100% of the patients were found to be treated with Haloperidol alone, 75.5% with Risperdal and Carbamazepine, and 71.4% with the combination. Haloperidol and Mg Valproate. The patient treated with Olanzapine and Lithium Carbonate had a satisfactory evolution. The differences found were not statistically significant.

**Table 3** Clinical status and treatment three months after hospital discharge of patients diagnosed with HPJMM Bipolar Disorder. 2009-2011

Treatment	Status				Total	
	Satisfactory		Not satisfactory		N	%
	N	%	N	%		
Risperdal	1	100.0	0	0.0	1	100.0
Quetiapine	0	0.0	2	100.0	2	100.0
Haloperidol	2	100.0	0	0.0	2	100.0
Magnesium Valproate	1	33.3	2	66.7	3	100.0
Carbamazepine	1	50.0	1	50.0	2	100.0
Risperdal and Magnesium Valproate	13	48.1	14	51.9	27	100.0
Risperdal and Carbamazepine	6	75.5	2	25.0	8	100.0
Quetiapine and Magnesium Valproate	0	0.0	1	100.0	1	100.0
Quetiapine and Carbamazepine	0	0.0	1	100.0	1	100.0
Olanzapine and Magnesium Valproate	1	50.0	1	50.0	2	100.0
Haloperidol and Magnesium Valproate	5	71.4	2	28.6	7	100.0
Haloperidol and Carbamazepine	4	40.0	6	60.0	10	100.0
Olanzapine and Lithium Carbonate	1	100.0	0	0.0	1	100.0
None	1	100.0	0	0.0	1	100.0
Total	36	52.9	32	47.1	68	100.0

Source: Clinical History; Statistical Significance  $\chi^2 = 12,9$   $p=0,46$

**Table 4** Clinical status and treatment six months after hospital discharge of patients diagnosed with HPJMM Bipolar Disorder. 2009-2011

Treatment	Status at 6 months				Total	
	Satisfactory		Not satisfactory		N	%
	N	%	N	%		
Quetiapina	0	0.0	1	100.0	1	100.0
Haloperidol	2	100.0	0	0.0	2	100.0
Magnesium Valproate	6	66.7	3	33.3	9	100.0
Carbamazepine	1	20.0	4	80.0	5	100.0
Risperdal and Magnesium Valproate	12	70.6	5	29.4	17	100.0
Risperdal and Carbamazepine	5	55.6	4	44.4	9	100.0
Quetiapina and Magnesium Valproate	0	0.0	1	100.0	1	100.0
Quetiapina and Carbamazepine	0	0.0	1	100.0	1	100.0
Olanzapina and Magnesium Valproate	0	0.0	1	100.0	1	100.0
Haloperidol and Magnesium Valproate	2	33.3	4	66.7	6	100.0
Haloperidol and Carbamazepine	3	60.0	2	40.0	5	100.0
Olanzapina and Lithium Carbonate	1	100.0	0	0.0	1	100.0
Haloperidol and Lithium Carbonate	0	0.0	1	100.0	1	100.0
Fluphenazine	0	0.0	1	100.0	1	100.0
None	2	66.7	1	33.3	3	100.0
Total	34	54.0	29	46.0	63	100.0

Source: Clinical History; Statistical Significance  $\chi^2 = 15,7$   $p=0,33$

Table 4 shows that the two patients who were taking Haloperidol as the only medication was diagnosed with satisfactory clinical status. Something similar happened with the one who took the combination of Olanzapine and Lithium Carbonate. At this evolutionary moment, seven out of 10 patients with the combination of Risperdal and Magnesium Valproate had a satisfactory condition, in addition, as already analyzed, this combination was the least associated with the appearance of recurrences. The use of Valproate as the only medication has a 66.7% satisfactory clinical status of the patients who used it. The differences found were not statistically significant.

Table 5 shows that Quetiapine alone, followed by the Risperdal-Carbamazepine combination and, to a lesser extent, combined with Valproate, were the drugs associated with satisfactory clinical status one year after evolution. The patient treated with Olanzapine and Lithium Carbonate had a satisfactory clinical condition. The differences were not statistically significant.

**Table 5** Clinical status and treatment twelve months after hospital discharge of patients diagnosed with HPJMM Bipolar Disorder. 2009-2011

Treatment	Status at 1 year				Total	
	Satisfactory		Not satisfactory		N	%
	N	%	N	%		
Quetiapine	2	66.7	1	33.3	3	100.0
Magnesium Valproate	6	46.2	7	53.8	13	100.0
Carbamazepine	4	50.0	4	50.0	8	100.0
Risperdal and Magnesium Valproate	8	47.1	9	52.9	17	100.0
Risperidone and Carbamazepine	4	80.0	1	20.0	5	100.0
Quetiapine and Magnesium Valproate	0	0.0	1	100.0	1	100.0
Haloperidol and Magnesium Valproate	1	25.0	3	75.0	4	100.0
Haloperidol and Carbamazepine	0	0.0	2	100.0	2	100.0
Olanzapine and Lithium Carbonate	1	100.0	0	0.0	1	100.0
Haloperidol and Lithium Carbonate	0	0.0	1	100.0	1	100.0
Flufenazine	0	0.0	1	100.0	1	100.0
Flufenazine and Magnesium Valproate	0	0.0	1	100.0	1	100.0
None	4	66.7	2	33.3	6	100.0
Total	30	47.6	33	52.4	63	100.0

Source: Clinical History; Statistical Significance  $\chi^2 = 10.8$   $p=0.54$

#### 4. Discussion

The frequency according to age and sex of the different types of BAD in this study match with that reported by other authors. It is suggested that the most frequent age of onset of BD in childhood and adolescence is between 15 and 19 years, there would be no differences between the sexes, the onset would be abrupt, of a complete depressive or manic episode and a higher prevalence of symptoms psychotics. This also match with what was found in this work (1, 2, 3, 7, 10, 11, 12, 13, 14).

According to Diller and Birmaher (6), in 16 open studies and 9 double-blind studies with more than 1, 200 participants reviewed by them, it is suggested "that monotherapy with lithium, valproate or carbamazepine has similar results in the treatment of non-psychotic episodes of mania and mania with mixed features, where the response of manic symptoms ranged from 23% to 55% (41% in the open studies and 40% in double-blind studies)".

In the reviewed bibliography, few studies were found on the maintenance treatment of TB patients in this evolutionary period, with which to be able to compare our results, however, in some works, it is stated in a general way that the

treatment with which clinical improvement of the acute episode was achieved, its duration depends on individual biological factors such as severity and the number of previous episodes, family history of the disease and response to medications and the occurrence of relapses (4, 6, 7, 8, 14, 15), which was strictly adhered to in all our patients.

In contrast to what was previously stated, some authors point out that when the patient is clinically stable, an attempt should be made to suspend the psychotropic drugs used in the acute episode (atypical or typical neuroleptics) and add that when there is a recurrence, symptoms or the patient is not responding at levels adequate to the stabilizing agent alone, the association with neuroleptics will be maintained (5, 6, 13).

Another study on maintenance treatment with antipsychotics in children with Bipolar Disorder, where atypical antipsychotics were used, resulted in improvement in more than 50.0% of the patients (6). Some authors point out normothymic properties for maintenance treatment of atypical antipsychotics, Quetiapine with 71% used from 10 to 17 years of age and which has shown positive results in Bipolar Depression as well as Aripiprazole with use from 10 to 17 years of age. 17 years and Olanzapine with use from 13 to 17 years of age. It is suggested that more Valproate alone or in combination with Risperdal is used in maintenance treatment, which also confers discrete antidepressant properties, or Quetiapine with Valproate or Lithium (4, 5, 6, 7, 8, 15, 16, 17).

In TB-I patients with manic episodes or mixed features, a significantly higher response rate was observed with Risperidone (68.5%) than with Lithium (35.6%) and sodium valproate (24%) (6, 18). This approach is similar with what was found in the present study.

The goals of long-term maintenance treatment are to reduce cycling frequency and emotional instability, maximize patient functioning, as well as achieve patient adherence to treatment (4, 6, 7, 8, 10, 16, 17, 18, 19).

The use of lithium is widely recommended in the literature as a first-line mood stabilizer, but monitoring of serum levels is necessary to avoid toxicity and the development of hypothyroidism and leukocytosis with its use, so it is dangerous to use it without blood control, especially in children and adolescents (6, 7, 8, 10, 18, 19).

In Cuba, its use is limited by difficulties in carrying out therapeutic control by performing lithium tests.

It should be noted that it has been found in the literature that about 25.0% of patients abandon treatment in the first month, 44.0% in the first trimester, and 60.0% within the initial six months. therefore, the continuity of the studies becomes difficult (6, 7, 12, 14, 19, 20). The percentage of patients who abandoned the present study is lower than that found by the authors referred to.

Despite Fluphenazine being an antipsychotic of the typical neuroleptic type, its use in Bipolar Disorder has not been sufficiently studied, although its effectiveness in other acute psychotic disorders in doses from 2.5 mg to 10 mg (21). Juan Manuel Márquez Pediatric Hospital has been used in cases refractory to treatment with Risperdal and Haloperidol.

In patients using Valproate and Lithium as the only medication, percentages of positive response as mood stabilizers ranged from 30.0% to 50.0%, reaching 73.5% in some cases, the first and 42 0.0% to 63.0% in the second. Carbamazepine and Lamotrigine between 34% and 54%. Of the antipsychotics, Quetiapine has shown the highest response rates, higher than 80.0%. It is followed by Risperidone in around 50.0% of patients and Olanzapine whose response rate is 40.0% (6, 8, 19).

There is some evidence that olanzapine may prevent further episodes of mood disorders in patients who have responded during an acute manic or mixed episode and who have not previously had a satisfactory response to lithium or valproate (1, 4, 5, 6, 19). Studies have shown that prophylactic treatment with Lithium Carbonate was effective, since it decreased the frequency, severity and duration of the episodes, with a decrease in the number of admissions and a reduction in hospital stays (6, 7, 14, 18, 19).

Other studies have found highly diverse results, with the following medications being more associated with a good patient evolution as monotherapy: the antipsychotics, Quetiapine, Aripiprasol, Asenapine and Olanzapine and Haloperidol to a lesser degree, as well as their combined treatment with anti-recurrence agents such as Valproate and Lithium, the latter also as monotherapy, in addition to Topiramate and Lamotrigine (5, 6, 7, 8, 19). The results of the current work match with this approach, although an association of satisfactory clinical status was also found in patients who used carbamazepine alone or in combination with Risperdal.



In the reviewed literature, the effectiveness of Olanzapine, Risperdal and Haloperidol in achieving a good patient evolution is widely described. Of the anti-recurrences, Lithium and Valproate are reported as the most effective (1, 4, 5, 6, 7, 8, 12, 17, 18, 19, 22, 23), similar to our results.

It is noteworthy that medications used alone or in combinations are well tolerated by patients and that allowed an acceptable recovery at discharge, at 3 months and 6 months, however at one year they are almost 50% linked to an unsatisfactory evolution. This raises questions about what the cause will be: the drugs used or a group of factors, such as the natural history of the disease itself, biological vulnerability, the presence of psychiatric or medical comorbidity, the use of other types of drugs, age of the patient, the stage of development he is in or the character traits. responsibility of the family in the control of the treatment, the management of the patient and the disease, their socioeconomic, intellectual and cultural level, the presence of psychiatric diseases in family members directly related to the care of these patients and the characteristics of the dynamics familiar. The school or work environment and their cooperation in the patient's pharmacological and non-pharmacological treatment and social support networks may also influence them.

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## 5. Conclusion

The treatments most associated with satisfactory clinical status were: Haloperidol alone, Quetiapine alone, as well as the combinations of Risperdal and Carbamazepine, Risperdal and Mg Valproate, Olanzapine and Lithium Carbonate, and Haloperidol with Mg Valproate.

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## Compliance with ethical standards

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### *Disclosure of conflict of interest*

The authors declare that they have no conflict of interest.

### *Statement of ethical approval*

The present research work does not contain any studies performed on animals/humans subjects by any of the authors.

### *Statement of informed consent*

All data published here are under consent for publication

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